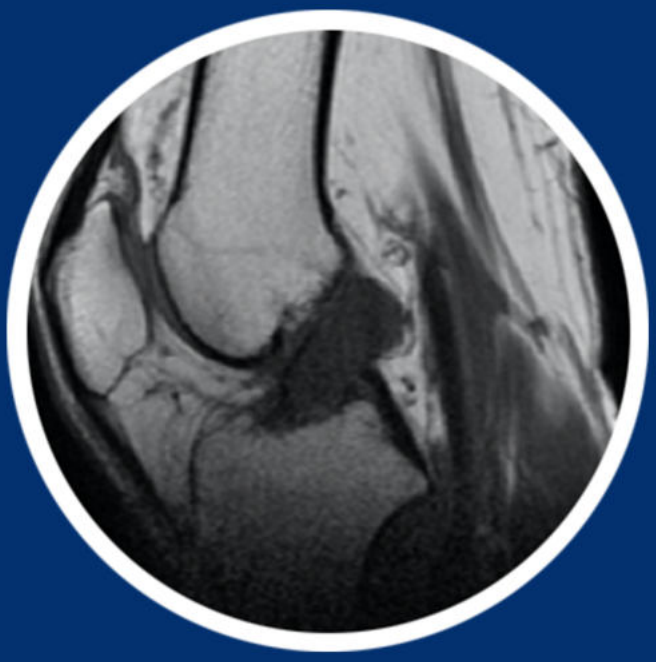
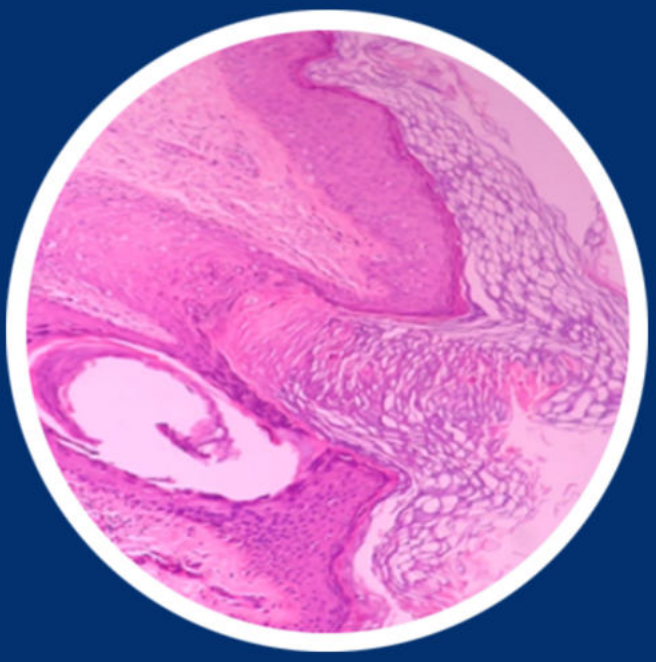
EuRJ

Volume 6 • Issue 3 • May 2020

e-ISSN: 2149-3189

The European Research Journal





Available at http://dergipark.org.tr/eurj

The European Research Journal

Aim and Scope

The European Research Journal (EuRJ) is an international, independent, double-blind peer reviewed, Open Access and online publishing journal, which aims to publish papers on all the related areas of basic and clinical medicine.

Editorial Board of the European Research Journal complies with the criteria of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), and Committee on Publication Ethics (COPE).

The journal publishes a variety of manuscripts including original research, case reports, invited review articles, technical reports, how-to-do it, interesting images and letters to the editor. The European Research Journal has signed the declaration of the Budapest Open Access Initiative. All articles are detected for similarity or plagiarism. Publication language is English. The journal does not charge any article submission or processing charges.

EuRJ recommends that all of our authors obtain their own ORCID identifier which will be included on their article.

The journal is published bimonthly (January, March, May, July, September, and November).

Abstracting and Indexing

The journal is abstracted and indexed with the following: TR Index (ULAKBİM TR Dizin), Google Scholar, Index Copernicus (ICV 2018: 100), EMBASE, ProQuest Central, ROAD, SciLit, MIAR, J-Gate, SHERPA/RoMEO, BASE, EZB, CrossRef, JournalTOCs, WorldCat, TURK MEDLINE, Turkish Citation Index.

Publisher

The European Research Journal (EuRJ)
The Association of Health Research & Strategy
Kırcaali Mah. Fevziçakmak Cd. Göktaş İş Mrk.
Kat:3 No:62/12
Osmangazi/BURSA-TURKEY
www.dergipark.org.tr/eurj/

THE ASSOCIATION OF HEALTH RESEARCH AND STRATEGY

e-ISSN: 2149-3189

EDITORIAL BOARD

EDITORS

Omer SENORMANCI, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training & Research Hospital,
Department of Psychiatry,
Bursa, Turkey

Rahmi DUMAN, MD,

Associate Professor,
Ankara LIV Hospital,
Department of Ophthalmology,
Ankara, Turkey

Ali ASAN, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training & Research Hospital,
Department of Infectious Disease,
Bursa, Turkey

Meliha KASAPOGLU AKSOY, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Physical Therapy & Rehabilitation,
Bursa, Turkey

Sinem KIYICI, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Endocrinology & Metabolism
Bursa, Turkey

Soner CANDER, MD

Associate Professor,
Uludag University Medical School,
Department of Endocrinology & Metabolism
Bursa, Turkey

Metin GUCLU, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Endocrinology & Metabolism
Bursa, Turkey

Cuma Bulent GUL, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Nephrology
Bursa, Turkey

Sedat ONER, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Urology
Bursa, Turkey

Burcu METIN OKTEN, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Physical Therapy & Rehabilitation,
Bursa, Turkey

Arda ISIK, MD

Associate Professor,
Binali Yildirim University School of Medicine,
Department of General Surgery,
Erzincan, Turkey

Emin USTUNYURT, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Physical Therapy & Rehabilitation,
Bursa, Turkey

Mehtap BULUT, MD

Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Emergency Medicine,
Bursa, Turkey

Mete KAYA, MD

Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Pediatric Surgery,
Bursa, Turkey

Melih CEKINMEZ, MD

Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Neurosurgery,
Bursa, Turkey

Serhat YALCINKAYA, MD

Associate Professor,
Kutahya University of Health Sciences,
Department of Thoracic Surgery
Kutahya, Turkey

Korgun OKTEM, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Anesthesiology & Reanimation,
Bursa, Turkey

Derya KARASU, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Anesthesiology & Reanimation,
Bursa, Turkey

Hasan ARI, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Cardiology,
Bursa, Turkey

Erhan TENEKECIOGLU, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Cardiology,
Bursa, Turkey

Kadir Kaan OZSIN, MD

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Cardiovascular Surgery,
Bursa, Turkey

INTERNATIONAL EDITORIAL BOARD MEMBERS

Elif EKINCI, MD

MBBS, FRACP, PhD
University of Melbourne
Department of Medicine,
Melbourne, Australia

Erdem CUBUKCU, MD

Associate Professor,
Uludag University School of Medicine,
Department of Medical Oncology,
Bursa, Turkey

Essam M MAHFOUZ, MD

Professor,
University of Mansoura School of Medicine
Department of Cardiology,
Mansoura, Egypt

Francesco CARELLI, MD

Professor,
University of Milan School of Medicine,
Department of Family Medicine,
Milan, Italy

Gary TSE, MD, PhD

Assistant Professor,
The Chinese University of Hong Kong,
Department of Medicine and Therapeutics,
Hong Kong, China

Ibrahim TAYMUR, MD,

Associate Professor,
University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital,
Department of Psychiatry,
Bursa, Turkey

Kendra J. GRUBB, MD, MHA, FACC

Assistant Professor,
Emory University School of Medicine,
Department of Cardiovascular Surgery,
Atlanta, GA, USA

Sait Ait BENALI, MD

Professor,
Cadi Ayyad University School of Medicine,
Department of Neurosurgery,
Marrakech, Morocco

Sedat ALTIN, MD

Professor,
University of Health Sciences,Yedikule Training & Research Hospital,
Department of Chest Diseases,
Istanbul, Turkey

Semih HALEZEROGLU, MD, FETCS

Professor,
Acibadem University School of Medicine,
Department of Thoracic Surgery,
Istanbul, Turkey

Veysel TAHAN, MD, FACP, FACG, FESBGH

Assistant Professor,
University of Missouri,
Division of Gastroenterology and Hepatology,
Columbia, Missouri, USA

Yenal DUNDAR, MD

University of Liverpool School of Medicine,
Department of Psychiatry,
Liverpool, UK

Table of Contents

Original Articles

Reviews

Case Report

Letter to the Editor

The European Research Journal 2020;6(3):187-192 Original Article

DOI: 10.18621/eurj.486547 *Cardiovascular Surgery*

Effects of coronary endarterectomy on postoperative early results in long segment coronary artery disease

Orhan Güvenç[1], Mehmet Tuğrul Göncü[2], Mesut Engin[3], Mustafa Çağdaş Çayır[4], Ahmet Fatih Özyazıcıoğlu[2]

[1]*Department of Cardiovascular Surgery, Ağrı State Hospital, Ağrı, Turkey*
[2]*Department of Cardiovasculer Surgery, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey*
[3]*Department of Cardiovasculer Surgery, University of Health Sciences, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey*
[4]*Department of Cardiovasculer Surgery, Pamukkale University School of Medicine, Denizli, Turkey*

ABSTRACT

Objectives: Main goal of coronary bypass surgery is complete revascularization. In some coronary endarterectomy applied patient groups, complete revascularization is inevitable. In this study, it was aimed to reveal factors affecting early mortality and morbidity in patients undergoing coronary endarterectomy.

Methods: Retrospective records of preoperative, operative, and postoperative data of 98 patients undergoing coronary artery bypass grafting (CABG) with coronary endarterectomy between January 1, 2012, and October 30, 2016, were reviewed.

Results: A total of 113 endarterectomies were performed in different coronary arteries. Of the patients, 22 (22.4%) were female and 76 (77.6%) were male. The mean of ages was 60.4 ± 9.9 (range; 36-81 years). A positive inotropic requirement was required in 68 (69.1%) patients and intra-aortic balloon pump was required for 23 (23.4%) patients. Mortality was observed in 10 patients (10.2%). Peroperative myocardial infarction was observed in 17 (17.3%) patients. Mortality rate was significantly higher in patients whose left ventricular ejection fraction was 30 or less and who had a higher risk in EuroSCORE ($p < 0.001$). When compared with the other vessels, mortality ratewas found to be higher for left anterior descending coronary artery endarterectomy ($p = 0.038$). Mortality in female patients undergoing endarterectomy was higher than male patients ($p = 0.023$).

Conclusions: Mortality and morbidity are higher in patients undergoing coronary endarterectomy when compared to conventional CABG operations. However, it is a method that can be applied by considering certain risk factors.

Keywords: Endarterectomy, bypass surgery, coronary artery

Coronary artery diseases (CADs) are one of the most important causes of death in our age. Coronary Artery Bypass Grafting (CABG) surgery is still the most valuable treatment option in the treatment of CAD despite the improvements in cardiology. Complete revascularization is intended in CABG operations. The aim is to provide blood flow to the disease-free region in the distal coronary artery. However, finding a disease-free zone is not possible in all operations. This is particularly important in patients with

Received: *December 5, 2018;* ***Accepted:*** *February 28, 2019;* ***Published Online:*** *May 22, 2019*

How to cite this article: Güvenç O, Göncü MT, Engin M, Çayır MÇ, Özyazıcıoğlu AF. Effects of coronary endarterectomy on postoperative early results in long segment coronary artery disease. Eur Res J 2020;6(3):187-192. DOI: 10.18621/eurj.486547

Address for correspondence: *Mehmet Tuğrul Göncü, MD., Professor, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, , Department of Cardiovascular Surgery, Bursa, Turkey. E-mail: drgoncu@gmail.com*

e-ISSN: 2149-3189

diffuse coronary disease. In this situation, it is necessary to remove the atheroma plaque from the coronary artery [1]. The frequency of this group of patients is reported between 0.8% and 25.1% [2].

The aim of this study was to investigate the early mortality and morbidity outcomes of patients undergoing elective coronary artery surgery.

METHODS

This study was performed in patients who underwent coronary endarterectomy between January 2012-October 2016, at Bursa Yüksek İhtisas Training and Research Hospital, Department of Cardiovasculer Surgery. The study protocol was approved by the local institutional Ethical Committee of University of Health Sciences. The patients were evaluated retrospectively and the effect of coronary endarterectomy on postoperative morbidity and mortality was evaluated with statistical methods.

Preoperative, operative and postoperative data of the patients were obtained by examining patient files and hospital information management system records. Patients who underwent CABG and no additional cardiac procedure were included in the study. Preoperative, intraoperative and postoperative data of patients were recorded and mortality and morbidity analyzes were performed.

Surgical Endarterectomy Technique

In patients who underwent closed (traction, pull out) endarterectomy technique; a small arteriotomy was performed in the coronary artery. The atheromatous lesion was dissected and taken out by traction. The arteriotomy and incision were continued until the atheromatous nucleus was reached and removed. If the incision was no longer needed, the bypass graft was anastomosed.

In patients undergoing open endarterectomy technique; with a long arteriotomy extending from the damaged vascular segment to the healthy vascular segment, it was ensured that the atheromatous nucleus was completely cleared from all the branches of the artery. Then, the arteriotomy was closed with internal thoracic artery (ITA) or saphenous vein graft. In some patients, arteriotomy was closed with saphenous vein patch and an ITA graft anastomosed on the patch.

Statistical Analysis

Statistical analysis data were analyzed with the Statistical Package for the Social Sciences (IBM SPSS Statistic Inc. version 16.0, Chicago, IL, USA). Continuous and ordinal variables were expressed as the mean ± standard deviation and nominal variables were expressed as frequency and percentage. Kolmogorov-Smirnov test and Shapiro-Wilk tests of normality were used to identify the distribution of variables. Student's t-test was used to compare two groups for continuous variables with normal distribution. Mann-Whitney U test was used to compare two groups for continuous variables without normal distribution. Chi-Square test was used to compare two groups for nominal variables. For all tests, a p-value of < 0.05 was considered statistically significant.

RESULTS

Of the 98 patients included in the study, 22 (22.4%) were female and 76 (77.6%) were male. The mean age was 60.4 ± 9.9 (range; 36-81 years). More than half of the patients (59.9%) were over 60 years old. There were 60 (60.4%) patients with a family history of coronary artery disease, 59 (60.2%) patients with anti-hypertensive treatment, and 44 (45%) patients with diabetes mellitus (DM). Fifty-nine (60.2%) of the patients had smoking habit. The body mass index of 32 (33%) patients was over 30. In the biochemical examination of the preoperative period, cholesterol and triglyceride levels of 71 patients were detected as above normal values (Table 1).

Fifty-seven (58.1%) of the patients had previously undergone coronary intervention (coronary balloon and/or stent). In terms of left ventricular ejection fraction (LVEF), 21 (21.4%) patients with LVEF ≤ 30%, 37 (37.7%) patients with LVEF 30-50% range and 40 (40.8%) patients with LVEF ≥ 50% were detected. The patients were classified for EuroSCORE as low risk (0-3 points), medium risk (4-6 points) and high risk (7 points and above) groups. There were 39 (39.7%) patients with low risk, 48 (48.9%) patients with medium risk and 11 (11.2%) patients with high-risk. Fourteen (14.2%) patients had a peripheral arterial disease (PAD), 33 (33.6%) patients had a chronic obstructive pulmonary disease (COPD), 6

Table 1. Demographic and clinic characteristics of the patients

Characteristics	Data
Age (years)	60.3 ± 9.9
Gender	
Male, n (%)	76 (77.6)
Female, n (%)	22 (22.4)
CAD history in family, n (%)	60 (61.2)
Obesity, n (%)	32 (32.6)
DM, n (%)	44 (44.8)
Smoking, n (%)	59 (60.2)
Hyperlipidemia, n (%)	71 (72.4)
Hypertension, n (%)	59 (60.2)
COPD, n (%)	33 (33.6)
PAD, n (%)	14 (14.2)
CVA, n (%)	6 (6.1)
Previous PCI, n (%)	57 (58.1)
EF ≤ 30, n (%)	21 (21.4)
EF = 30-50, n (%)	37 (37.7)
EF ≥ 50, n (%)	40 (40.8)
EuroScore = 0-3, n (%)	39 (39.7)
EuroScore = 4-6, n (%)	48 (48.9)
EuroScore = 7 and above, n (%)	11 (11.2)
CRF, n (%)	7 (7.1)

CAD = Coronary artery disease, DM = Diabetes mellitus, COPD = Chronic obstructive pulmonary disease, PAD = Peripheral artery disease, CVA = Cerobrovasculer accident, PCI = Percutaneur coronary intervention, EF = Ejection fraction, CRF = Chronic renal failure

(6.1%) patients had a cerebrovascular accident (CVA), and 7 (7.1%) patients had chronic renal failure (CRF). Coronary endarterectomy was performed to provide complete revascularization during coronary bypass in our patient group. Minimum 1or maximum 2 endarterectomies were applied (mean: 1.1 ± 0.3). A total of 113 endarterectomy procedures were performed. Forty-one (36.2%) were left anterior descending artery (LAD), 10 (8.8%) diagonal (Dx), 1 (0.8%) intermediary, 15 (13.2%) circumflex (Cx) and 46 (40.7%) right coronary artery (RCA) (Table 2).

In 15 (15.3%) patients, two endarterectomies were performed at the same time. The distribution of these coronary endarterectomy vessels was found as 5 (4.4%) LAD-Dx, 5 (4.4%) LAD-Cx, 3 (2.6%) LAD-RCA and 2 (1.7%) Cx-RCA (Table 2). While the patients were transferring to intensive care unit, a positive inotropic requirement was provided in 68 (69.3%) patients and intra-aortic balloon pump (IABP) support was provided in 23 (23.4%) patients. The duration of mechanical ventilation was 6-120 hours (mean: 15.5 ± 13.8) in the postoperative period. The number of patients intubated over 48 hours was 5. Total drainage volume of the patients in the first 48 hours in the intensive care unit was determined as minimum 300 ml, and maximum 1700 ml (mean: 760 ± 280 ml). In postoperative intensive care follow-up, 52 (53%) patients had various rhythm problems. The most common arrhythmia was atrial fibrillation and was seen in 37 (37.7%) of the patients. This was followed by ventricular rhythm problems (ventricular extrasystole, ventricular tachycardia, ventricular fibrillation) with 15 (15.3%) patients. These rhythm problems disrupt early postoperative hemodynamics. During the intensive care follow-up, 17 (17.3%) patients had elevated blood cardiac enzyme levels (postoperative MI). Postoperatively, 17 (17.3%) patients had elevation of liver function parameters and 19 (19.3%) patients had impaired levels of renal function markers. Four patients (4%) had cerebrovascular events and 2 of them had no previous complaints. The total length of stay of patients in the intensive care unit was 1-13 days (mean: 3.1 ± 2 days). The total hospital stay was 6-25 days (mean: 13.8 ± 3.6) (Table 3).

Table 2. Endarterectomy data of the patients

	n (%)
RCA endarterectomy	46 (46.9)
LAD endarterectomy	41 (41.8)
Cx endarterectomy	15 (15.3)
Dx endarterectomy	10 (10.2)
İntermedier endarterectomy	1 (1)
LAD-Cx endarterectomy	5 (5.1)
LAD-Dx endarterectomy	5 (5.1)
LAD-RCA endarterectomy	3 (3)
Cx-RCA endarterectomy	2 (2)

RCA = Right coronary artery, LAD = Left anterior descending, Cx = Circumflex, Dx: Diagonal

Table 3. Operative and postoperative data of the patients

Inotropic support, n (%)	68 (69.1%)
IABP support, n (%)	23 (23.4%)
Mean mechanical ventilation time (hours)	15.5 ± 13.8 (6-120)
Mean total drainage volume in the first 48 hours (ml)	760 ± 280 (300-1,750)
Arrhythmia, n (%)	52 (53%)
Postoperative MI, n (%)	17 (17.3%)
Posoperative impaired liver function, n (%)	17 (17.3%)
Postoperative renal failure, n (%)	19 (19.3%)
Postoperative CVE, n (%)	4 (4%)
Mortality, n (%)	10 (10.2%)

IABP = Intraaortic balloon pump, CVE = Cerebrovasculer event, MI = Myocardial infarction

Mortality was observed in 10 (10.2%) patients. The highest mortality rate was in LAD endarterectomy group. Among these patients, 8 (8.1%) with LAD and 1 (1%) with LAD-RCA. The highest mortality rate was observed in female; 6 (27.2%) deaths in female patients and 4 (5.2%) deaths in male patients (p = 0.023). Mortality in patients with moderate to low LVEF was significantly higher than in patients with normal LVEF. Mortality was observed in 10 patients with low LVEF 3 (3%) and 7 (7.1%) moderate patients. Mortality wasn't observed in normal LVEF group ($p < 0.001$). Mortality was observed in 6 (6.1%) patients in the high-risk group, 4 (4%) patients in the moderate risk group and in none of the patients in the lower risk group ($p < 0.001$). The mortality rate was 7.9% in patients who underwent LAD endarterectomy and 1.7% in the other patient group (p = 0.038). Total ICU stay, total hospital stay and total perfusion times were observed as longer in patients with mortality (Table 4).

Table 4. Distribution of mortality according to various parameters

		Survivors	Non-survivors	*p* value
Age (yeras)		59.4 ± 10.3	64.2 ± 17.2	0.381*
Total ICU stay (days)		3.1 ± 1.9	5.2 ± 2.7	**0.032****
Total hospital stay (days)		11 ± 3.7	17.7±6.6	**0.021****
X-clamp time (min)		49.3 ± 14.2	65.7 ± 28.1	0.301**
TPT (min)		89.4 ± 15.8	107.5 ± 8.2	**0.007****
Gender	Female (n)	16	6	**0.023*****
	Male (n)	72	4	
LVEF	Low-Moderate (n)	48	10	**< 0.001*****
	Normal (n)	40	0	
EuroSCORE	Low-Moderate (n)	82	4	**< 0.001*****
	High (n)	5	6	
Endarterectomy	LAD (n)	32	9	**0.038*****
	RCA (n)	44	2	
	Others (n)	26	0	

*Student-T test **Mann Whitney U test ***Chi-Square test. Data are shown are mean ± standard deviation or number. ICU = Intensive care unit, X-clamp time = Cross-clamp time, TPT = Total perfusion time, LVEF = Left ventriculer ejection fraction

DISCUSSION

Coronary endarterectomy was performed in 1957 by Bailey *et al*. [3], but no bypass was performed in those days. This method has always been discussed since the first implementation of this process to the present day. In the 1990s, this method was not recommended in routine practice because of high mortality and morbidity rates [4]. When we look at the literature, the rate of coronary endarterectomy application varies between 0.8 and 25% [5]. Considering that approximately 800 CABG surgeries are performed annually at our center so this ratio is compatible with the literature.

In our study, the rate of male patients was 77.6%. In many studies about coronary endarterectomy, the ratio of male patients was found to be high in accordance with our study [6]. The authors attributed this to the short diameters of the coronary arteries in female patients. In addition, in our study, we found that mortality rate in female patients who underwent coronary endarterectomy was higher with 27.2% compared to men with 5.2%.

The diffuse disease of LAD has a special importance since LAD feeds a significant portion of the heart. The importance of revascularization of this vessel has been demonstrated in many studies [7]. The rate of LAD endarterectomy varies between 9% and 74.8% in the literature [8]. In our study, 36.2% of the patients underwent LAD endarterectomy. We observed that RCA was the most common endarterectomy vessel with 40.6%. In the literature, this ratio varies between 21.1% and 83% [8, 9]. In some patients, multiple vascular endarterectomies may be required during the same operation. According to the literature, multiple coronary endarterectomies increase mortality [9]. In our study, we determined that two coronary endarterectomies were performed simultaneously in 15 patients. Of these, only two patients were treated with two vessels (RCA-Cx) except LAD.

Early extubation, intensive care, and less total hospital stay after open heart surgery are closely related to reduced mortality. In our study, the mean duration of intubation in the intensive care unit was 6-120 hours. Takanashi *et al*. [8] reported that the duration of intubation was 12.6 ± 18.7 hours. The duration of intensive care stay and total hospitalization period ranged from 1 to 13, 6 to 25 days, respectively. Schmitt *et al*. [10], found these durations as 5.6 ± 8.4 and 15.9 ± 13.9 days, respectively, in their coronary endarterectomy study.

Inotrope and IABP support may be required for avoiding from cardiopulmonary bypass after CABG operation. These need ratios may increase in patients undergoing coronary endarterectomy. In our study, the number ofa positive inotropic requirement was 68 (69.3%) and IABP support was required in 23 (23.4%) patients. Padhy *et al*. [11] statedthese rates as 64.2% and 16.6%, respectively.

The amount of drainage of the patients after surgery affects the amount of blood and blood product transfer, which affects the mortality and morbidity. The total amount of drainage in our patients ranged from 300 to 1700 ml (mean: 760 ± 280 ml). Yener *et al*. [12], found the mean amount of mediastinal bleeding as 650 ± 8.2 ml. Compared to this study, we can say that our drainage rates are acceptable.

Arrhythmias after open heart surgery may prolong hospital stay, serious arrhythmias can cause mortality and morbidity. Atrial fibrillation (AF) is the most common rhythm problem and ventricular arrhythmias can be seen less frequently. In our study, 52 (53%) patients had various rhythm problems. The most common arrhythmia was AF in 37.7% of the patients. In the literature, this ratio varies between 25% and 30% [8, 13]. The treatment of this arrhythmia is very important for cardiac surgery. Because it increases the morbidity in the early period, If it is permanent, it paves the way for future complications.

One of the most important factors in early mortality and morbidity in patients undergoing coronary endarterectomy is peroperative MI. Although, the most common cause of per-operative MI is incomplete revascularization, residual material to be left in the vessel, intimal flap, vasospasm, air embolism, inadequate protection of myocardium under the cross-clamp and obstruction of the newly constructed bypass graft may cause [14]. The incidence of perioperative MI varies between 1.5% and 19% [15]. This rate was found to be 17.3% in our study.

The mortality rate was 10.2% (10 patients) in our study. Nine of these ten patients had LAD endarterectomy. Especially, studies showing that mortality has increased in the patients who underwent

LAD endarterectomy support our study [16]. The 10% mortality rate we found in our study is very high when compared with the conventional surgical method. The studies in the literature are also in this direction. However, we can say that this increased mortality rate is affected by comorbid factors [17].

CONCLUSION

In conclusion, we suggest that coronary endarterectomy should be performed in the right patient group at the right time and with the right methods. We should consider this operation as a life-saving technique in patients with the common CAD, which is thought to be inoperable. Otherwise, these patients will either face death or we will consider more severe treatment methods such as heart transplantation and heart support devices.

Author Contribution

All authors have directly participated in the planning, execution, analysis or reporting of this research paper. All authors have read and approved the final version of the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Nishigawa K, Fukui T, Takanashi S. Coronary endarterectomy for the diffusely diseased coronary artery. Gen Thorac Cardiovasc Surg 2014;62:461-7.
2. Soylu E, Harling L, Ashrafian H, Athanasiou T. Does coronary endarterectomy technique affect surgical outcome when combined with coronary artery bypass grafting? Interact Cardiovasc Thorac Surg 2014;19:848-55.
3. Bailey CP, May A, Lemmon WM. Survival after coronary endarterectomy in man. JAMA 1957;164:641-6.
4. Shapira OM, Akopian G, Hussain A, Adelstein M, Lazar LH, Aldea GS, et al. Improved clinical outcomes in patients undergoing coronary artery bypass grafting with coronary endarterectomy. Ann Thorac Surg 1999;68:2273-8.
5. Ghatanatti R, Teli A. Coronary endarterectomy: recent trends. J Clin Diagn Res 2017;11:PE01-PE04.
6. Bagheri A, Masoumi A, Bagheri J. Early outcomes of coronary endarterectomy in patients undergoing coronary artery bypass surgery. Heart Surg Forum 2016;19:E059-63.
7. Gucu A, Goncu T, Yavuz S, Arican Özluk O, Eris C, Turk T, et al. Alternative option in patients with multisegmental left anterior descending coronary artery disease for providing complete myocardial revascularization. Int J Clin Exp Med 2014;7:142-7.
8. Takanashi S, Fukui T, Miyamoto Y. Coronary endarterectomy in the left anterior descending artery. J Cardiol 2008;52:261-8.
9. Stavrou A, Gkiousias V, Kyprianou K, Dimitrakaki IA, Challoumas D, Dimitrakakis G. Coronary endarterectomy: the current state of knowledge. Atherosclerosis 2016;249:88-98.
10. Schmitto JD, Kolat P, Ortmann P, Popov AF, Coskun KO, Friedrich M, et al. Early results of coronary artery bypass grafting with coronary endarterectomy for severe coronary artery disease. J Cardiothorac Surg 2009;4:52.
11. Padhy K, Narasimham SBR, Murthy GSRC, Chaganti VR, Kumar PVVNM, Rao MB, et al. Coronary endarterectomy for diffuse extensive coronary artery disease. Ind J Thoracic Cardiovasc Surg 2005;21:251-5.
12. Yener Ümit A, Kervan Ü, Korkmaz K, Gedik Selçuk H, Budak Baran A, Genç Bahadır S, et al. The impact of coronary artery endarterectomy on mortality and morbidity during coronary artery bypass grafting. Turk Gogus Kalp Dama 2014;22:734-41.
13. Byrne JG, Karavas AN, Gudbjartson T, Leacche M, Rawn JD, Couper GS, et al. Left anterior descending coronary endarterectomy: early and late results in 196 consecutive patients. Ann Thorac Surg 2004;78:867-73.
14. Sirivella S, Gielchinsky I, Parsonnet V. Results of coronary artery endarterectomy and coronary artery bypass grafting for diffuse coronary artery disease. Ann Thorac Surg 2005;80:1738-44.
15. Fuster V. Epidemic of cardiovascular disease and stroke: the three main challenges. Circulation 1999;99:1132-7.
16. Jones EL, Weintraub WS. The importance of completeness of revascularization during long-term follow-up after coronary artery operations. J Thorac Cardiovasc Surg 1996;112:227-37.
17. Tiruvoipati R, Loubani M, Lencioni M, Ghosh S, Jones PW, Patel RL. Coronary endarterectomy:impact on morbidity and mortality when combined with coronary artery bypass surgery. Ann Thorac Surg 2005;79:1999-2003.

The European Research Journal 2020;6(3):193-199 Original Article

DOI: 10.18621/eurj.475930 *Child Psychiatry*

The relation between preschool children's language development and their mothers' depression and anxiety symptoms: a cross-sectional study

Zeynep Göker[1], Havva Eser[2], Arzu Yılmaz[3]

[1]Department of Child Psychiatry, University of Health Sciences, Ankara Child Health and Diseases Hematology and Oncology Training and Research Hospital, Ankara, Turkey
[2]Department of Child Development and Education, Ankara Training and Research Hospital, Ankara, Turkey
[3]Department of Child Neurology, Ankara Training and Research Hospital, Ankara, Turkey

ABSTRACT

Objectives: In this study, the relationship between preschool age group children's language development and depression/anxiety symptoms of their mothers was investigated.

Methods: Children aged 13-75 months and their mothers were included. Denver-II test and Beck Depression and anxiety scales were utilized. SPSS 17.0 program was used and $p < 0.05$ was considered as significant.

Results: Of the 58 patients, 74.1% were male, with the mean age of 53.3 months. The mean maternal age was 31.5 years. The mean education level was 8.3 years for mothers. According to the Denver-II of language development, 53.4% of the cases were found to be "delayed" whereas 46.6% of all were "normal", with significantly lower in "delayed" children (47.4 vs. 60 months; t (56) = -3.431, $p = 0.001$). Delayed language was significantly associated with lower mothers' education level (7.4 vs. 9.3 years; t (56) = -2.466, $p = 0.017$). The median score of depression scale was significantly higher in the delayed language (18 vs. 13; z = -2.218, $p = 0.027$). Positive correlation was found between the mothers' education and the language development (r = .324, $p = 0.013$). The anxiety symptom levels of the mothers were not associated with language development ($p > 0.05$).

Conclusions: The level of education of mother seems to affect language development. There is a relationship between the depressive symptoms of the mother and the delay in language development. It seems important that the mothers of the cases whose children had language development to be directed to psychiatric evaluation.

Keywords: language development, child, mother's depression, mother's anxiety

Language is one of the important parameters of early childhood development [1]. It is thought that both the receptive language and the expressive language development through social communication skills in the first and second years of life, and then the progressive games, sharing common interests with others, and using gestures and gestures to indicate their needs and desires [2]. Therefore, being aware of the factors affecting language development in early childhood is very important for the healthy development of the child.

The attitude and behavior of the caregiver is the

Received: ***October 29, 2018;*** *Accepted:* ***December 27, 2018;*** *Published Online:* ***August 5, 2019***

How to cite this article: *Göker Z, Eser H, Yılmaz A. The relation between preschool children's language development and their mothers' depression and anxiety symptoms: a cross-sectional study. Eur Res J 2020;6(3):193-199. DOI: 10.18621/eurj.475930*

Address for correspondence: *Zeynep Göker, MD., University of Health Sciences, Ankara Child Health and Diseases Hematology and Oncology Training and Research Hospital, Department of Child Psychiatry, Ankara, Turkey. E-mail: zeynepgoker@hotmail.com, Fax: +90 312 347 2330*

e-ISSN: 2149-3189

leading one. Ekerim and Selcuk [3] showed in a study that the warm and supportive attitude of the mother towards her child influenced the effective use of the child's language. The factors that negatively affect the mother's outward behaviors such as depression or anxiety in the mother may negatively affect the child's developmental stages. Depression in mothers leads to both internal and external-problems [4], has a negative impact on children's language development [5], these children were shown to be less than their peers at the age of 1 to 3 years, with less vocabularies compared to children without depression in their mothers [6]. In a cohort study, Koutra *et al*. [7] showed that neuro-developmental steps including language development of 18 months-old children were adversely affected by depression in the mother. In another prospective study, it was reported that anxiety, perceived stress and depression in the mother had a slight negative effect on the cognitive development of the child [8].

The hypothesis of this study is that "mothers of children aged 12-75 months who have delayed language development have more depression and anxiety symptoms than children with normal language development.

METHODS

The sample of the study was conducted between May 2018 and June 2018 in Ankara Training and Research Hospital, Hüseyingazi District Polyclinic. Fifty-eight children and their mothers who did not use any language other than Turkish and accepted to participate in this study were formed. Patients with organic (eye, ear pathologies), neurological and syndromic reasons were excluded from the study.
Sociodemographic data were collected by a form prepared by the researchers. The monthly income level variable was reported in three categories as low income (1-1999 Turkish Liras [TL]), middle income (2000-4999 TL) and high income (5000- and above TL) level. Denver II-developmental screening test were applied to the children's mother by child development specialist and Beck depression and Beck anxiety scales were fullfilled by their mothers.

Children who were compatible with their peersas a result of Denver test were taken as control group. Mothers' depression and anxiety symptom levels were expressed in terms of total score of the scale.

The approval of the ethics committee of the study was obtained by the decision of the Ministry of Health, Ankara Health Research and Application Center Medical Research Institute 2018-45-462. Verbal and written informed consent of the mothers were included in the study.

Tools Used

Sociodemographic Data Form

It was created by the authors to gather information about the sociodemographic characteristics of children and their parents and siblings. The age of the child, gender, demographic variablesofparents (age, educational status and occupation), monthly income levels, number of children at home, and the presence of a medical or psychiatric disease history in the family and themselves were questioned.

Denver-II Development Screening Test (DDST)

Prepared in 1967 by Frankenburg *et al*. [9] is a standardized practice that is adapted to many countries' own communities. The validity and reliability study of the test was conducted by Anlar *et al*. [10]. It is a test which can be applied easily for children between 0-6 years of age and it has an important role in early development of child development and developmental deviations. Four areas are evaluated in the test:

1. **Personal-social:** Agreement with people, the ability to meet individual needs,
2. **Fine motor:** Hand-eye coordination, use of small objects, problem-solving ability,
3. **Language:** Hearing, comprehension and use of language, receptive and expressive language skills,
4. **Rough motor:** Movement of large muscles such as sitting, walking, jumping.

The results of the test are grouped in three classes as "normal", "suspicious" and "abnormal". Normal means no delay and no more than one warning, suspicious stands for that there is a delay and /or two or more warnings, Abnormal means there are two or more delays [11]. The cases with normal results are evaluated 3 months later and the suspected cases are evaluated with a test repetition after 1 month. Patients who are considered suspicious or abnormal results are referred to an advanced center for diagnostic evaluation. Since our study was based only on

language development, the results were reported as in delay and included in a 1-month cross-section.

Beck Depression Inventory (BDI)

This is a 21-item self-report scale developed by Beck *et al*. [12] in 1961, presenting the most common emotional, somatic, cognitive, and motivational symptoms in depression. It focuses more on the cognitive and emotional symptoms of depression, with less emphasis on somatic symptoms (including loss of appetite, weight loss, and libido). The items of the scale are rated between 0 and 3 and the lowest total score is 0 and the highest total score is 63. Increased score means that the level of depression symptoms increases. The Turkish validity of the scale was conducted by Hisli [13] in 1988.

Beck Anxiety Inventory (BAI)

It isa self-assessment scale used to determine the frequency of anxiety symptoms experienced by individuals developed by Beck *et al*. [14]. It is a Likert type scale which is composed of 21 items and scored from 0-3. The Turkish reliability and validity was conducted by Ulusoy *et al*. [15] in 1998.

Statistical Analysis

Statistical analysis of the data was performed using the SPSS 17.0 program (Chicago Inc., 2008). The conformity of continuous variables to normal distribution was tested with Kolmogorov-Smirnov. Categorical variables were given in terms of number and percentage, and continuous variables were given as arithmetic mean and standard deviation. Student-t test was used for paired group comparison because the data were normal distribution. In the correlation analysis of continuous variables, Pearson, categorical etc. Spearman correlation coefficients were used for correlation analysis of continuous variables. A $p < 0.05$ was considered significant.

RESULTS

Of 58 patients, 73.6 (n = 43) were male and 25.9% (n = 15) were female. The mean age was 53.3 ± 15.1 months (range: 13-75 months). The mean age of the mothers was 31.5 years (mean age: 36 years). The mean education level of the mothers was 8.3 ± 3.1 years and the mean education level of fathers was 8.6 ± 3.2 years.

According to the Denver-II developmental screening test, 34.5% (n = 20) of the cases were "normal", 36.2% (n = 21) were "suspicious" and 29.3% (n = 17) were "abnormal". When the results of the language-development subscale were evaluated, it was found that while 46.6% (n = 27) of the cases had normal language development, whereas 53.4% (n = 31) had delayed language development.

The mean age of the patients with delayed language development was significantly smaller than the normal ones (47.4 vs. 60 months; t (56) = - 3,431, $p = 0.001$). It was determined that maternal education duration (7.4 vs. 9.3 years; t (56) = - 2.466, $p = 0.017$) was significantly lower in patients with delayed language development.

Maternal age variables were found to be similar to those in normal or delayed language development according to Denver-II test ($p > 0.05$ for both, see Table 1).

Table 1. Demographics and their relation with language development

	Denver-II language outcome				
	Total (n = 58)	Normal (n = 27)	Delayed (n = 31)	Statistics	
				t	p
Age (months)	53.3 ± 15.1	60.0 ± 13.4	47.4 ± 14.2	-3.431	**0.001**
Mothers' age (years)	31.5 ± 5.4	30.5 ± 4.9	32.4 ± 5.8	1.369	0.176
Fathers' age (years)	36.4 ± 6.6	35.3 ± 5.4	37.3 ± 7.4	1.143	0.258
Mother education (years)	8.3 ± 3.1	9.3 ± 2.9	7.4 ± 3.0	-2.466	**0.017**
Father education (years)	8.6 ± 3.2	9.4 ± 3.1	7.9 ± 3.1	-1.822	0.074

Data are shown as mean ± standard deviation

Analysis of categorical variables

It was determined that 6.4% (n = 3) of the cases were parents / divorced. 91.5% (n = 43) of the patients were with their parents. 2,1% (n = 1) of the patients died. 85.1% (n = 40) of the mothers were housewives. 14.9% (n = 7) of the mothers were working.

Monthly income level: 48.9% (n = 23) of the cases were low (-1999 TL), 46.8% (n = 22) were medium (2000-4999 TL) and 4.3% (n = 2) high (5000TL and above) income level.

Number of children in the home: 23.4% (n = 11) of the cases were single children, 61.7% (n = 29) with two children, 12.8% (n = 6) with three children,2.1% (n = 1) were from family with four children.

Distribution of the birth order of the cases: 57.4% of the cases were first child (n = 27), 34% (n = 16) second child, 6.4% (n = 3) third child, 2.1% (n = 1) was the fourth child.

Table 2. Categorical variables in terms of Denver-II language development

	Denver-II language outcome				
	Total (n = 58)	Normal (n = 27)	Delayed (n = 31)	Statistics	
				χ2	*p* value
Gender, n (%)					
Male	43 (74.1)	19 (70.4)	24 (77.4)	0.374	0.541
Female	15 (25.9)	8 (29.6)	7 (22.6)		
Parents status, n (%)					
Together	52 (89.7)	22 (81.5)	30 (96.8)	3.537*	0.106
Divorced	5 (8.6)	4 (14.8)	1 (3.2)		
Father died	1 (1.7)	1 (3.7)	0		
Mothers' work, n (%)					
She is working	8 (13.8)	3 (11.1)	5 (16.1)	0.306*	0.712
Housewife	50 (86.2)	24 (88.9)	26 (83.9)		
Socio-economic level, n (%)					
Lower (-1999TL)	25 (43.1)	9 (33.3)	16 (51.6)	5.450*	0.052
Middle (2000-4999 TL)	30 (51.7)	18 (66.7)	12 (38.7)		
High (5000 TL-)	3 (5.2)	0	3 (9.7)		
Sibling number					
Alone, **n (%)**	12 (20.7)	3 (11.1)	9 (29.0)	9.045*	0.029
Two	36 (62.1)	22 (85.1)	14 (45.4)		
Three	8 (13.8)	1 (3.7)	7 (22.6)		
Four	2 (3.4)	1 (3.7)	1 (3.2)		
Birth order, n (%)					
First	31 (53.4)	16 (35.5)	15 (48.4)	1.890*	0.735
Second	20 (34.5)	9 (33.3)	11 (35.5)		
Thirth	5 (8.6)	1 (3.7)	4 (12.9)		
Fourth	2 (3.4)	1 (3.7)	1 (3.2)		
Mothers' health, n (%)					
Medical disease	3 (5.2)	2 (7.4)	1 (3.2)	0.514*	0.593
Psychiatric disorder	14 (24.1)	6 (22.2)	8 (25.8)	0.101	0.750

*Fisher's exact test

Table 3. Mothers' scale scores in terms of language development of their children

	Denver-II language outcome				
	Total (n = 58)	Normal (n = 27)	Delayed (n = 31)	Statistics	
	M (min-max)	M (min-max)	M (min-max)	z	*p* value
BDI-total	17 (3-40)	13 (3-29)	18 (4-40)	-2.218	**0.027**
BAI-total	12 (0-51)	10 (0-51)	13 (0-48)	-.320	0.749

M = Median, min = minimum, max = maximum
BDI = Beck depression inventory, BAI: Beck anxiety inventory

The medical history of the mother was 4.3% (n = 2), 95.7% (n = 45) of the cases. The family history of psychiatric disease was not present in 85.1% (n = 40) of the cases and 14.9% (n = 7). Gender, demographic data of the parents, socioeconomic level, the number of children, the presence of disease histories in the mother were similar in two groups (for all $p > 0.05$, see Table 2).

Comparison of scale total scores

The mean score of depression scale in the mother was significantly higher in cases with delay in language development (18 vs. 13 points, z = -2.218, $p = 0.027$). There was no significant effect of mother's anxiety symptoms on language development ($p > 0.05$) (Table 3).

Correlation analysis

There was a negative and significant correlation between language development and Beck depression scores (r = -. 294, $p = 0.025$). There was a positive and significant correlation between language development and child age (month) (r = .411, $p = 0.001$). There was a positive and significant correlation between mothers' educational level and language-development (r = .324, $p = 0.013$, see table 4).

DISCUSSION

In our country, there are studies investigating the developmental evaluation and the factors that affect it by using the Denver-II test. From these studies, Güneş [16] examined the effect of family functions and other demographic factors on the development of family functions using a Denver-II test in 201 mothers and their 0-6-year-old children (102 girls, 99 boys) enrolled in a family health center in a district of Bursa province [16]. They reported a positive correlation between the life satisfaction parameters of mothers and their children's developmental scores. Madan and Tekin [17] performed a total of 60 children who were selected by random sampling from children in the 0-6 age group living in the center of Antalya. Güven *et al*. [18] reported that 179 of the children underwent the Denver-II test to have a high socioeconomic level, factors affecting the child's development, being a child of a working mother, and being a child using breast

Table 4. Spearman correlation analysis of language development

	BDI-T	BAI-T	C-age (month)	M-edu (year)	F-edu (year)
Language	-.294*	NS	.411**	.324**	NS
BDI-T	1	.615**	NS	NS	NS
BAI-T		1	NS	NS	NS
C-age (month)			1	NS	NS
M-edu (year)				1	.670**

BDI-T = Beck depression inventory-Total score, BAI-T = Beck anxiety inventory-Total score, C = Children, M-edu = Mothers' education, F-edu = Fathers' education
*significance at the 0.05 level (2-tailed), **significance at the 0.05 level (2-tailed)

milk for longer periods[18]. Bayoglu *et al*. [19] conducted a total of 980 children under the Denver-II test and reported that the Denver-II test results of their children with low socioeconomic status were abnormal. Anlar *et al*. [20] investigated the effect of socioeconomic level on development and reported that fine-motor development was affected by this variable [20].

The common emphasis of all these studies is that this screening test is an effective tool in determining the level of development headings of children aged 0-6 with the Denver-II screening test and in following the improvements in the development steps after the required interventions.

Anlar *et al*. [20] found that mothers were more effective on their children's development steps than their fathers, and they indicate that this activity has reached a peak level around the age of 5 to around 32-72 months. In our study, it was shown that mothers' depression symptoms had a negative effect on the language development of their children. It was not possible to test what could have changed in the stages of development after none of the cases we called for a month to check and the interventions we proposed (the behaviorist suggestions towards the mother and her child). Nevertheless, based on the current results, we can say that the mother education levels of children in the developmental period affect the language development of children. Depression symptoms in mothers of pre-school age children are important and it seems necessary to be followed up. In our study, it was determined that anxiety symptoms did not affect language-development.

CONCLUSION

This study main outcome is that there is significantly increased depressive symptoms of the mothers whose children's language development had delayed. It is important that the mothers of patients with delayed language development are referred to psychiatric evaluation for the purpose of further evaluation of depression symptoms.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Tümkaya S. [Language development]. In: Deniz ME, ed., [Development in early childhood]. 8th ed., Pegem Akademi: Ankara, 2017: pp.28-52. [Article in Turkish]
2. McMurray B. Defusing the childhood vocabulary explosion. Science 2007;317:631.
3. Ekerim M, Selcuk B. Longitudinal predictors of vocabulary knowledge in Turkish children: the role of sensitive parenting and executive functions. Early Educ Dev 2018;29:324-41.
4. Garcia D, Bagner DM, Pruden SM, Nichols-Lopez K. Language production in children with and at risk for delay: mediating role of parenting skills. J Clin Child Adolesc Psychol 2015;44:814-25.
5. Stein A, Malmberg LE, Sylva K, Barnes J, Leach P; FCCC team. The influence of maternal depression, care giving, and socioeconomic status in the post-natal year on children's language development. Child Care Health Dev 2008;34:603-12.
6. Pan BA, Rowe ML, Singer JD, Snow CE. Maternal correlates of growth in toddler vocabulary production in low-income families. Child Dev 2005; 76:763-82.
7. Koutra K, Chatzi L, Bagkeris M, Vassilaki M, Bitsios P, Kogevinas M. Antenatal and postnatal maternal mental health as determinants of infant neurodevelopment at 18th months of age in a mother-child cohort (Rhea Study) in Crete, Greece. Soc Psychiatry Psychiatr Epidemiol 2013;48:1335-45.
8. Keim SA, Daniels JL, Dole N, Herring AH, Siega-Riz AM, Scheidt PC. A prospective study of maternal anxiety, perceived stress, and depressive symptoms in relation to infant cognitive development. Early Hum Dev 2011;87:373-80.
9. Frankenburg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of the Denver Developmental Screening Test. Pediatrics 1992;89:91-7.
10. Anlar B, Yalaz K. [Denver II Developmental Screening Test. Adaptation and standardization to Turkish children]. Hacettepe Çocuk Nörolojisi Gelişimsel Tıp Araştırmaları Grubu Yayını, Ankara. 1996. [Article in Turkish]
11. Anlar B, Bayoğlu B, Yalaz K. [Denver II test handbook adapted to Turkish children]. 2007. [Article in Turkish]
12. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71.
13. Hisli N. [A study on the validity of the Beck depression inventory]. Psikoloji Dergisi 1988;6:118-126. [Article in Turkish]
14. Beck AT, Epstein N, Brown G, Steer RA. An Inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1998;56:893-7.
15. Ulusoy M, Şahin N, Erkman H. Turkish version of the Beck anxiety inventory: psychometric properties. J Cogn Psychother 1998;12:163-72.
16. Günes N. [Investigation of the relationship between the

developmental level of children aged 0-6 and their family functions and life satisfaction]. Hacettepe Üniversitesi Sağlık Bilimleri Enstitüsü. Çocuk Gelişimi ve Eğitimi Programı Yüksek Lisans Tezi (Thesis). Ankara. 2017. [Article in Turkish]
17. Madan R, Tekin D. "Developmental follow-up of 0-6 age group children'' programs (PS007). Hacettepe University Faculty of Health Science Journal 2015;1(Suppl 2):641-50. [Article in Turkish]
18. Güven F, Say A, Sarı İ, Sarı E, Değirmenci S, Uygur Külcü N. [The effect of socio-economic level on Denver II test]. Zeynep Kamil Tıp Bülteni 2012;43:108-13. [Article in Turkish]
19. Bayoğlu B, Bakar E, Kutlu M, Karabulut E, Anlar B. Can preschool developmental screening identify children at risk for school problems? Early Hum Dev 2007;83:613-7.
20. Durmazlar N, Ozturk C, Ural B, Karaagaoglu E, Anlar B. Turkish children's performance on Denver II: effects of sex and mother's education. Dev Med Child Neurol 1998;40:411-6.

The European Research Journal 2020;6(3):200-203 Original Article

DOI: 10.18621/eurj.488170 *Otorhinolaryngology*

Efficacy and feasibility of 226 Hz and 1000 Hz tympanometry in healthy pediatric patients

Osman İlkay Özdamar[1], Gül Özbilen Acar[1], Emel Pektaş[2], Özlem Ertuğrul[2], Şayan Yiğit[2]

[1]Department of Otorhinolaryngology-Head and Neck Surgery, İstanbul Medeniyet University, Göztepe Training and Research Hospital, İstanbul, Turkey
[2]Department of Audiology, İstanbul Medeniyet University, Göztepe Training and Research Hospital, İstanbul, Turkey

ABSTRACT

Objectives: Tympanometric evaluation of middle ear with 226 Hertz (Hz) frequency probe has been widely used in patients with suspected middle ear and Eustachian tube disorders. However most of the recent studies were demonstrated that tympanometric examination with 1000 Hz frequency probe was superior to 226 Hz frequency probe examination to detect middle ear disorders affecting middle ear admittance especially for infants. The objective(s) of this study was to compare the reliability and feasibility of 226 Hz and 1000 Hz tympanometric results in normal hearing healthy pediatric group of patients.

Methods: In this study, we evaluated normal healthy pediatric patients with 226 and 1000 Hz frequency probe tympanometry for the aim of comparing efficacy and detecting the rate of false negative tympanometric findings in these subjects. Forty-nine (98 ears) healthy pediatric patients (25 males and 24 females) were enrolled in the study and all of the patients were younger than 18 years of age. Oto-microscopic examination was performed to all of the patients as a gold standard.

Results: The mean age was 9.3 ± 4.46 years old with a range from 3 to 17 years. The mean values of 226 Hz tympanometric measurement of right ears for ear volume, compliance, pressure and gradient were 74 ± 28.10, 59 ± 38.96, -46 ± 92.38 and 36 ±3 3.22, respectively; these values for the left ears were 84 ± 65.94, 51 ± 31.00, -57 ± 102.05 and 30 ± 23.35, respectively. The mean values of 1000 Hz tympanometric measurement of right ears for ear volume, compliance and pressure were 78 ± 23.03, 172 ± 85.04 and -22 ± 110.70, respectively; these values for the left ears were 64 ± 32.05, 147 ± 104.70, and 0 ± 98.20, respectively.

Conclusions: We found that there was no superiority of the usage of 1000 Hz tympanometry to 226 Hz tympanometry in normal hearing healthy pediatric patients who were equal or older than 3 years of age.

Keywords: 1000 Hz tympanometry, 226 Hz tympanometry, children, normal hearing

Tympanometry is a useful diagnostic tool to detect middle ear pathologies especially otitis media with effusion (OME). It reflects the middle ear elasticity, stiffness and compliance which are disrupted in some middle ear pathologies. The most common conventional method for tympanometric measurement is performed by using 226 Hertz (Hz) probe tone. The other common, especially in infants, used 1000 Hz probe tone frequency have been found superior to 226 Hz probe tone in infants younger than 9 months [1, 2].

In recent years, 1000 Hz probe tone tympanometry in infants has been increasingly studied with the widely committed national hearing programs in more countries for the aim of early detection of hearing loss

Received: *er 27, 2018;* ***Accepted:*** *July 23, 2019;* ***Published Online:*** *February 10, 2020*

How to cite this article: *Özdamar Oİ, Özbilen Acar G, Pektaş E, Ertuğrul Ö, Yiğit Ş. Efficacy and feasibility of 226 Hz and 1000 Hz tympanometry in healthy pediatric patients. Eur Res J 2020;6(3):200-203. DOI: 10.18621/eurj.488170*

Address for correspondence: *Osman İlkay Özdamar, MD., İstanbul Medeniyet University, Göztepe Training and Research Hospital, Department of Otorhinolaryngology-Head and Neck Surgery, Otorhinolaryngology-Head and Neck Surgery, Turkey*
E-mail: osmanilkay73@yahoo.com, Tel: +90 216 5664072, Fax: +90 216 4674951

e-ISSN: 2149-3189

in neonates. Middle ear dysfunctions in which the most common reason is OME are the main reason for false-positive results in these screening programs, therefore it is crucial to detect clearly OME if it is present [3]. Tympanometry is an objective, useful, non-invasive and reusable clinical diagnostic tool to detect middle ear function, and also external ear as well.

Although studies regarding with comparing feasibility of 1000 Hz and 226 Hz probe tone tympanometries in children, especially in infants, have presented for patients with normal and middle ear pathologies in the literature, there are a few studies comparing the feasibility and usefulness of 1000 Hz and 226 Hz probe tone tympanometries in children older than 3 years of age with normal functioning middle ears. Therefore, it would be possible to detect false-positive results and compare with this method in the patients.

In this retrospective study, we aimed to compare the feasibility and usefulness of 1000 Hz and 226 Hz probe tone tympanometries in children older than 3 years of age with normal otomicroscopic examination and normal hearing detected with behavioral audiometry, transient-evoked otoacoustic emissions (OAE) and/or click-evoked auditory brainstem audiometry (ABR).

METHODS

In this retrospective study, we evaluated normal healthy pediatric cases with 226 and 1000 Hz frequency probe tympanometries for the aim of comparing efficacy and detecting the rate of false positive tympanometric findings in these subjects. Forty-nine (98 ears) healthy pediatric subjects (25 males and 24 females) were enrolled in the study, and all of the cases were younger than 18 years of age. The mean age was 9.3 ± 4.46 years old with a range from 3 to 17 years. Oto-microscopic examination was performed to all of the children as a gold standard to detect pathologies in middle ear and external ear as well. All of the children had normal hearing that were detected by means of behavioral audiometry, Otoacoustic emission (OAE) and/or Auditory Brainstem Response (ABR).

All of the tympanometric tests were performed with both of the 226 Hz and 1000 Hz probe tones (Interacoustics AT 235 h tympanometer, Denmark) in each child. Tympanometry types for 226 Hz tone probe were noted as type A, type B, type C, type D and type Du; and for 1000 Hz tone probe as type 1, type 2, type 3, type 4 and type 4u as based on Lidén [4] and Jerger [5].

RESULTS

The mean values of 226 Hz tympanometric measurement of right ears for ear volume (EV), compliance (C), tympanometric peak pressure(TPP) and gradient (G) were 74 ± 28.10 ml, 59 ± 38.96 ml, -46 ± 92.38 daPa and 36 ± 33.22 ml, respectively; these values for the left ears were 84 ± 65.94 ml, 51 ± 31.00 ml, -57 ± 102.05 daPa and 30 ± 23.35 ml, respectively. The mean values of 1000 Hz tympanometric measurement of right ears for EV, C and TPP were 78 ± 23.03 ml, 172 ± 85.04 ml and -22 ± 110.70 daPa, respectively; these values for the left ears were 64 ± 32.05, 147 ± 104.70, 0 ± 98.20, respectively. TPP

Table 1. 226 Hz and 1000 Hz tympanometry results of the patients

	226 Hz. Tympanometry		1000 Hz. Tympanometry	
	Right Ears	Left Ears	Right Ears	Left Ears
Normal tympanogram*	42	41	42	42
Anormal tympanogram**	7	8	7	7
Other anormal tympanograms†	None	None	None	None
Total	49	49	49	49

*Type A in 226 Hz probe tone typmpanometry, and type 1 in 1000 Hz tympanometry.
**Type C in 226 Hz probe tone typmpanometry, and type 3 in 1000 Hz tympanometry.
†Type B, D and Du in 226 Hz probe tone typmpanometries, and type 2, 4 and 4u in 1000 Hz tympanometries.

around 0 daPa (between +100 daPa and -150 daPa) were classified as Type A or Type 1 in 226 Hz tone probe and 1000 Hz tone probe tympanometries, respectively. We detected 86% (42/49 patients) type A tympanometry for the right ears and 84% (41/49 patients) for the left ears in 226 Hz tympanometric measurements, and 86% (42/49 patients) type 1 tympanometry for the right ears and 86% (42/49 patients) for the left ears in 1000 Hz tympanometric measurements (Table 1). Additionally, we detected 14% (7/49 patients) type C tympanometry (TPP at lower than -150 daPa pressure) for the right ears and 16% (8/49 patients) for the left ears in 226 Hz tympanometric measurements, and 14% (7/49 patients) type 1 tympanometry (TPP at lower than -150 daPa pressure) for the right ears and 14% (7/49 patients) for the left ears in 1000 Hz tympanometric measurements. There were no type B, type D and type Du tympanometries in any patient with 226 Hz tympanometry and no type 2, type 4 and type 4u in any patient with 1000 Hz tympanometry.

DISCUSSION

In this study, we compared the 266 Hz tone probe tympanometry results with 1000 Hz tone probe tympanometry results that were performed in normal hearing and healthy pediatric patients older than 3 years of age. However, there is a study from Korea that recommends usage of 1000 Hz probe tone tympanometry for infants up to 12 months of age [6]. Type of tympanogram in the clinician perspective is the main objective to consider normality or abnormality of this objective measurement with regarding to external ear canal, tympanic membrane and middle ear function. Therefore we considered the type of tympanometry as normality standard.

Alaerts et al. [3] found that type 1 tympanogram were detected in 91% of infants younger than 3 months of age with 1000 Hz tone probe tympanometry; on the other hand, 75% of the cases had type A tympanometry with 226 Hz tympanometry in children between 9-32 months of age. We found that 86% (42/49 patients) type A tympanometry for the right ears and 84% (41/49 patients) for the left ears in 226 Hz tympanometric measurements, and 86% (42/49 patients) type 1 tympanometry for the right ears and 86% (42/49 patients) for the left ears in 1000 Hz tympanometric measurements.

Park et al. [6] studied on Korean infants (up to 13 months of age) whether having OME or not by using 226 Hz and 1000 Hz tympanometry. They found that more than 90% of tympanometries with 226 Hz were normal in infants without OME as well as with 1000 Hz tympanometry. On the contrary, in infants with OME more than 90% of tympanometries with 226 Hz were normal but more than 90% of tympanometries with 1000 Hz were abnormal which means more reliable results. In normal functioning middle ears, the tympanometry results were similar with 226 Hz and 1000 Hz but in middle ear pathologies, such as OME, the results of 1000 Hz were more reliable and false-negative results were detected with 226 Hz tympanometry [6].

Other important tympanometric finding in first 6 weeks of life in neonates is DP (double peak curve) tympanogram which was compatible with rapid anatomical growth of ear structures during this period, and this tympanometric finding is decreased with increasing age [3, 7]. Also, we detected no DP tympanometric finding in normal hearing healthy pediatric patients who were equal or older than 3 years of age which is compatible with the literature.

In current study, nearly 85% of normal functioning ears had normal type A or type 1 tympanometry but remaining nearly 15% subject had abnormal tympanometry on both of 226 Hz and 1000 Hz tympanometry in normal hearing and normal functioning middle ear system (false-positive results) in healthy children with older than 3 years of age.

CONCLUSION

We found that there was no superiority of the usage of 1000 Hz tympanometry to 226 Hz tympanometry in normal hearing healthy pediatric patients who were equal or older than 3 years of age. It needs studies with large series of cases to assess the reliability of these results.

Authors' contribution

OİÖ = writing of the article, substantial contributions to conception and design, revising it critically for important intellectual content and final

approval of the article; GÖA = revising it critically for important intellectual content, substantial contributions to conception and design,and final approval of the article; EP = analysis and interpretation of data, performing of tympanometric measurements, data collection drafting the article andfinal approval of the version; ÖE = analysis and interpretation of data,performing of tympanometric measurements, data collection, drafting the article andfinal approval of the version; ŞY = Analysis and interpretation of data,performing of tympanometric measurements, data collection,drafting the article and final approval of the version.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Acknowledgement

This study was presented as a poster presentation at 9th EAONO Instructional Workshop & Consensus on Auditory Implants, June 20-23, 2018, Copenhagen/Denmark.

REFERENCES

1. Hoffmann A, Deuster D, Rosslau K, Knief A, Am Zehnhoff-Dinnesen A, Schmidt CM. Feasibility of 1000 Hz tympanometry in infants: tympanometric trace classification and choice of probe tone in relation to age. Int J Pediatr Otorhinolaryngol 2013;77:1198-203.
2. Carmo MP, Costa NT, Momensohn-Santos TM. Tympanometry in infants: a study of the sensitivity and specificity of 226-Hz and 1,000-Hz probe tones. Int Arch Otorhinolaryngol 2013;17:395-402.
3. Alaerts J, Luts H, Wouters J. Evaluation of middle ear function in young children: clinical guidelines for the use of 226- and 1,000-Hz tympanometry. Otol Neurotol 2007;28:727-32.
4. Lidén G. The scope and application of current audiometric tests. J Laryngol Otol 1969;83:507-20.
5. Jerger J. Clinical experience with impedance audiometry. Arch Otolaryngol 1970;92:311-24.
6. Park M, Han KH, Jung H, Kim MH, Chang HK, Kim SH, et al. Usefulness of 1000-Hz probe tone in tympanometry according to age in Korean infants. Int J Pediatr Otorhinolaryngol 2015;79:42-6.
7. Mazlan R, Kei J, Hickson L, Stapleton C, Grant S, Lim S, et al. High frequency immittance findings: newborn versus six-week-old infants. Int J Audiol 2007;46:711-7.

The European Research Journal 2020;6(3):204-209 Original Article

DOI: 10.18621/eurj.513297 *Urology&Psychiatry*

The effects of total laser pubic hair removal on sexual functions, body perception and self-esteem in women

Mustafa Murat Aydos[1], Sinay Önen[2], Efe Önen[1]

[1]*Department of Urology, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey*
[2]*Department of Psychiatry, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey*

ABSTRACT

Objectives: Both males and females carried out pubic hair removal by various methods usually for visual/aesthetic or psychosexual reasons. The aim of the present study was to evaluate self-esteem, body image and sexual functions of women before and after total laser pubic hair removal (TLPHR) which is frequently being prefered due to its long-lasting effects.

Methods: A total of 45 sexually active women between 20 and 50 years of age who underwent total laser pubic hair removal were included in the study. The sociodemographic features, Female Sexual Function Index (FSFI), Rosenberg Self Esteem Scale (RSES), Body Cathexis Scale (BCS), Beck Depression Inventory (BDI) of the participants were assessed before the first session and after the 6th session of TLPHR procedure.

Results: Total RSES, total BCS scores and the 40th item of the BCS score significantly decreased after the TLPHR procedure ($p < 0.001$). Total FSFI scores and also FSFI subscales of desire, arousal, lubrication and satisfaction scores were significantly increased after TLPHR ($p < 0.001$).

Conclusion: Our study results demonstrated that self-esteem, genital and total body image, sexual desire, sexual arousal and sexual satisfaction was improved after TLPHR procedure. Wider sampled studies examining the effects of laser pubic hair removal on individual, relational and psychosocial issues in both males and females are needed.

Keywords: Pubic, Rosenberg, hair removal, self-estem, laser

Both males and females carried out pubic hair removal for many reasons for over the centuries. Modern pubic hair removal is often done for visual/aesthetic or psychosexual reasons rather than for health reasons. [1]. Women are willing to remove their pubic hair for the reasons like hygiene, sexual attractiveness, sexual enhancement, religious-social beliefs and before any gynecological examination [2, 3]. Also by removing pubic hair women are found to have higher levels of body shame, self consciousness and self objectification [4]. In addition to this some researches proposes males prefer sexual partners to be hairless [5]. Anecdotal reports indicate that pubic hair removal provide increased aesthetic appearance and increased tactile sensitivity of the genitals such as the clitoris, but unfortunately there is insufficient scientific data to support this view [1]. Moreover, unwanted hair loss might be an extremely distressing condition and might cause reduction of self-esteem, well-being and sexuality which was previously demonstrated in women treated for breast cancer and women with hypotrichosis [6, 7].

razor blade, waxing, plucking, bleaching, depilatory creams, electrolysis, laser therapy are the most

Received: *January 16, 2019;* ***Accepted:*** *February 7, 2019;* ***Published Online:*** *February 11, 2019*

How to cite this article: *Aydos MM, Önen S, Önen E. The effects of total laser pubic hair removal on sexual functions, body perception and self-esteem in women. Eur Res J 2020;6(3):204-209. DOI: 10.18621/eurj.513297*

e-ISSN: 2149-3189

Address for correspondence: *Efe Önen, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Urology, Mimar Sinan Mah., Emniyet Cad., Yıldırım, 16310 Bursa, Turkey. E-mail: drefeonen@gmail.com, Fax: +90 224 366 0416*

known methods for pubic hair removal [2]. Shaving and waxing are the most common methods of genital hair removal wherefore they are cheap and easy to applicate. Because of avoiding frequent side effects and having longer persistence, the number of women who prefer laser depilation is increasing nowadays. Not only pubic hair removal is recommended by Islam as a tradition of hygiene, but also total pubic hair removal performed to put forth femininity for sexuality in Turkish population [8]. Although in many countries the number of women who have genital grooming is increasing, total pubic hair removal is still the most preferred modality in our country for these reasons.
In several studies, sexual intercourse and sexual satisfaction frequency correlated with total pubic hair removal, particularly in young women. This practice has an interesting psychosexual basis that has not yet been fully explored in sexual medicine. The aim of the present study was to compare self-esteem, body image and sexual functions of women before and after total laser pubic hair removal (TLPHR) procedure.

METHODS

The present cross-sectional study comprised of 45 women who underwent laser depilation for pubic hair removal between June 2018 and Nowember 2018 at a referral private clinic and our clinic. Sexually active women between 20 and 50 years of age who volunteered to participate and did not have any psychiatric diagnosis were included in the study. Ethics committee approval was obtained from the local ethics committee of Bursa Yuksek Ihtisas Training and Research Hospital (ID:2011-KAEK-25 2018/06-15). And all the women gave written consent, were seen by a doctor at entry to the study.

Participants were asked to fill in self-administered questionnaires before and after the laser depilation sessions. Laser depilation sessions was performed by a 755 nm diode laser once a month. Participants fulfilled the Female Sexual Function Index (FSFI), Rosenberg Self Esteem Scale (RSES), Body Cathexis Scale (BCS), Beck Depression Inventory (BDI) before the first session and after the 6th session of TLPHR procedure. BMI was calculated by dividing weight (in kilograms) by height (in meters squared). Since increased body weight and depressive disorder may affect self-esteem, body image and sexual functioning, women with a BMI below 18.5 and above 25 and with a BDI score above 17 were excluded from the study.

Instruments

Sociodemographic Data Form

This form was developed by the researchers and contained questions directed at determining the women's sociodemographic characteristics including age, height, weight, marital status, education level, occupation, economic status, medical illness, smoking status, alcohol and drug use.

Female Sexual Function Index (FSFI)

FSFI questionnaire was created by Rosen *et al*. for the assessment of female sexual functioning [9]. The instrument was validated and adapted to Turkish population by Öksüz and Malhan [10]. Based on clinical interpretations of a principal components analysis, a 6-domain structure was identified including sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. Participants completed the instrument by choosing the option that best described their situation. Each question was associated with a value corresponding to the degree of gratification of the participant. A score of '0' indicates no sexual activity in the last four weeks, and the others are numbered from 1 to 5 on an incremental scale.

Rosenberg Self-Esteem Scale (RSES)

RSES is a 10-item likert type scale which was developed by Morris Rosenberg in 1965 to evaluate global self-worth by measuring both positive and negative feelings about one's self [11]. In our country, reliability and validity studies of the scale were performed by Korkmaz [12]. The score received from the first 10 items is evaluated as high self-esteem for a total score of 0-1, average self-esteem for a total score from 2-4, and low for 5-6. Lower scores indicate higher levels of self-esteem [12].

The Body Cathexis Scale (BCS)

It is a 40-item scale which was developed by Secord and Jourand in 1953 to measure the level of body satisfaction and attitude to body image [13]. The reliability and validity of Turkish version was performed by Hovardaoğlu and Özdemir in 1990 [14]. The items are in a 5-point likert type scale that ranges

from 1 = I don't like at all to 5 = I really like. The lowest possible score from the scale is 40 and the highest is 200 and higher scores indicate less satisfaction from the body parts. The Cronbach alpha coefficient obtained from this tool in our study was determined to be 0.85.

Beck Depression Inventory (BDI)

BDI is a self-report scale consisting of 21 items which is used to evaluate physical, emotional, cognitive and motivational symptoms of depression [15]. Validity and reliability of Turkish version of BDI was performed by Hisli Şahin [16]. The total score vary between 0-63, and the cut-off value is accepted as 17.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows version 20.0 (SPSS Inc., Chicago, IL, USA). The data were analyzed for normal distribution of continuous variables using histograms and the Shapiro-Wilk test. The normally distributed continuous variables were reported as mean ± standard deviation (SD). Categorical variables were reported as frequencies and percentages. To examine the differences between before and after the laser procedure, the continuous covariates were analyzed based on paired samples t test and Wilcoxon signed-rank tests.

RESULTS

The mean age of the study group was 34.1 ± 4.3 years. Thirty-seven (82.2%) women were employed and 31 (68.9%) women had high education level. All women were heterosexual and sexually active with a partner. Thirty-five (77.8%) women were married and 7 (15.6%) were single. The mean BMI of the study group was 21.9 ± 2.8 kg/m2. The sociodemographic features of the study group is given in Table 1.

The mean BDI score was 8.9 ± 4.6 before the first session of TLPHR and there was no statistically significant change in BDI scores after the procedure ($p > 0.05$). The mean RSES scores of the study group were 2.3 ± 0.7 before and 1.4 ± 0.5 after TLPHR. The mean RSES change was statistically significantly decreased after the laser sessions ($p < 0.001$). Total

Table 1. Demographic characteristics (n = 45)

Age (mean ± SD)	**34 ± 4.3**
Marital Status, n (%)	
Single	7 (15.6)
Married	35 (77.8)
Widowed/Divorced	3 (6.6)
Education Level, n (%)	
Literate	4 (8.9)
Primary School	10 (22.2)
High School	15 (33.3)
University	16 (35.6)
Economic status, n (%)	
Low	8 (17.8)
Average	20 (44.4)
High	17 (37.8)
BMI (kg/m2) (mean ± SD)	21.9 ± 2.8

BMI = Body mass index

BCS scores were 174.42 ± 17.32 before and 156 74 ± 16.22 after the procedure ($p < 0.001$). Especially the BCS scale 40th item, which indicates the satisfaction from genital organs, was evaluated separately and statistically significantly decreased score was found after the TLPHR procedure ($p < 0.001$) (Table 2).

The mean total FSFI scores of participants were 26.2 ± 3.4 before TLPHR and 32.5 ± 3.9 after TLPHR procedure. Total FSFI scores significantly increased after the laser depilation ($p < 0.001$). FSFI subscales of desire, arousal, lubrication and satisfaction scores were significantly increased after TLPHR ($p < 0.001$). The mean scale scores before and after TLPHR procedure are given in Table 3.

DISCUSSION

The present study evaluated the alteration of self-esteem, body image and sexual functions of women who was applied total laser pubic hair removal. Our study results demonstrated that self-esteem, genital and total body image, sexual desire, sexual arousal and sexual satisfaction of study population was improved after TLPHR procedure.

Regular cleaning and grooming of the pubic hair is an important doctrine in Muslim societies. Thus, the

Table 2. The FSFI scores of the volunteers before and after the laser hair removal procedure

		Mean ± SD	*p value*
FSFI total			**< 0.001**
	Before TLPHR	26.2 ± 3.4	
	After TLPHR	32.5 ± 3.9	
Desire			**< 0.001**
	Before TLPHR	3.7 ± 0.4	
	After TLPHR	5.2 ± 0.7	
Arousal			**< 0.001**
	Before TLPHR	3.9 ± 0.3	
	After TLPHR	5.1 ± 0.5	
Lubrication			**< 0.001**
	Before TLPHR	4.5 ± 0.7	
	After TLPHR	5.6 ± 0.8	
Orgasm			> 0.05
	Before TLPHR	4.1 ± 0.6	
	After TLPHR	5.5 ± 0.8	
Satisfaction			**< 0.001**
	Before TLPHR	4.3 ± 0.7	
	After TLPHR	5.4 ± 1.1	
Pain			> 0.05
	Before TLPHR	5.5 ± 0.9	
	After TLPHR	5.4 ± 1.2	

FSFI = Female Sexual Function Index, TLPHR = Total Laser Pubic Hair Removal

Table 3. RSES, BCS, BDI scores before and after the TLPHR procedure

	Before TLPHR	After TLPHR	*p value*
RSES total	2.3 ± 0.7	1.4 ± 0.5	**< 0.001**
BCS	174.42 ± 17.32	156.74 ± 16.22	**< 0.001**
BCS (40^{th} item)	2.39 ± 0.25	1.77 ± 0.14	**< 0.001**
BDI	8.9 ± 4.6	9.0 ± 4.8	0.91

Data are show as mean±standard deviation. RSES = Rosenberg Self Esteem Scale, BCS = Body Cathexis Scale, BDI = Beck Depression Inventory, TLPHR = Total laser pubic hair removal

hygiene of the pubic area and to be hair-free before sexual intercourse, is a cultural and religious expectation both for women and their spouses that can affect the sexual functions and marital adjustment of the couple. Muallazaziz *et al*. [8] reported that laser was the third preferred hair removal method among muslim women according to their study results. Also in a study with a larger Turkish population laser pubic hair removal was indicated to be preferred by 16.8% of the participants [17]. Although it is not the most commonly used method but the increased tendency to prefer LPHR for pubic hair removal in recent years was the reason for the preference of LPHR method in the present study.

The study of Sangiorgi *et al*. [18] showed that Brazilian women who are satisfied with the appearance of their own genitalia have a stronger preference for complete removal of pubic hair. Herbenick *et al*. [19] indicated similar results in their study with 2451 women. In a study of DeMaria *et al*. [20] which was carried on with 663 female participants who had been removing pubic hair, it was demonstrated that women who were hair-free had a significantly more positive genital self-image than women with at least some hair on their genitals. In our study there was an improvement in the genital body image of women after total laser pubic hair removal (TLPHR) procedure, supporting previous findings.

Hirsutism is defined in females as male type terminal hair growth and distribution occurring in approximately 60% of cases with Polycystic Ovary Syndrome (PCOS) [21, 22]. Previous studies have reported that women who have PCOS are more prone to depression, anxiety and have lower self-esteem, negative body image, and psychosexual dysfunction [23, 24]. Clayton *et al*. [25] evaluated the impact of laser hair removal among hirsute women with PCOS and suggested that laser treatment reduced the severity of facial hair, depression and anxiety and improved quality of life over the 6-month study period. Our study results support the previous findings that the decrease of unwanted body hair provide an improvement in body image and sexual functions, and result in an increase in the one's self-esteem.

In a study of Herbenick *et al*. [19] 2451 women between the ages of 18-65 were compared in terms of pubic hair removal type and sexual dysfunction, and found that women who had done total pubic hair removal had higher scores of total FSFI, desire, arousal, lubrication, pain and sexual satisfaction than women with no hair removal and partial hair removal. Also Bercaw-Pratt *et al*. [26] point to association between complete depilation and greater sexual activity. According to our study results, total FSFI score and desire, arousal, lubrication and satisfaction subscale scores were significantly increased after TLPHR compared to baseline scores. These findings show that there is a prominent improvement in both sexual functions and sexual satisfaction of the participants after TLPHR procedure. The increase in both sexual desire and sexual arousal might be attributed to the previous asseverations claiming that pubic hair removal provide increased aesthetic appearance and increased tactile sensitivity of the clitoris.

A study of DeMaria *et al*. [2] revealed that there was no significant differences between body esteem scores among low-income Hispanic, Black, and White women who were current groomers compared to those who were not [2]. In contrary our findings indicate an improvement in the body image and satisfaction in women after total laser pubic hair removal (TLPHR) procedure. This contradiction between the results of the studies can be attributed to the fact that the participants in our study have higher income levels, and increased economic status may be related to the more importance given to the body image and the increase in expectations on aesthetic issues.

Limitations

This study had several limitations. First, it was limited to mid/high-income women seeking at our clinic in the Bursa region and therefore studying in wider groups could provide more effective results. The cohort of this study could be accepted as a representation of a Muslim society; thus, our findings may not be generalized to other religious, ethnic and cultural populations.

CONCLUSION

The present study findings indicate that body satisfaction, self-esteem and sexual functions improve after total laser pubic hair removal in women. The results of the study will be valuable for future studies investigating psychosocial-sociocultural effects of pubic hair removal such as quality of life, psychosocial functionality and marital adjustment. Also more studies with larger groups of patients are required about this topic.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Ramsey S, Sweeney C, Fraser M, Oades G. Pubic hair and sexuality: a review. J Sex Med 2009;6:2102-10.
2. DeMaria AL, Berenson AB. Prevalence and correlates of pubic hair grooming among low-income Hispanic, black, and white women. Body Image 2013;10:226-31.
3. Braun V, Tricklebank G, Clarke V. "It shouldn't stick out from your bikini at the beach": Meaning, gender, and the hairy/hairless body. Psychol Women Q 2013;37:478-93.
4. Smolak L, Murnen SK. Gender, self-objectification and pubic hair removal. Sex Roles 2011;65:506-17.
5. Butler S, Smith NK, Collazo E, Caltabiano L, Herbenick D. Pubic hair preferences, reasons for removal and associated genital symptoms: comparisons between men and women. Sex Med 2014;12:48-58.
6. Freedman TG. Social and cultural dimensions of hair loss in women treated for breast cancer. Cancer Nurs 1994;17:334-41.
7. Lee YR, Lee SJ, Kim JC, Ogawa H. Hair restoration surgery in patients with pubic atrichosis or hypotrichosis: review of technique and clinical consideration of 507 cases. Dermatol Surg 2006;32:1327-35.
8. Muallaaziz D, Yayci E, Ataçağ T, Kaptanoğlu AF. Pubic hair removal practices in Muslim women. Basic Clin Sci 2014;3:39-44.
9. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, et al. The female sexual function index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000;26:191-208.
10. Öksüz E, Malhan S. [Reliability and validity of the Female Sexual Function Index in Turkish population]. Sendrom 2005;17:54-60. [Article in Turkish]
11. Rosenberg M. The association between self-esteem and anxiety. J Psychiatr Res 1962;1:135-52.
12. Korkmaz M. Yetişkin örneklem için bir benlik saygısı ölçeğinin güvenirlik ve geçerlik çalışması. (Yayımlanmış yüksek lisans tezi). İzmir: Ege Üniversitesi Sosyal Bilimler Enstitüsü, 1996.
13. Secord PF, Jourand SM. The appraisal of body-cathexis and the self. J Consult Psychol 1953;17:343-7.
14. Hovardaoğlu S, Özdemir YD. Vücut Algısı Ölçeği'nin güvenirlik ve geçerlik çalışması/ Şizofrenik ve major depresif hastaların beden imgelerinden doyum düzeyleri (Yayımlanmamış yüksek lisans tezi). Ankara: Gazi Üniversitesi Sosyal Bilimler Enstitüsü, 1990.
15. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71.
16. Hisli Şahin N. Beck depresyon Envanterinin geçerliği üzerine bir çalışma. Psikoloji Dergisi 1988;6:118-26.
17. Kutlubay Z. Alexandrite laser hair removal results in 2359 patients: a Turkish experience. J Cosmet Laser Ther 2009;11:85-93.
18. Sangiorgi MLPO, Lara LADS, Lerri MR, Ferriani RA, Romão APMS. The Preference of Women and Men Regarding Female Genital Depilation. Rev Bras Ginecol Obstet 2017;39:488-95.
19. Herbenick D, Schick V, Reece M, Sanders S, Fortenberry JD. Pubic hair removal among women in the United States: prevalence, methods, and characteristics. J Sex Med 2010;7:3322-30.
20. DeMaria AL, Sundstrom B, McInnis SM, Rogers E. Perceptions and correlates of pubic hair removal and grooming among college-aged women: a mixed methods approach. Sexual Health 2016;13:248-56.
21. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet 2007;370:685-97.
22. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Androgen Excess Society: Position statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J Clin Endocrinol Metab 2006;91:4237-45.
23. Coffey S, Mason H. The effect of polycystic ovary syndrome on health related quality of life. Gynecol Endocrinol 2003;17:379-86.
24. Deeks A, Gibson-Helm M, Teede H. Anxiety and depression in polycystic ovary syndrome (PCOS): a comprehensive investigation. Fertil Steril 2010;93:2421-3.
25. Clayton WJ, Lipton M, Elford J, Rustin M, Sherr L. A randomized controlled trial of laser treatment among hirsute women with polycystic ovary syndrome. Br J Dermatol 2005;152:986-92.
26. Bercaw-Pratt JL, Santos XM, Sanchez J, Ayensu-Coker L, Nebgen DR, Dietrich JE. The incidence, attitudes and practices of the removal of pubic hair as a body modification. J Pediatr Adolesc Gynecol 2012;25:12-4.

The European Research Journal 2020;6(3):210-215 Original Article

DOI: 10.18621/eurj.470881 *Medical Oncology*

The effects of fulvestrant treatment on hormone receptor-positive metastatic breast cancer

Serdar Arıcı[1], Çağlayan Geredeli[1], Şaban Seçmeler[1], Abdullah Sakin[2], Orçun Can[3], Nurgül Yaşar[1], Şener Cihan[1]

[1]Department of Medical Oncology, University of Health Sciences, Okmeydanı Training and Research Hospital, İstanbul, Turkey
[2]Department of Medical Oncology, Yüzüncü Yıl School of Medicine, Van, Turkey
[3]Department of Medical Oncology, Nevşehir State Hospital, Nevşehir, Turkey

ABSTRACT

Objectives: To determine fulvestrant efficacy and tolerability in Turkish patients with hormone receptor-positive metastatic breast cancer.

Methods: Patients who developed metastasis while taking tamoxifen or aromatase inhibitors in the adjuvant period or metastatic disease at the diagnosis. Fulvestrant 500 mg was administered intramuscularly every 28 days. Progression-free survival (PFS) and overall survival (OS) durations were calculated.

Results: In this particular research, totally 137 patients were participated. Median PFS was 9 months (95% CI, 5.7-10.3). The 12-month PFS rate was calculated as 42%, and the 36-month PFS rate was 17%. The median PFS was not reached in the first line use of fulvestrant in the metastatic period but 9 months and 7 months in the second and subsequent lines respectively. Results indicated that this difference was statistically significant ($p = 0.002$). It was shown that patients with liver and brain metastasis had lower PFS compared patients with no liver and no brain metastasis. The estimated median OS was 38 months after fulvestrant started. The 12-month OS rate was calculated as 82.4%, and the 36-month OS rate was 50%.

Conclusions: Fulvestrant contributes both PFS and OS in patients with hormone receptor-positive metastatic breast cancer and this effect is more clear in using fulvestrant as first-line treatment.

Keywords: fulvestrant, breast cancer, endocrine treatment

Endocrine therapy has preferred a form of treatment for hormone receptor (HR) positive early stage breast cancer and advanced stage breast cancer. Endocrine therapy agents that are not cross-resistant to sequential administration prolong the chemotherapy-free period and have limited toxicity-effective disease stabilization. Tamoxifen has been the backbone of endocrine therapy for almost the last 30-40 years. In metastatic disease, response rate increases up to approximately 30% by using tamoxifen [1-3]. Tamoxifen and its metabolites are linked to the estrogen receptor (ER) and this receptor modulation also causes the antagonistic effect as an estrogenic effect [4]. Another group of drugs used in endocrine therapy is aromatase inhibitors (AI). In randomized clinical trials, AI was superior to tamoxifen in postmenopausal women [1, 3]. Fulvestrant, a 17 beta-estradiol analog, is a selective ER antagonist that suppresses estrogen signaling by binding to ER and inducing a conformational change [5, 6]. Dimerization is subsequently blocked, triggering accelerated degradation and downregulation of the ER protein [5]. Fulvestrant exhibits lack of

Received: **October 15, 2018;** *Accepted:* **January 31, 2019;** *Published Online:* **August 27, 2019**

How to cite this article: *Arıcı S, Geredeli Ç, Seçmeler Ş, Sakin A, Can O, Yaşar N, et al. The effects of fulvestrant treatment on hormone receptor-positive metastatic breast cancer. Eur Res J 2020;6(3):210-215.DOI: 10.18621/eurj.470881*

Address for correspondence: *Serdar Arıcı, MD., University of Health Sciences, Okmeydanı Training and Research Hospital, Department of Medical Oncology, İstanbul, Turkey. E-mail: serdararici@hotmail.com*

e-ISSN: 2149-3189

cross-reactivity with tamoxifen. The clinical efficacy of fulvestrant was initially demonstrated in two phases III trials that compared fulvestrant 250 mg per month with anastrozole 1 mg daily as a secondline therapy for advanced breast cancer [7, 8]. A combined analysis of these trials demonstrated that time to progression (TTP) with fulvestrant 250 mg was noninferior to anastrozole [9]. The phase III CONFIRM trial found that fulvestrant 500 mg was associated with improved progression-free survival (PFS) and overall survival (OS) compared with the 250 mg dose in patients who experienced disease recurrence or progression after previous endocrine therapy [10, 11]. The FIRST study reported that improved OS with fulvestrant 500 mg treatment compared with anastrozole in the first-line setting for ER-positive advanced breast cancer, with an approximately 30% reduction in mortality risk [12] In this retrospective study, we investigated fulvestrant efficacy and tolerability in Turkish patients with hormone receptor-positive metastatic breast cancer.

METHODS

This study was planned as a retrospective single center study. Istanbul Okmeydanı Training and Research Hospital obtained medical information from the archive files of patients who were treated with hormone receptor positive and HER 2 negative metastatic breast cancer in the medical oncology clinic. Patients who developed metastasis while taking tamoxifen or aromatase inhibitors in the adjuvant period or metastatic disease at the diagnosis. Fulvestrant 500 mg was administered intramuscularly every 28 days (500 mg loading after 14 days from the first dose). PFS and OS durations were calculated by obtaining the date of starting Fulvestrant treatment, date of progression and date of the last visit from patient files.

Statistical Analysis

SPSS 15.0 for Windows program was used for statistical analysis. Comparisons of ratios in groups were made with Chi Square Analysis. Monte Carlo simulation was applied when conditions were not met. The survival analyzes were performed with Kaplan Meier Analysis. A statistical significance level of alpha was accepted as $p < 0.05$.

RESULTS

In this particular research, totally 137 patients were participated . The median age was 53 (min.: 27 - max.: 91). The median follow-up time was 20 months (0-78 months). 20.9% patients were metastatic stage at the diagnosis. 22% of patients had not received any endocrine treatment before fulvestrant (Table1). During the follow-up period, 65% of the patients developed progression, 35% had no progression and still continued to use Fulvestant. Median PFS was 9 (95% CI 5.7-10.3) months (Figure 1). The 12-month PFS rate was calculated as 42%, and the 36-month PFS rate was 17% (Table 2). The median PFS was not reached in the first line use of fulvestrant in the metastatic period but 9 months and 7 months in the second and subsequent lines respectively. Results indicated that this difference was statistically significant ($p = 0.002$) (Table-3). There was no significant difference in PFS according to age, hormone and cerb-2 status in subgroup analyzes. It was clear that patients with liver and brain metastasis had lower PFS compared patients with no liver and no brain metastasis, the median PFS in patients with liver metastasis was 6 months (no liver metastasis 11 months) and in patients with brain metastasis was 3 months (no brain metastasis 10 months) these differences were statistically significant ($p = 0.004$ and $p= 0.011$ respectively in patients liver metastasis and brain metastasis). But PFS in patients with bone or lung or lymph node metastasis not statistically significant difference compared patients with no metastasis at these sites ($p = 0.235$, $p = 0.632$ and $p = 0.156$ respectively) (Table-4). The estimated median OS was 38 months after fulvestrant started. The 12-month OS rate was calculated as 82.4%, and the 36-month OS rate was 50%. 12-month (Table 5). OS rate was 95% in the first line use of fulvestrant in the metastatic period but 81.8%, 82.6 %, 75.5% in the second, third and fourth line respectively. But this difference was not statistically significant ($p = 0.149$). Also median OS, in patients using fulvestrant as first-line, was 48 months (Table 6). In subgroup analyzes, there was a statistically significant OS difference in patients with liver metastasis compared with patients had no liver metastasis, the median OS was 18 months and 52 months respectively ($p = 0.049$). Also in patients with brain metastasis compared with patients

Table 1. Patient Characteristics

		Mean ± SD	Min-Max
Age (years)		53.0 ± 13.4	27-91
		n	%
Menopause	Post	69	51.1
	Pre	66	48.9
Hystology	Ductal	119	87.5
	Lobular	13	9.6
	Others	4	2.9
Adjuvant ET	No	28	22.0
	Tamoxifen	61	48.0
	Tamoxifen+anastrazole	24	18.9
	Tamoxifen+letrozole	14	11.0
Metastasis at diagnosis		27	20.9
Metastasis site at starting fulvestrant	Bone	102	74.5
	Lymph nodes	27	19.7
	Liver	24	17.5
	Lung	33	24.1
	Brain	3	2.2
	Others	9	6.6
Follow-up time (months)		20.0 ± 14.9 (0-78)	

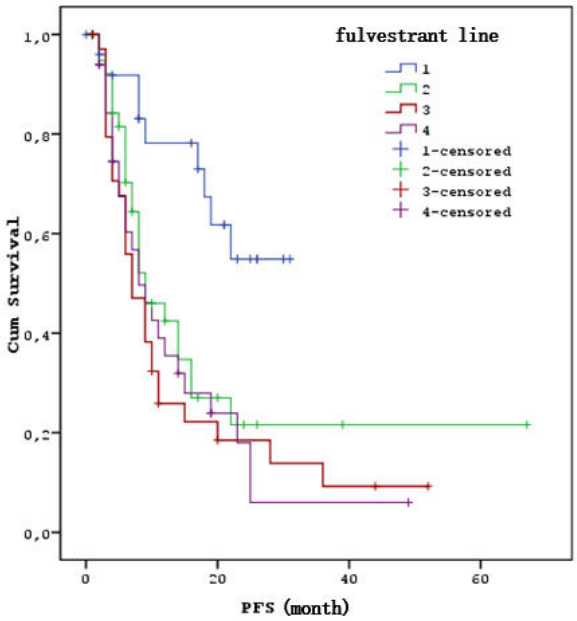


Fig. 1. Cumulative proportion surviving. PFS = progression free survival.

Table 2. **Progression free survival**

		PFS
Estimate median for PFS (95% CI) month		9 (6.8-11.2)
Cumulative proportion surviving (%)	12	42.4
	24	26.0
	36	17.1

PFS = progression free survival

Table 3. **Fulvestrant line and PFS**

			Cumulative Proportion Surviving (%)		
		Median (%95 CI)	12.month	24.month	36.month
Fulvestrant line	1	Not reached	78.2	54.9	-
	2	9 (5.2-12.8)	42.5	21.6	
	3	7 (4.1-9.9)	25.9	18.5	9.2
	4	8 (4.2-11.8)	35.5	18.0	-
Log Rank *p*			0.002		

PFS = progression free survival

Table 4. **Site of metastasis and PFS-OS**

Site		Median PFS	Median OS	OS *p* value	PFS *p* value
Bone	no	9	52	0.818	0.235
	yes	10	35		
Lymph	no	11	38	0.646	0.156
	yes	7	77		
Liver	no	11	52	0.049	0.004
	yes	6	18		
Lung	no	9	35	0.936	0.632
	yes	9	52		
Brain	no	10	38	0.001	0.011
	yes	3	12		

OS = overall survival, PFS = progression free survival

Table 5. **Overall survival**

		OS
Estimate Median for Survival Time (%95 CI)	month	38 (17.1-58.9)
Cumulative Proportion Surviving (%)	12	82.4
	24	61.5
	36	50.5
	60	40.2

OS = overall survival

Table 6. Cumulative proportion surviving

		Cumulative Proportion Surviving (%)		
		Median (95% CI)	12. month	36. month
Fulvestrant line	1	48	95.0	79.8
	2	35	81.8	46.5
	3	27 (0-60.3)	82.6	45.9
	4	26 (15.2-36.5)	75.5	46.1
Log Rank *p*			0.149	

had no brain metastasis, the median OS was significantly lower (12 months and 38 months respectively, $p = 0.001$) (Table 4). In all patients, toxic effects such as myalgia, arthralgia, fever and bone complications were observed in 23.9% of the patients and grade 3-4 toxic effect was not observed.

DISCUSSION

This particular research was a retrospective study that had been analyzed the clinical outcomes of fulvestrant treatment in post-menopausal patients with advanced breast cancer. It is found that median PFS had been 9 months. In two studies on Japanese women with advanced breast cancer treated with fulvestrant were reported that PFS was 5.4-5.5 months [13, 14]. In another study by Ishida *et al*. [15], fulvestrant in Japanese women with metastatic breast cancer that progressed after endocrine therapy was found that the median time to progression was 6.1 months.

In CONFIRM study, the median PFS was 6.5 months. In this study, fulvestrant treatment had been only located in the second line [10]. In this study there had been patients treating with fulvestrant first to the fourth line, but approximately 50% of patients were in the first line group. In this study trial, The median PFS had not reached in the first line use of fulvestrant in the metastatic period but 9 months and 7 months in the second and subsequent lines respectively ($p = 0.002$).

In the univariate analysis of this particular study found a lower PFS, regarding the presence-absence of liver and or brain metastasis. Similarly, FALCON study reported that in the presence of visceral disease PFS was significantly lower [16]. Kawaguchi *et al*. [13] found a similar PFS in the presence or absence of visceral disease. In contrast to the results found in this study and the FALCON study sub-analysis, a meta-analysis by Graham *et al*. [17] of four randomized controlled trials found that fulvestrant was associated with greater benefit in advanced breast cancer patients with visceral metastasis.

The estimated median OS was 38 months after fulvestrant started, in this particular study. The FIRST study was eveluated overall survival of patients who were postmenopausal women with estrogen receptor-positive, locally advanced/metastatic breast cancer who had no previous therapy for advanced disease received either fulvestrant 500 mg (days 0, 14, 28, and every 28 days thereafter) or anastrozole 1 mg (daily). The median OS was reported 54.1 months in the FIRST study [12]. But in the FACT trial, the median OS was 37.8 months in patients receiving fulvestrant plus anastrazole. The patients in FACT trial was received fulvestrant and anastrazole in first-line at metastatic disease but fulvestrant was used 250 mg [18]. In our trial, aproximately half of patients have used fulvestrant at second and further lines and median OS, in patients using fulvestrant as first-line, was 48 months.

In the FIRST study, 70.1% of patients experienced at least one adverse effects; the incidence of serious adverse effects was 11.9% with fulvestrant [12]. In the FALCON trial, 73% of patients in the fulvestrant group reported the adverse event and serious adverse events were reported by 13%. The most common side effects were arthralgia [17]. In our retrospective study, toxic effects such as myalgia, arthralgia, fever and bone complications were observed in 23.9% of the patients and grade 3-4 toxic effect was not observed.

CONCLUSION

In conclusion, fulvestrant contributes both PFS and OS in patients with hormone receptor-positive metastatic breast cancer and this effect is more clear in using fulvestrant as first-line treatment.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Bonneterre J, Buzdar A, Nabholtz JM, Robertson JF, Thürlimann B, von Euler M, *et al*. Anastrozole is superior totamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma. Cancer 2001;92:2247-58.
2. Bajetta E, Procopio G, Ferrari L, Martinetti A, Zilembo N, Catena L, et al. A randomized, multicenter prospective trial assessing long-acting release octreotide pamoate plus tamoxifen as a first line therapy for advanced breast carcinoma. Cancer 2002;94:299-304.
3. Paridaens R, Dirix L, Lohrisch C, Beex L, Nooij M, Cameron D, et al. Mature results of a randomized phase II multicenter study of exemestane versus tamoxifen as first-line hormone therapy for postmenopausal women with metastatic breast cancer. Ann Oncol 2003;14:1391-8.
4 Dutertre M, Smith CL. Molecularmechanisms of selectiveestrogenreceptormodulator (SERM) action. J Pharmacol Exp Ther 2000;295:431-7.
5. Wakeling AE, Dukes M, Bowler J. A potent specific pure antiestrogen with clinical potential. Cancer Res 1991;51:3867-73.
6 Wakeling AE. Similarities and distinctions in the mode of action of different classes of antioestrogens. Endocr Relat Cancer 2000;7:17-28.
7. Osborne CK, Pippen J, Jones SE, Parker LM, Ellis M, Come S, et al: Double-blind, randomized trial comparing the effi- cacy and tolerability of fulvestrant versus anastrozole in postmenopausal women with advanced breast cancer progressing on prior endocrine therapy: Results of a North American trial. J Clin Oncol 2002;20:3386-95.
8. Howell A, Robertson JFR, Quaresma Albano J, Aschermannova A, Mauriac L, Kleeberg UR, et al. Fulvestrant, formerly ICI 182,780, is as effective as anastrozole in postmenopausal women with advanced breast cancer progressing after prior endocrine treatment. J Clin Oncol 2002;20:3396-403.
9. Robertson JFR, Osborne CK, Howell A, Jones SE, Mauriac L, Ellis M, et al. Fulvestrant versus anastrozole for the treatment of advanced breast carcinoma in postmenopausal women: A prospective combined analysis of two multicenter trials. Cancer 2003;98:229-38.
10. Di Leo A, Jerusalem G, Petruzelka L, Torres R, Bondarenko IN, Khasanov R, et al. Results of the CONFIRM Phase III trial comparing fulvestrant 250 mg with fulvestrant 500 mg in postmenopausal women with estrogen receptor– positive advanced breast cancer. J Clin Oncol 2010;28:4594-600.
11. Di Leo A, Jerusalem G, Petruzelka L, Torres R, Bondarenko IN, Khasanov R, et al. Final overall survival: fulvestrant 500 mg vs 250 mg in the randomized CONFIRM trial. J Natl Cancer Inst 2014;106:djt337.
12. Ellis MJ, Llombart-Cussac A, Feltl D, Dewar JA, Jasiówka M, Hewson N, et al. Fulvestrant 500 mg versus anastrozole 1 mg for the first-line treatment of advanced breast cancer: overall survival analysis from the phase II FIRST study. J Clin Oncol 2015;33:3781-7.
13. Kawaguchi H, Masuda N, Nakayama T, Aogi K, Anan K, Ito Y et al. Outcomes of fulvestrant therapy among Japanese women with advanced breast cancer: a retrospective multicenter cohort study (JBCRG-C06; Safari). Breast Cancer Res Treat 2017;163:545-54.
14. Araki K, Ishida N, Horii R,Takahashi S, Akiyama F, Ito Y, et al. Efficacy of fulvestrant 500 mg in Japanese postmenopausal advanced/recurrent breast cancer patients and factors associated with prolonged time-to-treatment failure. Expert Opin Pharmacother 2015;16:2561-8.
15. Ishida N, Araki K, Sakai T, Kobayashi K, Kobayashi T, Fukada I, et al. Fulvestrant 500 mg in postmenopausal patients with metastatic breast cancer: the initial clinical experience. Breast Cancer 2016;23:617-23.
16. Robertson JFR, Bondarenko IM, Trishkina E, Dvorkin M, Panasci L, Manikhas A, et al. Fulvestrant 500 mg versus anastrozole 1 mg for hormone receptor-positive advanced breast cancer (FALCON): an international, randomised, double-blind, phase 3 trial. Lancet 2016;388:2997-3005.
17. Graham J, Pitz M, Gordon V, Grenier D, Amir E, Niraula S. Clinical predictors of benefit from fulvestrant in advanced breast cancer: a meta-analysis of randomized controlled trials. Cancer Treat Rev 2016;45:1-6.
18. Bergh J, Jönsson PE, Lidbrink EK, Trudeau M, Eiermann W, Brattström D, et al. FACT: an open-label randomized phase III study of fulvestrant and anastrozole in combination compared with anastrozole alone as first-line therapy for patients with receptor-positive postmenopausal breast cancer. J Clin Oncol 2012;30:1919-25.

The European Research Journal 2020;6(3):216-224 Original Article

DOI: 10.18621/eurj.455476 *Nursery*

The analysis of occupational accidents among the healthcare staffs

Songül Özenir[1], Vesile Ünver[2]

[1]*Department of Nursery, Tuzla State Hospital, İstanbul, Turkey*
[2]*Department of Nursery, Acıbadem Mehmet Ali Aydınlar University, Faculty of Health Sciences, İstanbul, Turkey*

ABSTRACT

Objectives: The aim of the study is to identify the attitudes of healthcare professionals towards the potential occupational accidents and the safe use of sharp instruments in their work environment.

Methods: The study was carried out between February 2017 and March 2017 with the participation of 173 health care personnel. The data collection forms consist of two parts, "Questionnaire about the occupational accidents that the participants might experience" and the"Attitude scale about the safe use of sharp objects and instruments by the participants".

Results: The number of injuries they experienced in the same period varied between 1 and 12 and the mean injury cases were found to be 2.76 ± 2.59. The total score of the participants from the Attitude scale was found to vary between 68 and 112, with a mean total score of 81.65 ± 7.03.

Conclusions: The participants of the study are subject to serious occupational accidents and occupations risks which may negatively affect their health.

Keywords: Healthcare workers, occupational injuries, sharp objects and instruments

Hospitals are defined as high risk working areas. Some of the risks they face include the inevitable contact with sick people or their blood and other body fluid. Therefore, they are subject to several occupational accidents due to the working conditions [1, 2].

Healthcare professionals are 12% of the total working population in the world [3]. In Turkey, there were 787,352 healthcare professionals in 2015 [4]. As it is well known that healthcare professionals try to care about other people's health and treat them without thinking about their health in a self-sacrificing manner and they are subject to serious threats which may lead to many negative effects in their life.

Hospitals have much more complex structures in contrast to many other work settings. In such a complex structure, healthcare professionals may be subject to both traditional occupational dangers such as musculoskeletal system illness (i.e. backache or neck ache), stress, and more specific and much riskier health problems, including sharps injuries, radiation exposure, latex allergy [5, 6]. In comparison to other professionals, healthcare professionalsare reported to experience musculoskeletal system pain much more frequently. On the other hand, such health problems are common among healthcare professionals and they are also subject to infections transmitted by blood such as Hepatitis B (HBV), Hepatitis C (HCV), and Human Immunodeficiency Virus (HIV) as a result of injuries caused by sharp instruments [6, 7].

Received: *August 28, 2018;* ***Accepted:*** *January 18, 2020;* ***Published Online:*** *February 1, 2020*

How to cite this article: *Özenir S, Ünver V. Occupational accident exposed to healthcare workers and views of the safe use of sharp medical instruments. Eur Res J 2020;6(3):216-224. DOI: 10.18621/eurj.455476*

Address for correspondence: *Vesile Ünver, PhD., RN, Associate Professor, Acıbadem Mehmet Ali Aydınlar University, Faculty of Health Sciences, Department of Nursery, İstanbul Turkey. E-mail: vunver1@gmail.com*

e-ISSN: 2149-3189

Healthcare staff is subject to numerous risks of getting an infection in their work environment. Such infections mostly occur through contact with blood and other body fluids [2]. Such diseases, that are the results of contact with blood and other body fluids, have higher rates of morbidity and mortality and occur frequently due to the injuries caused by sharp objects or instruments and percutaneous injuries [2, 8].

The data reported by the Centers for Disease Control and Prevention (CDC) indicate that healthcare professionals in the USA experience the injuries caused by needle tip and percutaneous injuries of which the number increases each year and that the yearly cases of the injuries caused by injectors among healthcare professionals are 385,000 and the daily mean of the injuries caused by sharp instruments is 1,000 [9]. The World Health Organization (WHO) reported that each year in Europe, nearly 304,000 healthcare professionals are diagnosed with HBV, 149,000 healthcare professionals are diagnosed with HCV and 22,000 healthcare professionals are diagnosed with HIV due to the injuries caused by sharp objects and instruments [10]. The findings of a meta-analysis suggest that the frequency of the HCV infection is much higher among healthcare professionals in contrast to the general population [11].

The findings of the CDC suggest that the injuries caused by contact with blood and body fluids occur due to percutaneous injuries (82%), in inpatient treatment sections (36%) and operating theatres (29%). The contact with blood and body fluids has been observed mostly among nurses, physicians and technicians (42%, 30%, and 15%, respectively) [12].

In the health sector, there are more occupational accidents and injuries, but the reporting of these cases is not so common. For instance, in the European health sector, the rate of occupational accidents is 34% more than those in other professional sectors [9]. The rate of reporting occupational accidents and injuries varies from one country to another. The findings of the CDC indicate that the rate of reporting the injuries caused by sharp instruments is about 46% and that those reported such cases are technicians (66%), nurses (53%), physicians (53%) and surgeons (30%) [13]. In a study carried out in India which covered the period between September 2012 and August 2014, it was found that there were 401 cases involving the contact with blood and body fluids by healthcare professionals and 208 cases were reported among them (52%). Those who reported such cases included physicians (77.5%, 93/120), nurses (42.1%) and laboratory technicians (25%) [9]. A study conducted in Turkey concluded that the rate of reporting such incidents is just 12.7% [12]. In Turkey, a regulation named "Patient and Employee Safety Regulation" was issued to establish safety committees at hospitals and to identify the necessary steps to be taken [14]. However, there are no data concerning the healthcare staff who experienced occupational accidents, how many of them became incapable of working or died and the specifics of the working conditions in the health sector in Turkey [9].

All these figures given above suggest that one of the serious threats caused as a result of the occupational accidents is the injury occurred during the use of sharp instruments and contact with blood and other types of bodily fluids. Therefore, it is significant to be informed about the attitudes of healthcare professionals towards the use of sharp instruments in their work environment. This study was carried out to identify the attitudes of healthcare professionals towards potential occupational accidents and the safe use of sharp instruments in their work environment. The data of the study are thought to be useful in improving the health of healthcare staff and in developing and shaping the related policies.

METHODS

Subjects

The study targeted healthcare professionals working at a public hospital during the period between February 2017 and March 2017 (n = 191). There were 51 physicians, 83 nurses/midwives/healthcare staff, 11 X-ray technicians, 7 anesthesia technicians, 8 laboratory technicians, 5 pharmacists, 2 audiologists and 24 medical secretaries/public servants. There was no specific sampling method used in the study. Instead, all of the healthcare professionals whose characteristics given above were attempted to be includedin the study. The participants of the study were 173 healthcare professionals who volunteered to take part in the study. The others did not volunteer or were not working at the hospital during the specified period due to several reasons (being on leave, being on sick leave, etc.). The participants represent 91% of

the targeted sample.

Data Collection

The data of the study were collected through questionnaires performed by one of the authors; the participants were informed about the study before the application. The questionnaires were administered at the related divisions where the participants were working at. The administration of the questionnaires lasted about 25 minutes.

Data Collection Form

The data collection form included two sections, which are given as follows:

•A questionnaire which included items about the occupational accidents that the participants might experienced

•An attitude scale about the safe use of the sharp objects and instruments by the participants

Questionnaire about the occupational accidents that the participants might experienced:

The questionnaire administered to the participants is composed of two sections. The first one included a total of eleven items about the socio-demographical characteristics of the participants, such as age, gender, marital status, educational background and their roles at the hospital as well as other specific information about their profession at the hospital.The second section includes nineteen items that were concerned with the occupational accidents that the participants experienced in the past. One of the items in this section, namely "Please indicate your status in terms of Hepatitis B", was not endorsed by the hospital where the participants were working at. Therefore, it was reworded as the following and endorsed by the hospital.

"Item 19. Do you know your status in terms of Hepatitis B? Yes (--) No (--)"

Attitude scale about the safe use of the sharp objects and instruments by the participants:

The validity and reliability analysis of the attitude scale about the safe use of the sharp objects and instruments was carried out by Uzunbayır [15], and the Cronbach's alpha coefficient of the scale was found to be 0.80. In the current study, the Cronbach's alpha coefficient of the scale was found to be 0.822.

The scale is a 5-point Likert-type scale. It includes twenty-five items about the views of the healthcare professionals concerning the safe use of the sharp objects and instruments. The potential answers to the positive statements in the scale are as follows: 1) Strongly agree (5 points), 2) Agree (4 points), 3) No idea (3 points), 4) Disagree (2 points), and 5) Strongly disagree (1 point).

The potential answers to the negatively stated items are as follows: 1) Strongly agree (1 point), 2) Agree (2 points), 3) No idea (3 points), 4) Disagree (4 points), and 5) Strongly disagree (5 points).

The scale has three subdimensions: cognitive, affective and behavioral. For the score of the cognitive scale, the following items are taken into consideration: 1, 4, 8, 11, 13, 16, 18, 19, 20, 23, 24 and 25. The maximum score from the cognitive sub-dimension is 60, while the minimum score is 12. For the score of the affective scale, the following items are taken into consideration: 2, 7, 9, 10, 14 and 22. The maximum score from the affective sub-dimension is 30, while the minimum score is 6. For the score of the behavioral scale, the following items are taken into consideration: 3, 5, 6, 12, 15, 17 and 21. The maximum score from the affective sub-dimension is 35, while the minimum score is 7.

Ethical issues

In order to carry out the study, ethical permissions were received from Acıbadem Mehmet Aydınlar University through Acıbadem Healthcare Institutions' Medical Research Ethics committee dated 24.11.2016 and numbered 2016/19 and from the Ministry of Health through its Public Hospitals' General Directorate's Istanbul Province Anatolian South region Public Hospitals Association General Secretariat dated 07.02.2017 and numbered 35778018 774.99.

Statistical Analysis

For the statistical analysis of the data, the SPSS software was used. The normality of the data distribution was analyzed by the Shapiro Wilk test. The analysis showed that the data had a normal distribution. The data were analyzed using both the descriptive statistics (means, standarddeviation, frequency) and t-test which was employed to make comparisons between two groups. The ANOVA test was used to make comparisons among the groups

more than two. The correlations among the data were analyzed through the Pearson correlation analysis. The significance level was set at $p < 0.05$.

RESULTS

The age of the participants varied between 23 years and 62 years and the mean age of them was 38.32 ± 7.82. It was also found that 31% of the participants were either 34 years or younger (n = 35), 24.3% of them were between the age group of 35 and 39, 26.6% of them were between the age group of 40-44 and 17.3% were either 45 yeras or older. Most of the participants were female (60.1%; n = 104) and married (75.1%; n = 130). Concerning the educational background, it was found that 32.4% of them had a two-year higher education (n = 56). Among the participants, 47.4% were either nurses or midwives (n = 82). The period of working at the units of the participants was found to vary between 0.5 year and 30 years, with the mean period of 5.38 ± 4.99. The professional experience of the participants was found to vary between 0.5 year and 37 years, with the mean period of 14.74 ± 8.11. The weekly working hours of the participants varied between 35 hours and 100 hours with the mean hour of 45.14±8.85. The rate of the participants who worked at outpatient clinics was found to be 27.2% (n = 47). It was also found that 74.6% of the participants had night shifts at their respective units (n = 129).

Table 1 shows the occupational accidents that the participants experienced in the last year. It is seen that 18.2% of them had injuries caused by a sharp object or instrument (n = 32) and that 23.3% of them contacted with the body fluids of the patients they

Table 1. Occupational accidents experienced by the participants in the last year

Occupational accidents	Data
Injuries caused by sharp objects and instruments, n (%)	
Yes	32 (18.2)
No	144 (81.8)
Contact with the body fluids of patients, n (%)	
Yes	41 (23.3)
No	135 (76.7)
Both injuries by sharp instruments and contact with the body fluids of patients, n (%)	
Yes	57 (32.9)
No	116 (67.1)
Reasons for injuries (n = 57), n (%)	
Taking medicine from an ampoule	12 (21.1)
Separating pinpoint from an injector	9 (15.8)
Recapping the pinpoint	5 (8.8)
During subcutaneous medicine practices	5 (8.8)
While taking suture	5 (8.8)
During surgery and medical dressing	5 (8.8)
During disposal	5 (8.8)
IV set and branule insertion	3 (5.3)
IV medicationadministration	1 (1.8)
While bending the needle	1 (1.8)
Taking blood from the patients	1 (1.8)
The number of injuries by sharp objects and instruments, mean ± SD (min-max)	2.76 ± 2.59 (2-12)

Table 2. Practices followed by the participants after the occupational accidents

Practices performed following the occupational accident	Data
Practices following the injury (n = 57), n (%)	
Washing with an antiseptic solution	36 (63.2)
Having a medical inspection	20 (35.1)
Informing the unit responsibleabout the incident	16 (28.1)
Filling the report form about the case	12 (21.1)
Taking prophylactic medicine	3 (5.3)
Vaccination	2 (3.5)
Having an Ig	1 (1.8)
Reporting the accident, n (%)	
Yes	37 (21.0)
No	139 (79.0)
Unit/persons informed through a report, n (%)	
Infection controlnurse	28 (75.7)
Occupational health and safety unit	9 (24.3)
Unit responsible	7 (18.9)

treated (n = 41).

Table 2 shows that following the injury cases 63.2% of the participants wash the injured part with antiseptic solution (n = 36), 35.1% of them apply for medical investigation (n = 20), 28.1% of them inform the unit responsible about the incident (n = 16), 21.1% of them fill the incident report form (n = 12), 5.3% of them take prophylactic drug (n = 3), 3.5% of themvaccinate (n = 2) and 1.8% of them have an IG (n = 1). It was found that the rate of the participants who reported occupational accidents is 21% (n = 37). Of them, 75.7% report the incident to infection control nurses (n = 28), 24.3% report it to the occupational health safe unit (n = 9) and 18.9% report it to the unit responsible (n = 7). It was found that 32.9% of the participants experienced either an injury case caused by a sharp object or instrument or was subject to contact with the body fluid in the last year (n = 57). The average injury rate to the average weekly working hours of nurses (45.14) was found to be 1.32.

Table 3 shows the scores of the participants from the attitude scale for the safe use of sharp objects and instruments by healthcare professionals based on the subdimensions of the scale. Their scores from the cognitive subdimension vary between 32 and 56, and their mean score was found to be 42.92 ± 3.73. The scores of the participants from the affective subdimension of the scale were found to vary between 15 and 29 with a mean of 21.55 ± 2.46. It was found that the scores of the participants from the behavioral subdimension of the scale were between 7 and 28, and the mean score was 17.17 ± 3.13. The total score of the participants from the scale was found to vary between 68 and 112, with a mean total score of 81.65

Table 3. Scores of the participants from the attitude scale about the safe use of sharp objects and instruments, and subdimensions (n = 173)

Sub-categories of the scale	Minimum-Maximum scores	Mean ± SD
Cognitive	32-56	42.92 ± 3.73
Affective	15-29	21.55 ± 2.46
Behavioral	7-28	17.17 ± 3.13
Total	68-112	81.65 ± 7.03

Table 4. Comparison of the scores of the participants from the attitude scale and subdimensions based on some variables

Socio-demographical		Cognitive	Affective	Behavioral	Total
Age group	< 35	42.44 ± 3.05	21.58 ± 2.48	16.84 ± 2.83	80.85 ± 5.33
	36-39	43.31 ± 3.69	21.6 ± 2.49	17.00 ± 3.51	81.9 ± 7.37
	40-44	43.22 ± 3.89	21.57 ± 2.29	17.76 ± 3.39	82.54 ± 8.07
	≥ 45	42.83 ± 4.65	21.43 ± 2.75	17.13 ± 2.67	81.4 ± 7.76
	F	0.559	0.030	0.795	0.509
	p value	0.643	0.993	0.498	0.677
Gender	Female	42.63 ± 3.11	21.3 ± 2.5	17.03 ± 2.69	80.96 ± 5.6
	Male	43.36 ± 4.5	21.94 ± 2.37	17.39 ± 3.71	82.7 ± 8.71
	F	-1.258	-1.695	-0.745	-1.595
	p value	0.210	0.092	0.457	0.113
Marital status	Married	43.15±3.9	21.51±2.56	17.15±3.27	81.81±7.46
	Single	42.26±3.09	21.7±2.16	17.23±2.69	81.19±5.58
	F	1.360	-0.438	-0.143	0.501
	p value	0.176	0.662	0.887	0.617
Educational background	Two-year university education or less	42.87 ± 4.63	21.91 ± 2.63	17.6 ± 3.34	82.38 ± 8.54
	Undergraduate	42.62 ± 2.72	21.17 ± 2.34	17.04 ± 2.9	80.83 ± 5.01
	Graduate	43.39 ± 2.94	21.39 ± 2.25	16.59 ± 2.96	81.36 ± 6.1
	F	0.521	1.538	1.526	0.802
	p value	0.595	0.218	0.220	0.450
Profession	Nurse/midwife	42.99 ± 3.31	21.22 ± 2,23	17.27 ± 2.86	81.48 ± 6.11
	Physician	43.31 ± 2.63	21.48 ± 2,47	16.26 ± 2.24	81.05 ± 5.4
	Other	42.49 ± 5.02	22.18 ± 2,74	17.8 ± 3.98	82.47 ± 9.4
	F	0.565	2,424	2,848	0,509
	p value	0.569	0,092	0,061	0,602
Working unit	Policlinic	42.66 ± 3.15	21.15 ± 2.34	16.36 ± 2.98	80.17 ± 5.78
	Emergency unit	43.7 ± 3.44	21.65 ± 2.02	17.19 ± 2.94	82.54 ± 6.47
	Administrative unit	41.43±3.37	21.29 ± 2.24	17.67 ± 4.21	80.38 ± 6.62
	Clinic	42.78 ± 2.84	21.35 ± 2.23	17.09 ± 2.33	81.22 ± 5.35
	Laboratory	43.46 ± 2.93	21.23 ± 2.8	18.38 ± 3.59	83.08 ± 7.47
	Radiological unit	40.7 ± 2.91	22.5 ± 2 .64	16.5 ± 1.65	79.7 ± 3.56
	Surgery room	44.14 ± 3.42	21.93 ± 2.7	16.93 ± 1.9	83.0 ± 5.55
	Other	45.0 ± 9.21	23.50 ± 4.28	20.13 ± 4.36	88.63 ± 17.44
	F	1.935	1.267	1.977	1.948
	p value	0.067	0.270	0.061	0.065
Involving in the night shift at the unit	Yes	43.36 ± 3.86	21.64 ± 2.56	17.3 ± 3.3	82.3 ± 7.56
	No	41.66 ± 3.03	21.3 ± 2.13	16.8 ± 2.57	79.75 ± 4.77
	F	-2.651	-0.809	-0.927	-2.099
	p value	**0.009**	0.419	0.355	**0.037**

Data are shown as mean ± standard deviation.

± 7.03. Lower total mean scores from the scale indicate that healthcare professionals do not use these materials in a safe manner. Higher scores, on the other hand, suggest that the materials are used safely by healthcare professionals.

Table 4 presents a comparison of the scores of the participants from the attitude scale about the safe use of sharp objects and instruments based on the following variables: age, gender, marital status, educational background, occupation, the unit they work at and night shift. Of these variables, the age, gender, marital status, educational background and occupation were found to have no statistically significant difference in the scores of the participants on the subdimensions of cognitive, affective and behavioral as well as on the total score ($p > 0.05$). It is found that the variable of the unit where the participants working athad also no statistically significant difference in the scores of the participants on the subdimensions of cognitive, affective and behavioral as well as on the total score ($p > 0.05$). However, the scores of those participants who had night shifts had statistically significantly higher scores from the cognitive subdimension ($p = 0.009$; $p < 0.01$). Their total score was also found to be statistically higher than those who did not have night shifts ($p = 0.037$; $p < 0.05$).

DISCUSSION

The CDC reported that nearly 5.6 million healthcare staff has a risk of infections contacted with bloodborne [16]. In the study, it was found that 57 (32.9%) participants experienced either injuries caused by sharp objects and instruments and/or contact with blood or body fluid in the last year. It was also found that 18.2% of the healthcare professionals sampled had an injury caused by a sharp object or instrument in the last year (n = 32) (See Table 1). In the study by Omac *et al*. [17], it was found that the 62.7% of the nurses who participated in the study experienced at least one injury caused by a sharp instrument in the last three months. Dikmen *et al*. [9] found that 63.4% of the healthcare professionals (664 people) had injury due to the sharp objects and instruments at least once during their professional life and that 64.4% of them contacted with blood, body fluid and secretions at least once during their professional life. Altıok *et al*. [18] concluded that 79.1% of the healthcare professionals experience injuries caused by sharp instruments and that 60.9% of such injury cases occur due to the contact with an object which became entangled in blood. One of the major causes of injuries is reported to be injector needles [18]. Ottino *et al*. [19] state that most of the injuries occur due to the use of standard needles. Güney *et al*. [20] analyzed the work by healthcare professionals in the emergency unit and found that 105 of the participants had an injury caused by a sharp instrument in the last year (32.2%). Taşçıoğlu [21] concluded that in the last six months, 56.6% of the participants experienced an occupational accident and among these accidents, the most frequent one was the injuries caused by a sharp instrument (43 participants–43.4%). Samancıoğlu *et al*. [22] found that 65.8% of the emergency unit nurses had one or three injury incidents caused by a sharp instrument in the last twelve months. Bush *et al*. [16] concluded that pathogens contaminated through contact with blood occur in the form of percutaneous injuries. It was also reported in the same study that the rate of percutaneous injuries among healthcare staff sampled varies between 74.2% and 92.3%. The findings of the study also indicated that the most frequently injured groups were medical students and nurses. It may be a result of the fact that nurses frequently involve in medical practices. In short, Bush *et al*'s study [16] suggests that there is a close relationship between occupational experience and the rate of injuries. However, the current study does not focus on the correlation between occupational experience and the rate of injuries.

In the present study, the majority of the participants experienced the injuries during taking the medicine from a vial (21.1%, n = 12). It was followed during the case of separating the needle from an injector (15.8%, n = 9) and during the recapping of the needle (8.8%, n = 5) (See Table 1). The related studies similarly indicate that the injury cases occur during the preparation of materials or recapping of needle [23].

In the study, it was also found that the majority of the participants did not report any injury cases (79%) (See Table 2). Of those who reported such incidents, 75.7% were found to report the incident to infection

control nurses (n = 28), 24.3% of these participants reported it to the occupational health and safety unit (n = 9), and 18.9% of them reported the incidents to the unit responsible (n = 7). Samancıoğlu *et al*. [22] concluded thatin the case of injuries caused by sharp instruments, 80% of the nurses sampled reported the incident to infection control nurse. Akkaya *et al*. [24] concluded that 32 of the nurses reported such incidents to the infection control committee.

The total mean score of the participants from the scale was found to vary between 68 and 112 with a mean of 81.65 ± 7.03 (See Table 3). Özyiğit *et al*. [25] found that the total mean score of the participants from the same scale was 84.21 ± 5.23 (min: 68 - max:110). In the study, some of the variables (namely, age, gender, marital status, educational background and occupation) were found to have no statistically significant effect on the scores of the participants from the attitude scale about the safe use of sharp objects and instruments (see Table 4). Their specific occupation did not affect the total scores and subdimension scores in a statistical manner. In the study of Özyiğit *et al*. [25], no significant difference was found in the scores of the nurses, physicians and other healthcare staff who participated from the cognitive section of the scale. However, the behavioral mean scores of the nurses (20.09 ± 2.71) were higher than those of the physicians (19.12 ± 2.08) and cleaning staff members (19.14 ± 2.10). Another interesting finding of the study was that although it was not statistically significant, the scores of the physician's samples from the cognitive subdimension of the scale were higher than those of the other participants, but their scores from the behavioralsubdimension were the lowest. Özyiğit *et al*. [25] similarly concluded that the physicians sampled in their study had the lowest behavioral scores. Therefore, it can be argued that physicians do not pay much attention to the necessary behaviors in using sharp medical instrumentsand that they perceive their working conditionsless risky. Given that, in-service training activities at hospitals mostly address nurses and other auxiliary healthcare staff and it can be stated that physicians have lower levels of awareness about the potential occupational accidents. Therefore, in-service training activities should be attended by all healthcare staff at hospitals.

CONCLUSION

The participants of the study are subject to serious occupational accidents and occupations risks which may negatively affect their health. In the last year, the participants mostly experienced either an injury caused by sharp instruments orcontact with blood. Such occupational accidents were mostly experienced by nurses and midwives. The injuries are experienced during the preparation of materials and the injection needles. Therefore, it is suggested that safe medical instruments should be used to avoid and reduce the potential occupational accidents, that personal protective environment should be provided by the healthcare institutions as well as the safe medical instruments should be easily accessed and that common steps should be taken and strictly followed to avoid the contact with the infection. In the study, it is revealed that not all occupational accidents are reported by the healthcare staff. Therefore, necessary steps should be taken to improve the rate of such reports which should contain the type of injury and the cause of the injury. In order to maintain a systematic reporting, there should be standard procedures.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Authors' Contribution

All of the authors have contributed to the study on conception and design, drafting the article, revising it critically for important intellectual content, and final approval of the version to be published. All authors are in agreement with the content of the manuscript. SÖ = Study design, data collection and preparation manuscript; VÜ = Thesis advisor, Study design and preparation manuscript.

Acknowledgement

We would like to thank all staff who gave their time and made this study possible. We would like to thank Ayca Pamukcu who did statistical analysis.

REFERENCES

1. İnci Eİ, Bilişli Y, Hizay D. [Assessment of notifications by healthcare staff suffering from occupational accidents: case of university hospital]. Health Care Acad J 2016;3:83-8. [Article in Turkish]
2. Salman E, Karahan ZC. [Infection risks for healthcare workers and protection I: infections transmitted by blood and body fluids]. Ankara Üniversitesi Tıp Fakültesi Mecmuası 2014;67:43-9. [Article in Turkish]
3. Goniewicz M, Włoszczak-Szubzda A, Niemcewicz M, Witt M, Marciniak-Niemcewicz A, Jarosz MA. Injuries caused by sharp instruments among healthcare workers -- International and Polish Perspectives. Ann Agric Environ Med 2012;19:523-7.
4. Ministry of Health, Health Statistics 2015. http://www.sagem.gov.tr/dosyalar/SIY_2015_Haber_Bulteni.pdf, Accessed: February 10, 2017.
5. Meydanlıoğlu A. [Health and safety of healthcare workers]. Balıkesir Sağlık Bilimleri Dergisi 2013;2:192-9. [Article in Turkish]
6. Ndejjo R, Musinguzi G, Yu X, Buregyeya E, Musoke D, Wang J-S, et al. Occupational health hazards among healthcare workers in Kampala, Uganda. J Environ Public Health 2015;2015:913741.
7. Andersen LL, Clausen T, Mortensen OS, Burr H, Holtermann A. A prospective cohort study on musculoskeletal risk factors for long-term sickness absence among health care workers in elder care. Int Arch Occup Environ Health 2012;85:615-22.
8. Swetharani K, Vinod KV, Hamide A, Dutta TK, Harichandrakumar KT. Awareness of blood-borne infections and burden of occupational exposures to blood and body fluids among healthcare personnel in a tertiary care teaching hospital. Indian J Occup Environ Med 2016;20:138-43.
9. Dikmen AU, Medeni V, Uslu İ, Aycan S. [Assessment of work accidents in health care workers in a university hospital in Ankara]. Türk Tabibler Birliği Mesleki Sağlık ve Güvenlik Dergisi 2014;14:22-8. [Article in Turkish]
10. Puro V, De Carli G, Cicalini S. European occupational post-exposure prophylaxis study group. European recommendations for the management of healthcare workers occupationally exposed to hepatitis B virus and hepatitis C virus. Euro Surveill 2005;10:260-4.
11. Westermann C, Claudia Peters C, Lisiak B, Lamberti M, Nienhaus A. The prevalence of hepatitis C among healthcare workers: a systematic review and meta-analysis. Occup Environ Med 2015;72:880-8.
12. Ucak A. Saglık personelinin maruz kaldığı iş kazaları ve geri bildirimlerinin değerlendirilmesi. Afyon Kocatepe University Institute of Health Sciences Master Thesis, Afyonkarahisar, 2009.
13. Centers for Disease Control and Prevention. National Institute for Occupational Safety and Health.Guidelines for Protecting the Safety and Health of HealthCare Workers. https://www.cdc.gov/niosh/docs/88-119/pdfs/88-119.pdf Accessed April 17, 2017.
14. [Regulation on the ensuring the safety of patients and employees]. Official Gazette Issue: 27897, 6 April 2011. [Article in Turkish]
15. Uzunbayır N. [An attitude scale towards safe medical device usage of healthcare workers]. Ege University, Graduate School of Health Sciences, Master Thesis, 2009. [Article in Turkish]
16. Bush C, Schmid K, Rupp ME, Watanabe-Galloway S, Wolford B, Sandkovsky U. Blood borne pathogen exposures: difference in reporting rates and individual predictors among healthcare personnel. Am J Infect Control 2017;45:372-6.
17. Omac M, Eğri M, Karaoğlu L. [Evaluation of occupational needle stick - Sharp injuries and status of Hepatitis B immunization on nurses working at Malatya province hospitals]. İnönü Üniversitesi Tıp Fakültesi Dergisi 2010;17:19-25. [Article in Turkish]
18. Altıok M, Kuyurtar F, Karaçorlu S, Ersöz G, Erdoğan S. [Healthcare workers experiences with sharps and needlestick injuries and precautions they took when injuring]. Maltepe Üniversitesi Hemşirelik Bilim ve Sanatı Dergisi 2009;2:70-9. [Article in Turkish]
19. Ottino MC, Argentero A, Argentero PA, Garzaro G, Zotti CM. Needlestick prevention devices: data from hospital surveillance in Piedmont, Italy-comprehensive analysis on needlestick injuries between healthcare workers after the introduction of safety devices. BMJ Open 2019;9:2-10.
20. Güney SB, Köksal O, Durak VA. [The needlestick and sharp injuries among emergency service workers and analysis of prevention methods]. Uludağ Üniversitesi Tıp Fakültesi Dergisi 2017;43:1-5.
21. Taşçıoğlu I. [To fix the risks which arise from work and working environment and the level of nurses' perception of these risks in Lüleburgaz state Hospital and Lüleburgaz 82. Yil State Hospital]. Trakya University, Faculty of Health Science, Master Thesis, Edirne, 2007. [Article in Turkish]
22. Samancıoğlu S, Unlu D, Akyol AD. [The evaluation of needlestick and sharp injuries among intensive care nurses]. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi 2013;16:43-9. [Article in Turkish]
23. Motaarefi H, Mahmoudi H, Mohammadi E, Hasanpour-Dehkordi A. Factors associated with needlestick injuries in healthcare occupations: a systematic review. J Clin Diagn Res 2016;10:IE01-04.
24. Akkaya S, Sengoz G, Pehlivanoğlu F, Özdemir EG, Tek SA. [Evaluation of the survey results concerning sharps injuries]. Klimik Dergisi 2014;27:95-8. [Article in Turkish]
25. Özyiğit F, Küçük A, Altuntaş Ö, Arıkan İ, Kumbasar H, Fener S, et al. [The attitude of healthcare workers to safe use of medical instruments in a training and research hospital]. Med Bull Haseki 2014;52:168-71. [Article in Turkish]

The European Research Journal 2020;6(3):225-231 Original Article

DOI: 10.18621/eurj.486608 *Anesthesiology and Reanimation*

Evaluation of the parental satisfaction of developmentally delayed pediatric patients undergoing dental surgery with the "pediatric anesthesia parent satisfaction (PAPS)" survey

Mehmet Sargın[1], Hatice Toprak[2], Jale Bengi Çelik[1]

[1]*Department of Anesthesiology and Reanimation, Selçuk University School of Medicine, Konya, Turkey*
[2]*Department of Anesthesiology and Reanimation, Konya Training and Research Hospital, Konya, Turkey*

ABSTRACT

Objectives: The aim of the present study was to assess parental satisfaction of developmentally delayed pediatric patients undergoing dental surgery and compare this to satisfaction with anesthesia care for children without developmentally delayed.

Methods: Therefore, two different groups were approached and compared to matching controls. "Pediatric anesthesia parent satisfaction (PAPS)" survey was used to evaluate parental satisfaction in the present study. The PAPS survey was administered to 50 parents of developmentally delayed pediatric patients (Group I) and 30 parents of children without developmentally delayed (Group II). However, due to the shortcomings in the questionnaires, 5 participants from Group I and 4 from Group II were excluded from the study.

Results: In the "Before anesthesia", "After anesthesia", "Hospital team" and "Anesthesia team" parts of survey no statistically significant difference was found between the groups. In the ‘‘Before anesthesia’’ part the lowest score was given in response to Q5 item (The anesthesia team explained to me how my child might feel physically and emotionally after anesthesia and surgery). The mean score of Q5 item was 2.73 ± 1.77 in Group I and 2.36 ± 1.40 in Group II.

Conclusions: In conclusion, it was found that there is no difference between parental satisfaction of children with developmentally delayed and parental satisfaction of developmentally delayed pediatric patients.

Keywords: Parental satisfaction, pediatric, anesthesia, dental surgery, survey

Nowadays, the main purpose of medical procedures is to reduce costs, protect resources and increase patient satisfaction without endangering patient safety [1]. Therefore, patient satisfaction has become an important component of the quality of medical care. Patient-centered outcomes are the primary tool for measuring health service quality and effectiveness [2]. Patient satisfaction improves care quality and communication, resulting in better clinical results [3, 4]. Various patient satisfaction surveys have been developed rapidly in recent years [5-7]. The incentive payments of private insurance companies are shown as the reason for this rapid increase [7, 8]. Based on the rapid progress in information technologies, patients and their relatives have become more important in health care quality and satisfaction and have made

Received: ***November 22, 2018;*** *Accepted:* ***May 14, 2019;*** *Published Online:* ***February 1, 2020***

How to cite this article: *Sargın M, Toprak H, Çelik JB. Evaluation of the parental satisfaction of developmentally delayed pediatric patients undergoing dental surgery with the "pediatric anesthesia parent satisfaction (PAPS)" survey. Eur Res J 2020;6(3):225-231. DOI: 10.18621/eurj.486608*

Address for correspondence: *Mehmet Sargın, MD.,Selçuk University School of Medicine, Department of Anesthesiology and Reanimation, Konya, Turkey. E-mail: mehmet21sargin@yahoo.com*

e-ISSN: 2149-3189

their choices in this direction [8, 9].

Postoperative patient satisfaction is an important measure of hospital care. Because it enables the patient to be evaluated throughout the entire hospitalization period [7, 8]. Children's satisfaction can be difficult to assess or express themselves, so parents' satisfaction in terms of anesthesia can be used as a measure of their satisfaction. Parental satisfaction is closely related to the quality of medical care and communication. Parental satisfaction was evaluated in previous studies [10-12]. The satisfaction rate is closely related to many factors such as accessibility to the physician, communication with the family and emotional state of the family and empathy [13, 14].

Evaluation of patient satisfaction in anesthesia services is mixed. There is very little validated satisfaction scale, and there is a lack of pediatric anesthesia [15]. There are also doubts about the widespread use of these scales. Although there are departments related to anesthesia in various surgical care questionnaires, they do not qualify [16]. Also not approved by ASA. Pediatric Anesthesia Parent Satisfaction (PAPS) aimed to eliminate these deficiencies was developed by Milliken-Glabe *et al*. [17].

The aim of this study was to assess parental satisfaction of developmentally delayed pediatric patients undergoing dental surgery with the "Pediatric anesthesia parent satisfaction (PAPS)" survey and compare this to satisfaction with anesthesia care for children without developmentally delayed.

METHODS

Institutional ethics committee approval and written consent from the parents of each patient was obtained for the study. Inclusion criteria were children aged <16 years, parents able to speak, read and write Turkish, parents willing to participate in this study, and elective procedures under general anesthesia.

"Pediatric anesthesia parent satisfaction (PAPS)" survey was used to evaluate parental satisfaction in the present study. This questionnaire was developed by Milliken-Glabe *et al*. [17] and which contained 15 closed-ended items, one open-ended items. Responses of the survey were recorded using a 5-point Likert scale: 1 (Disagree very much), 2, 3, 4, and 5 (Agree very much). Closed-ended questions consist of 5 parts: "Before anesthesia", "Before and after anesthesia", "After anesthesia", "Hospital team" and "Anesthesia team". While evaluating this Likert type scale, we evaluated the highest value as the highest score because it reflects the best satisfaction.

The PAPS survey was administered to 50 parents of developmentally delayed pediatric patients and 30 parents of children without developmentally delayed undergoing dental surgery in the PACU prior to discharge. They had been informed that their answers would not affect the care given to their children. Parents were asked to answer questions regarding their level of satisfaction. In addition to the questionnaire, parents were also asked to specify their demographic characteristics (Age, gender, education level, monthly income of the family, where the family lived). And also, operation time, nausea and vomiting in PACU, pain score in PACU and shivering in PACU were recorded.

With a 0.65 effect size and 1/2 allocation ratio, (n1/n2) 22/44 subjects were required for an α value of 0.05 and a power of 80%.

Statistical Analysis

Statistical analyses were performed with SPSS 15.0 software (SPSS Institute, Chicago, IL, USA). The comparisons in both groups were carried out using the Student t-test and Pearson Chi-Square test. Parental satisfaction score between the two groups was evaluated using Student t-test. A $p < 0.05$ value was considered statistically significant.

RESULTS

The PAPS survey was administered to 50 parents of developmentally delayed pediatric patients (Group I) and 30 parents of children without developmentally delayed (Group II) however, due to the shortcomings in the questionnaires, 5 participants from Group I and 4 from Group II were excluded from the study.

Patients' demographic, clinical characteristics are summarised in Table 1, and there were no significant differences between the groups regarding patients' gender, operation time, nausea and vomiting in PACU, pain score in PACU and shivering in PACU ($p = 0.844$, $p = 0.269$, $p = 0.444$, $p = 0.170$, and $p = 0.444$, respectively). The mean age of the patients in Group I

Table 1. Patients' demographic, clinical characteristics

	Group I (n = 26)	Group II (n = 45)	*p* value
Age, years	5.92 ± 2.86	11.56 ± 3.81	**< 0.001**[a]
Gender, M/F, n (%)	14 (53.8)/12 (46.2)	23 (51.1)/22 (48.9)	0.844[b]
Height, cm	113.65 ± 17.12	133.16 ± 22.8	**< 0.001**[a]
Weight, kg	21.85 ± 9.13	35.98 ± 16.36	**< 0.001**[a]
Operation time, min	36.15 ± 20.99	41.56 ± 18.88	0.269[a]
Nausea and vomiting in PACU, n	0	1	0.444[b]
Pain score in PACU	2.46 ± 1.27	2.09 ± 0.97	0.170[a]
Shivering in PACU, n	0	1	0.444[b]

Values are given as mean ± standard deviation or n (%). M = Male, F = Female, PACU = Postanesthesia care unit. [a]Student t-test, [b]Pearson Chi-Square test

was 5.92 ± 2.86 years while in Group II it was 11.56 ± 3.81 years (p <0.001). When the height and weight of the patients were compared between the groups, there was a statistically significant difference (p < 0.001 and p < 0.001, respectively). Parents' demographic characteristics are summarised in Table 2. There was a statistically significant difference between the groups when the age of the parents was compared (p < 0.001). However, there were no significant differences between the groups regarding

Table 2. Parents' demographic characteristics

	Group I (n = 26)	Group II (n = 45)	*p* value
Parent age, years	31.23 ± 5.25	37.53 ± 7.10	**< 0.001**[a]
Parent gender, M/F, n (%)	6 (23.1)/20 (76.9)	5 (11.1)/40 (88.9)	0.179[b]
Parent education level, n (%)			0.131[b]
Primary schoo	17 (65.3)	39 (86.6)	
High school	4 (15.4)	5 (11.1)	
University	5 (19.2)	1 (2.2)	
Monthly income of the family (TL), n (%)			0.054[b]
0-1999 TL	11 (42.3)	32 (71.1)	
2000-4999 TL	12 (46.2)	11 (24.4)	
5000 and more	3 (11.5)	2 (4.4)	
Where the family live, n (%)			0.567[b]
City center	24 (92.3)	43 (95.6)	
District	2 (7.7)	2 (4.4)	

Values are given as mean ± standard deviation or n (%). M = Male, F = Female, PACU = Postanesthesia care unit. [a]Student t-test, [b]Pearson Chi-Square test

surveyed gender and education level of the parent, monthly income of the family, and where the family lived ($p = 0.179$, $p = 0.131$, $p = 0.054$, and $p = 0.567$, respectively).

Pediatric anesthesia parent satisfaction survey scores are summarised in Table 3. There were Q1, Q2, Q3 and Q5 items in the "Before anesthesia" part and no statistically significant difference was found between the groups ($p = 0.096$, $p = 0.625$, $p = 0.223$ and $p = 0.329$, respectively). In the ‘‘Before anesthesia’’ part the lowest score was given in response to Q5 item (The anesthesia team explained to me how my child might feel physically and emotionally after anesthesia and surgery). The mean score of Q5 item was 2.73 ± 1.77 in Group I and 2.36 ± 1.40 in Group II ($p = 0.329$).

There were Q6 and Q7 items in the "After anesthesia" part and no statistically significant difference was found between the groups ($p = 0.823$ and $p = 0.344$, respectively). Q4 item was the only item included in the ‘‘Before and after anesthesia’’ part, and there was no statistical difference between the groups ($p = 0.847$). In the "Hospital team" part there were Q9, and Q15 items and no statistically significant difference was found between the groups ($p = 0.168$ and $p = 0.257$, respectively).

There were Q8, Q10, Q11,Q12, Q13, and Q14 items in the "Anesthesia team" part and no statistically significant difference was found between the groups ($p = 0.309$, $p = 0.446$, $p = 0.239$, $p = 0.828$, $p = 0.206$ and $p = 0.960$, respectively). In the "Anesthesia team" part the lowest score was given in response to Q13 item [I know who the anesthesiologist (physician) was and his/her role in my child's care]. The mean score of Q13 item was 2.58 ± 1.15 in Group I and 2.13 ± 1.32 in Group II ($p = 0.206$).

Q16 (Please tell us more about your anesthesia experience) item was open-ended, and 16 parents fill

Table 3. Pediatric anesthesia parent satisfaction survey scores

	Group I (n = 26)	Group II (n = 45)	*p* value
Before anesthesia			
Q1	4.50 ± 0.86	4.13± 0.12	0.096[a]
Q2	4.27 ± 1.11	4.38 ± 0.74	0.625[a]
Q3	3.92 ± 1.26	4.27 ± 1.05	0.223[a]
Q5	2.73 ± 1.77	2.36 ± 1.40	0.329[a]
Before and after anesthesia			
Q4	4.62 ± 0.89	4.58 ± 0.72	0.847[a]
After anesthesia			
Q6	4.23 ± 0.95	4.18 ± 0.96	0.823[a]
Q7	4.58 ± 0.36	4.69 ± 0.79	0.344[a]
Hospital team			
Q9	4.80 ± 0.23	4.80 ± 0.54	0.168[a]
Q15	4.23 ± 0.76	4.44 ± 0.75	0.257[a]
Anesthesia team			
Q8	4.96 ± 0.19	4.84 ± 0.56	0.309[a]
Q10	4.80 ± 0.43	4.80 ± 0.45	0.446[a]
Q11	4.38 ± 1.09	4.64 ± 0.74	0.239[a]
Q12	4.65 ± 0.84	4.69 ± 0.51	0.828[a]
Q13	2.58 ± 1.15	2.13 ± 1.32	0.206[a]
Q14	4.65 ± 0.89	4.64 ± 0.67	0.960[a]

Values are given as mean ± standard deviation. [a]Student t-test.

this part in the Group I and 19 parents fill in the Group II. In Group I, 15 out of 16 parents stated extreme satisfaction statements like "Thank you", "We are very satisfied", while one parent stated that "We could not get enough information before anesthesia". In Group II, all 19 parents used satisfaction statements.

DISCUSSION

In the present study, we have investigated the parental satisfaction of developmentally delayed pediatric patients undergoing dental surgery with the "Pediatric anesthesia parent satisfaction (PAPS)" survey and compare this to satisfaction with anesthesia care for children without developmentally delayed. It has been shown that there are similar characteristics in terms of parents satisfaction. While satisfaction was generally high in both groups, only two items' scores were low. These two items were related to informing parents beforehand by the anesthesia team.

Parents of children with developmental disabilities tend to be well informed about their children's condition and may have high expectations when they arrive at the hospital. Also, it is likely that parents in these two different groups may have differences in informational trends and levels of health professionals.

Patient satisfaction is an important component of the quality of medical care and is used to measure the effectiveness of health care delivery [2]. In pediatric patients, presentation efficiency is mostly evaluated on parental satisfaction. Pediatric anesthesia-related questionnaires have already been performed and are difficult to implement in the routine because of their complexity and length [18]. The PAPS survey is very simple with only 17 questions, and the available parent assessment allows the evaluation of pediatric anesthesia services regardless of the patient's age. Although it was not preferred in our study, the PAPS survey can be applied easily electronically [18-20].

In a study evaluating parental satisfaction of pediatric patients who underwent outpatient surgery, high parental satisfaction was demonstrated similar to our results [21]. However, it was stated that better physical conditions, operation schedules would be made more regularly, and the increase in anesthesia consultations would contribute positively to parental satisfaction.

In a study comparing parental satisfaction in the pediatric sedation unit and operating room, parents reported that the operation room was better informed in comparison to the pediatric sedation unit [22]. Also, it was stated that the operations in the main operating room started at the specified time, while the pediatric sedation unit could be delayed. However, there are no clear statements evaluating the period before and after anesthesia in this study. In our study, parents did not give any feedback on the time of the operation.

In another study evaluating the parental satisfaction of pediatric patients undergoing ambulatory anesthesia, high satisfaction with care before and after anesthesia was noted [23]. Parents need to be more careful about transport and information. While the deficiencies related to preoperative information were revealed in our results, the parents did not mention any disruption related to the transport of the patients.

In a study evaluating the satisfaction of parents with the pediatric surgery patients, Brenn *et al*. stated that the dissatisfaction reported by the parents was independent of the complication rate and was more because of the operational factors such as waiting times [24].

Chan *et al*. found a decrease in the level of anxiety in parents and increased parental satisfaction in their parents' education program [25]. In this training, information was given about the roles of midwives during and after anesthesia.

Also, it was indicated that the anxiety, fear, and trauma during anesthesia induction could be reduced by the necessary parental preparation [26]. The majority of the parents prefer to have broad information before their children's surgery, including possible complications [27].

In the literature, it is suggested that some variables such as parental gender, gender, and age of children and previous surgical experiences have important effects on parental anxiety. It was reported that mothers were more anxious than fathers [28]. It was also stated that the children under one year of age and the parents of children with first surgical experience were more anxious [28]. In our study, there was no patient under one year of age. There was an age difference between the groups. The reason for this difference; the fact that children with developmentally delayed ta in older ages allow dental treatment without

anesthesia is only the developmentally delayed pediatric patients need anesthesia for dental procedures at almost any age. There was no difference in parental gender between the groups, while the majority of the parents were mothers in the present study.

CONCLUSION

In conclusion, it is seen that there is no difference between parental satisfaction of children with developmentally delayed and parental satisfaction of developmentally delayed pediatric patients. In addition, consistent with the literature, it is seen that patients be informed and their parents are outstanding as a common problem all over the world.

Authors' contribution

Conception: MS, HT; Design: MS; Supervision: MS, HT; Fundings: MS, HT; Materials: MS, HT; Data collection and/or processing: MS, HT; Analysis and/or interpretation: MS, JBC; Literature review: MS, JBC; Writting: MS, HT, JBC; Critical review: MS, JBC.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Kassmann BP, Docherty SL, Rice HE, Bailey DE Jr, Schweitzer M. Telephone follow-up for pediatric ambulatory surgery: parent and provider satisfaction. J Pediatr Nurs 2012;27:715-24.
2. Bolus R, Pitts J. Patient satisfaction: the indispensable outcome. Manag Care 1999;8:24-8.
3. Greenfield S, Kaplan S, Ware JE Jr. Expanding patient involvement in care. Effects on patient outcomes. Ann Intern Med 1985;102:520-8.
4. Kaplan SH, Greenfield S, Ware JE Jr. Assessing the effects of physician-patient interactions on the outcomes of chronic disease. Med Care 1989;27(3 Suppl):S110-27.
5. Eagle CJ, Davies JM. Current models of "quality" – an introduction for anesthetists. Can J Anaeth 1993;40:851-62.
6. Darby C, Hays RD, Kletke P. Development and evaluation of the CAHPS Hospital Survey. Health Serv Res 2005;40:1973-6.
7. Giordano LA, Elliot MN, Goldstein E, Lehrman WG, Spencer PA. Development, implementation and public reporting of the HCHAPS survey. Med Care Res Rev 2010;67:27-37.
8. https:// www.cms.gov/ Medicare/ Quality-Initiatives-Patient-Assessment-instruments/ HospitalQualityInits/ HospitalHCAHPS. html. Accessed 1 August, 2015.
9. Hospital Compare. www.hospital-compare.hhs.gov. Accessed 1 August, 2015.
10. Odegard KC, Modest SA, Laussen PC. A survey of parental satisfaction during parent present induction of anaesthesia for children undergoing cardiovascular surgery. Paediatr Anaesth 2002;12:261-6.
11. Matziou V, Boutopoulou B, Chrysostomou A, Vlachioti E, Mantziou T, Petsios K. Parents' satisfaction concerning their child's hospital care. Jpn J Nurs Sci 2011;8:163-73.
12. Ebrahim S, Singh S, Parshuram C. Parental satisfaction, involvement, and presence after pediatric intensive care unit admission. J Crit Care 2013;28:40-5.
13. Fumis RR, Nishimoto IN, Deheinzelin D. Families' interactions with physicians in the intensive care unit: the impact on family's satisfaction. J Crit Care 2008;23:281-6.
14. McCormick MC, Escobar GJ, Zheng Z, Richardson DK. Factors influencing parental satisfaction with neonatal intensive care among the families of moderately premature infants. Pediatrics 2008;121:1111-8.
15. Barnett SF, Alagar RK, Grocott MPW, Giannaria S, Dick JR, Moonesinghe SR. Patient satisfaction measures in anesthesia: qualitative systematic review. Anesthesiology 2013;119:452-78.
16. https://www.facs.org/advocacy/quality/cahps/surgical-care-survey. Accessed 1 August, 2015.
17. Milliken-Glabe SJ, Zuk J, Ziniel SI, Bjur KA, Alvarez M, Szolnoki JM, et al. First steps in validating the pediatric anesthesia parent satisfaction (PAPS) survey. Paediatr Anaesth 2017;27:153-61.
18. Schiff JH, Russ N, Ihringer K. Paediatric Perianesthesia Questionnaire: development and data from eight hospitals across Germany. Br J Anaesth 2011;106:88-95.
19. Odegard KC, Modest SA, Laussen PC. Asurvey of parental satisfaction during parentpresent induction of anaesthesia for children undergoing cardiovascular surgery. Paediatr Anaesth 2002;12:261-6.
20. Iacobucci T, Federico B, Pintus C, de Francisci G. Evaluation of satisfaction level by parents and children following pediatric anesthesia. Pediatr Anesth 2005;15:314-20.
21. Erden IA, Pamuk AG, Ocal T, Aypar U. Parental satisfaction with pediatric day case surgery. Middle East J Anaesthesiol 2006;18:1113-21.
22. Connor MP, Dion GR, Borgman M, Maturo S. The pediatric sedation unit: a prospective analysis of parental satisfaction. Int J Pediatr Otorhinolaryngol 2014;78:2165-8.
23. Boonmak S, Boonmak P, Pothiruk K, Hoontanee N. Parents' satisfaction with pediatric ambulatory anesthesia in northeast of Thailand. J Med Assoc Thai 2009;92:1640-5.
24. Brenn BR, Choudhry DK, Sacks K. Outpatient outcomes and

satisfaction in pediatric population: data from the postoperative phone call. Paediatr Anaesth 2016;26:158-63.
25. Chan CS, Molassiotis A. The effects of an educational programme on the anxiety and satisfaction level of parents having parent present induction and visitation in a postanaesthesia care unit. Paediatr Anaesth 2002;12:131-9.
26. Hannallah FS. Who benefits when parents are present during anaesthesia induction in their children? Can J Anaesth 1994;4:271-5.
27. Kain ZN, Wang SM, Caramico LA, Hofstadter M, Mayes LC. Parental desire for perioperative information and informaed consent: a two-phase study. Anesth Analg 1997;84:299-306.
28. Litman RS, Berger AA, Chhibber A. An evaluation of preoperative anxiety in a population of parents of infants and childrenundergoing ambulatory surgery. Paediatr Anesth 1996;6:443-7.

The European Research Journal 2020;6(3):232-237 Original Article

DOI: 10.18621/eurj.476438 *Internal Medicine*

Evaluation of serum vitamin D levels in premenopausal women with iron deficiency anemia

Eray Atalay[1], Gökhan Bilgehan[2], Pınar Şişman[3], Halil İbrahim Erdoğdu[1]

[1]*Department of Internal Medicine, Kafkas University School of Medicine, Kars, Turkey*
[2]*Department of Internal Medicine, Kulu State Hospital, Konya, Turkey*
[3]*Department of Endocrinology and Metabolism, Medicana Hospital, Bursa, Turkey*

ABSTRACT

Objectives: In recent years, many effects of vitamin D except on bone metabolism have been discovered. Vitamin D contributes to the correction of the anemia by acting on the erythroid precursors in the bone marrow via Vitamin D Receptor and provides the elimination of free radicals and prooxidant substances secondary to iron deficiency due to its antioxidant effect in iron deficiency anemia (IDA).

Methods: A total of 97 female premenopausal women aged 18-44 were included in the study. Fifty patients with hemoglobin levels below 12 mg/dl and iron deficiency were classified as IDA group, and 47 subjects with hemoglobin levels of 12 mg/dl and above were classified as control group. The demographic data and biochemical parameters of all patients included in the study were analyzed.

Results: The vitamin D of the patient group was found to be 7.87 ± 3.63 ng/ml and the vitamin D of the control group was 11.84 ± 6.72 ng/ml. The difference between the groups was statistically significant. There was a positive correlation between serum vitamin D and serum hemoglobin, hematocrit, serum MCH, serum iron level, transferrin saturation index, ferritin.

Conclusions: In the light of the results of our study and other studies in the literature, we think that vitamin D deficiency may be important in patients with IDA and that vitamin D deficiency in these individuals will contribute to the regulation of anemia due to positive effects of vitamin D on both erythropoiesis and hepcidin in IDA are considered. However, larger studies are needed to clarify this issue.

Keywords: Vitamin D, iron deficiency anemia, anemia

Iron, is a vital element and essential for erythropoiesis, oxidative metabolism and cellular immune response. It has important functions in oxygen transport, catalysis of many enzymes in the energy system and the synthesis of deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and protein [1, 2]. As a result of cell metabolism, free radicals and reactive oxygen derivatives are formed. Free radicals show their effects on the cell membrane, organelles and DNA by causing protein, lipid, carbohydrate and DNA oxidation. These free radicals and reactive oxygen derivatives are neutralized by a complex antioxidant system [3]. It is accepted that oxidative stress increases in iron deficiency anemia (IDA) due to both increased oxidant amount and decreased antioxidant enzyme capacity [4]. The production of iron-containing proteins such as cytochrome, myoglobin, catalase and peroxidase is also affected in iron deficiency [5]. It has been shown in

Received: ***October 31, 2018;*** *Accepted:* ***March 16, 2019;*** *Published Online:* ***February 1, 2020***

How to cite this article: *Atalay E, Bilgehan G, Şişman P, Erdoğdu Hİ. Evaluation of serum vitamin D levels in premenopausal women with iron deficiency anemia. Eur Res J 2020;6(3):232-237. DOI: 10.18621/eurj.476438*

Address for correspondence: *Pınar Şişman, MD., Bursa Medicana Hospital, Department of Endocrinology and Metabolism, Bursa, Turkey. E-mail: drpinarsisman@gmail.com*

e-ISSN: 2149-3189

many studies that the activity of enzymes that protect cells against oxidative damage is impaired and thus tissues are exposed to oxidative stress in IDA [2].

In recent years, the determination of vitamin D receptor (VDR) in many tissues has revealed new opinions about the function of this vitamin. Many studies have shown the role of vitamin D deficiency in the formation of autoimmune diseases, inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, diabetes, infectious diseases, many types of cancer and heart diseases [6-8]. It was also determined modulator, antiinflammatory, antioxidant, antidiabetic, antihypertensive and renoprotective effectsof vitamine D [9]. Studies have shown that active vitamin D decreases proliferation and production of immunoglobulin [10] and affects erythropoiesis [11, 12]. Vitamin D levels are hundreds of times higher in the bone marrow compared to plasma and have been shown to be effective in regulating the functions of bone marrow. Red blood cells are prevented from becoming active in vitamin D deficiency [13]. It was also found to directly stimulate erythroid precursors [14]. Vitamin D, due to it's antioxidant and antiinflammatory effect, eliminate free radicals and prooxidant substances as well as through the VDR in the bone marrow contribute to the correction of anemia by acting on erythroid precursors. The aim of this study was to evaluate the effect of vitamin D levels on IDA in premenopausal women.

METHODS

A total of 97 female premenopausal women aged 18-44 were included in the study. Fifty patients with hemoglobin levels below 12 mg/dl and iron deficiency were classified as IDA group, and 47 subjects with hemoglobin levels of 12 mg/dl and above were classified as control group. Ethics Committee approval was obtained from the Ethics Committee of our center on 11.11.2015 and numbered 136. Exclusion criteria in our study; (i) detection of vitamin B12 or folic acid deficiency along with IDA, (ii) usage any iron preparation in the last 6 months before the study, (iii) presence of active infection, rheumatoid arthritis, ankylosing spondylitis, collagen tissue disease, celiac, hypo-hyperthyroidism, hypo-hyperparathyroidism, (iv) usage preparations such as calcium and vitamin D, bisphosphonates, calcitonin, selective estrogen receptor modulators, immunosuppressive drugs, antiepileptics, steroid, (v) presence of bone diseases, cushing syndrome, liver and kidney disease presence of malignancy, malnutrition and malabsorption. In the selection of individuals in the control group; the absence of any additional disease and the absence of IDAwas taken as the criterion. The demographic data and biochemical parameters of all patients included in the study were analyzed.

Complete blood counts were taken to tubes containing ethylenediaminetetraacetic acid (EDTA) and analyzed with Bt pro 2401. Serum AST, ALT, ALP, urea, creatinine, calcium, phosphorus, iron, total iron Binding Capacity (TIBC) levels were determined by the biochemistry analyzer Cobas 6000 C501 (Roche Diagnostics GmbH, Mannheim, Germany). Serum 25-Hydroxyvitamin D (25(OH)D), parathormone, vitamin B12, folic acid, ferritin levels were determined by Cobas e 411 (Roche Diagnostics GmbH, Mannheim, Germany).Body Mass Index (BMI); was calculated by dividing the weight of the patient by the square of his/her height (kg/m^2) by using Quetlet index.

Statistical Analysis

Statistical analyzes were performed using SPSS 22.0 program (SPSS Inc. Chicago, IL).The normal distribution of the variables was tested by Kolmogorov smirnov and the variance equation was tested with the Levene test. Because of the normal distribution of the data, all analyzes were performed using parametric tests. Continuous variables were expressed as mean ± standard deviation and categorical variables as percentage. Independent-Samples t-test was used for numerical variables and chi-square test was used for categorical ones. The relationship between vitamin D and other laboratory values was evaluated by Pearson correlation analysis. In the paired comparisons, the parameters which were statistically significant were included in the multivariate model. Stepwise logistic regression analysis was used to determine the independent risk factors of IDA. A receiver operator characteristic (ROC) curve was used to determine the cut-off value of vitamin D level for IDA. The area under the curve (AUC) was calculated for the accuracy of the test. A $p < 0.05$ was considered significant in all comparisons.

Table 1. Demographic and laboratory datas of the groups

Variables	PatientGroup (n: 50)	Control Group (n: 47)	*p* value
Age (years)	28.80 ± 8.06	28.27 ± 6.53	0.727
BMI (kg/m²)	23.83 ± 3.82	23.64 ± 3.12	0.796
Hg (gr/dl)	10.39 ± 1.09	14.06 ± 0.65	**< 0.001**
Hct (%)	30.63 ± 3.14	41.33 ± 2.13	**< 0,001**
Iron (µg/dl)	28.22 ± 8.98	104.02 ± 30.8	**< 0.001**
TIBC	433.28 ± 59.09	352.43 ± 52.61	**< 0.001**
TSI (%)	6.591 ± 2.32	29.98 ± 9.61	**< 0,001**
Ferritin (ng/ml)	5.95 ± 2.87	36.88 ± 17.93	**< 0.001**
Vitamin D (ng/ml)	7.87 ± 3.63	11.84 ± 6.72	**0.01**

BMI = Body mass index, TSI = Transferrin saturation index, TIBC = Total iron binding capacity

RESULTS

The mean age of the patients included in our study was 28.80 ± 8.06 years in the patient group and 28.27 ± 6.33 years in the control group. There was no statistically significant difference between the groups (p = 0.727) (Table 1). In the statistical analysis of vitamin D levels, the vitamin D level of the patient group was found to be 7.87 ± 3.63 ng/ml and the vitamin D level of the control group was 11.84 ± 6.72 ng/ml. The difference between the groups was statistically significant (p = 0.01) (Fig. 1) (see Table 1).

In the statistical analysis, there was independent correlation between vitamin D level and IDA in logistic regression analysis (B = 1.168, p = 0.02). The cut-off value of vitamin D level 9.12 was 74% sensitive and 40% specific for IDA. In the ROC curve analysis, the AUC value was 0.681 (95% CI = 0.575-0.778, p < 0.02) (Fig. 2).

In our study, the correlation between serum vitamin D level and hemogram and iron parameters was found; There was a positive correlation between serum vitamin D level and serum hemoglobin level (r = 0.393, p < 0.001) between serum vitamin D level and serum hematocrit level (r = 0.419, p < 0.001). And

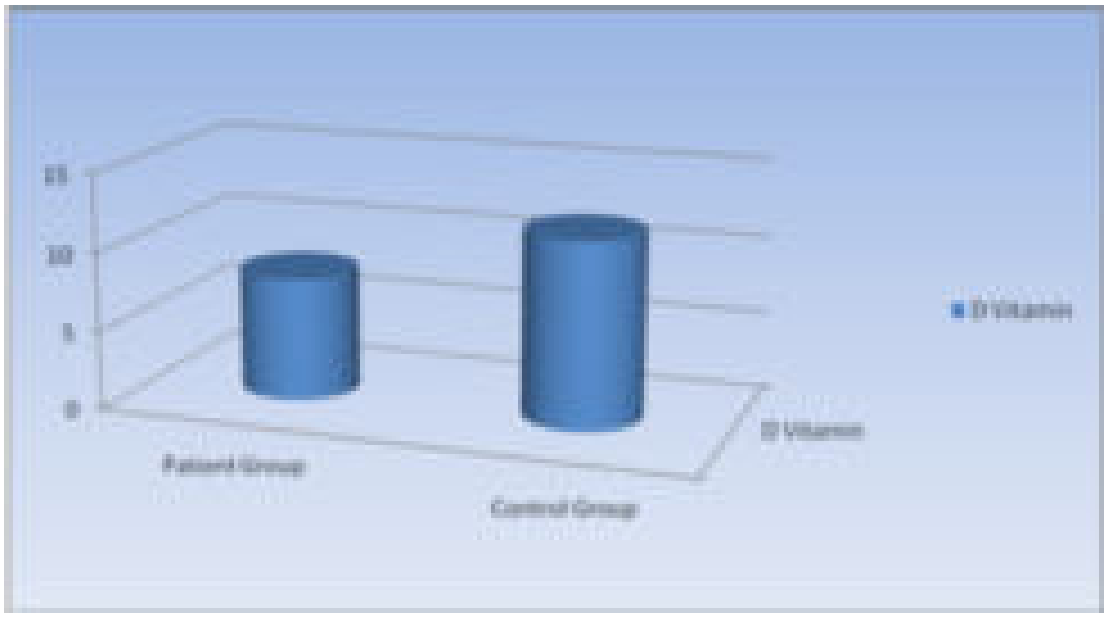


Fig. 1. Vitamin D levels of the groups.

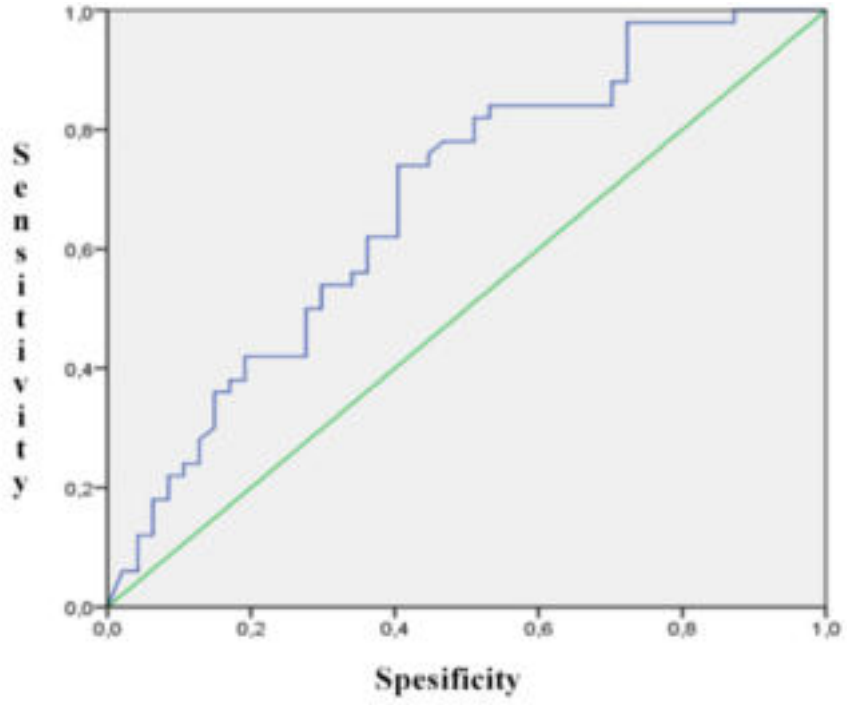


Fig. 2. Logistic regression graph of iron deficiency anemia parameters with vitamin D.

also positive correlation was found between serum vitamin D and serum MCH level (r = 0.298, *p* = 0.003), serum iron level (r = 0.301, p = 0.003), TSI (r = 0.249, *p* = 0,014), serum ferritin level (r = 0.225, *p* = 0.026). But there was a negative correlation between serum vitamin D level and serum RDW level (r = -0,225, *p* = 0.027).

DISCUSSION

Iron is an essential trace element for erythropoiesis, oxidative metabolism and cellular immune response, which has an effect on many systems [2, 15]. In many studies, it has been suggested that IDA has effects on cellular functions, growth, motor and mental development, behavior and cognitive functions, immune system, gastrointestinal system and physical capacity [16]. The main task of erythrocytes is to carry oxygen. Erythrocytes, where oxidative events occur at any time, because they are constantly exposed to oxygen, are equipped with an extremely effective antioxidant defense system.

Unlike other cell types, there are many active antioxidant enzymes such as super oxide dismutase (SOD) and catalase. Decreased enzymatic antioxidant capacity of erythrocytes in IDA has been reported [17-19]. Oxidative stress caused by the decrease in antioxidant enzyme activities in erythrocyte negatively affects oxidant/antioxidant system in serum. Serum antioxidant capacity cannot improve the increased oxidative state and result in increased oxidative stress [20]. In the study performed by Yoo *et al*. [21], oxidative capacity was significantly higher in the IDA group compared with the control group, and total antioxidant and catalase activity were found to be low. After four months of treatment, oxidant, antioxidant and catalase activity were found to be similar with control group [21].

Vitamin D has an immunomodulatory, anti-inflammatory, antioxidant, antidiabetic, antihypertensive and renoprotective positive effects [9]. Active vitamin D has been reported to reduce the production of many inflammatory cytokines (IL-2, IL-6, IL-12, IFN-tı, TNF-α, TNF-ß), [22], to cause cellular proliferation and to reduce the production of immunoglobulin [23].

Decreases in 25(OH)D levels may suppress erythropoiesis in bone marrow by decreasing local calcitriol production. Calcitriol has a direct proliferative effect on erythroid series cells. Endogenous erythropoietin and calcitriol have a

synergistic effect. In addition, calcitriol upregulate erythropoietin receptors in erythroid progenitor cells [24, 25]. In addition, calcitriol has a key role on the immune system and has an inhibitory effect on proinflammatory cytokine expression.Vitamin D is thought to be an inhibitory effect of anemia by its inhibitory effect on specific inflammatory pathways [26]. In the study conducted by Sim *et al*. [27], the probability of developing anemia was 1.86 times higher in people living in the south of the USA with vitamin D deficiency (< 30 ng/ml). But there is no difference according to gender [27]. A total of 2,526 people were included in the study to investigate the relationship between vitamin D deficiency and IDA in Korean girls and boys and adolescents. It was found that the socioeconomic level of patients with IDA was lower, BMI was higher and vitamin D level was lower.As vitamin D levels increased, it was observed that IDA was less frequent but this difference was not found in men [28]. In another study, 158 pregnant women were included in the study. Vitamin D and iron levels were measured at the 25th and 40th weeks of gestation and the risk of IDA was found to be eight times higher in patients with vitamin D levels below 50 nmol/l [29]. Anemia that occurs in patients with vitamin D deficiency was previously attributed to the deficiency of erythropoietin production [30, 31]. However, recent studies also emphasize the role of hepcidin, a hepatic peptide [32]. Hepcidin is a systemic iron-regulating hormone. High plasma hepcidin levels lead to iron sequestration in macrophages, contributing to the pathogenesis of anemia by restricting the flow of iron into the erythropoietic bone marrow.Vitamin D deficiency was found to cause hepcidin upregulation [33].

In our study, the vitamin D levels were 7.87 ± 3.63 ng/ml and 11.84 ± 6.72 ng/ml in the IDA group and control group, respectively. There was a significant difference between the groups (p = 0.01). However, vitamin D level of both groups is deficient. Vitamin D deficiency in most of the participants shows that vitamin D deficiency is a public health problem in our country which should be taken seriously. One of the factors affecting the level of vitamin D is the degree of utilization of sunlight according to the latitude and longitude of the geographic region and also one of the personal factors affecting the vitamin D level is the style of clothing. Clothes constitute an important barrier between UV heat and skin [34]. The fact that most of the participants in our study have a closed clothing style may be another reason why vitamin D levels are so low.

Limitations

Our study has some restrictive aspects. In this cross-sectional, retrospective study, it is not possible to determine the exact pathophysiology of the relationship between vitamin D and IDA.The fact that hepcidin levels were not measured limit the explanation of the pathogenesis of anemia in patients.

CONCLUSION

In our study, although the serum vitamin D level of the patient group and the control group was below the reference value (< 20 ng/ml), the difference between the groups was statistically significant (p = 0.01). There was a positive correlation between serum vitamin D level and serum hemoglobin, hematocrit, MCV, MCH, iron, transferrin saturation index, ferritin level, and negative correlation between serum RDW levels.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Authors' Contribution

All of the authors have contributed to the study on conception and design, drafting the article, revising it critically for important intellectual content, and final approval of the version to be published. All authors are in agreement with the content of the manuscript.

REFERENCES

1. Ganz T, Nemeth E. Iron imports. IV. Hepcidin and regulation of body iron metabolism. Am J Physiol Gastrointest Liver Physiol 2006;290:G199-203.
2. Oner AF, Bay A. [Iron deficiency anemia]. Türkiye Klinikleri

J Pediatr Sci 2005;1:7-15. [Article in Turkish]
3. Diaz-Castro J, Alferez MJ, Lopez-Aliaga I, Nestares T, Granados S, Barrionuevo M, et al. Influence of nutritional iron deficiency anemia on DNA stability and lipid peroxidation in rats. Nutrition 2008;24:1167-73.
4. Aslan M, Horoz M, Kocyigit A, Ozgonul S, Celik H, Celik M, et al. Lymphocyte DNA damage and oxidative stress in patients with iron deficiency anemia. Mutat Res 2006;601:144-9.
5. Coghetto Baccin A, Lauerman Lazzaretti L, Duarte Martins Brandao V, Manfredini V, Peralba MC, Silveira Benfato M. Oxidative stress in older patients with iron deficiency anaemia. J Nutr Health Aging 2009;13:666-70.
6. Hollick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancer and cardiovascular disease. Am J ClinNutr 2004; 80 (6suppl): S1678-88.
7. Ward LM. Vitamin D deficiency in the 21st century: a persistent problem among Canadian infants and mothers. CMAJ 2005;172:769-70.
8. Heaney RP. Long-latency deficiency disease: insights from calcium and vitamin D. Am J Clin Nutr 2003;78:912- 9.
9. Pilz S, Tomaschitz A, Drechsler C, de Boer RA. Vitamin D deficiency and heart disease. Kidney Int Suppl 2011;1:111-5.
10. Chen S, Sims GP, Chen XX, Gu YY, Chen S, Lipsky PE. Modulatory effect of 1,25 dihydroxyvitaminD3 on human B cell differentiation. J Immunol 2007;179:1634-47.
11. Blazsek I, Farabos C, Quittet P, Labat ML, Bringuier AF, Triana BK, et al. Bone marrow stromal cell defects and 1 alpha, 25-dihydroxyvitamin D3 deficiency underlying human myeloid leukemias. Cancer Detect Prev 1996;20:31-42.
12. Reichel H, Koeffler HP, Norman AW. The role of the vitamin D endocrine system in health and disease. N Engl J Med 1989;320:980-91.
13. Norman AW. Minireview: vitamin D receptor: new assignments for an already busy receptor. Endocrinology 2006;147:5542-8.
14. Alon DB, Chaimovitz C, Dvilansky A, Lugassy G, Douvdevani A, Shany S, et al. Novel role of 1, 25 (OH)(2)D(3) in induction of erythroid progenitor cell proliferation. Exp Hematol 2002;30:403-9.
15. Lanzkowsky P. İron-deficiency anemia. Manual of Pediatric Hematology and Oncology 3rd ed., USA: Academic Press, 2000;33-47.
16. Prasad AN, Prasad C. Iron deficiency; non-hematological manifestations. Prog Food Nutr Sci 1991;15:255-83.
17. Ramakrishnan U, Aburto N, McCabe G, Martorell R. Multimicronutrient interventions but not vitamin A or iron interventions alone improve child growth: results of 3 meta-analyses. J Nutr 2004;134:2592-602.
18. Isler M, Delibas N, Guclu M, Gultekin F, Sutcu R, Bahceci M, Kosar A. Superoxide dismutase and glutathione peroxidase in erythrocytes of patients with ıron deficiency anemia: effects of different modalities. Croat Med J 2002;43 16-9.
19. Vural H, Erel Ö, Koçyiğit A, Sabuncu T. [Oxidative stress in erythrocytes of patients with iron deficiency anemia]. Genel Tıp Dergisi 1997;7:77-80. [Article in Turkish]
20. Kumerova A, Lece A, Skesters A, Silova A, Petuhovs V. Anaemia and antioxidant defence of the red blood cells. Mater Med Pol 1998;30:12-5.
21. Yoo JH, Maeng HY, Sun YK, Kim YA, Park DW, Park TS, et al. Oxidative status in iron-deficiency anemia. J Clin Lab Anal 2009;23:319-2.
22. İmazeki I, MatsuzakiJ, Tsuji K, Nishimura T. Immunomodulating effect of vitamin D3 derivaties on type-1 cellular immunity. Biomed Res 2006;27:1-9.
23. Modan M, Halkın H, Karasık A, Lusky A. Elevated serum uric acid: a facet of hyperinsulinemia. Diabetologia 1987;30:713-8.
24. Saab G, Young DO, Gincherman Y, Giles K, Norwood K, Coyne DW. Prevalence of vitamin D deficiency and the safety and effectiveness of monthly ergocalciferol in hemodialysis patients. Nephron Clin Pract 2007;105:c132-8.
25. Aucella F, Scalzulli RP, Gatta G, Vigilante M, Carella AM, Stallone C. Calcitriol increases burst-forming unit-erythroid proliferation in chronic renal failure. A synergistic effect with r-HuEpo. Nephron Clin Pract 2003;95:c121-7.
26. Perlstein TS, Pande R, Berliner N, Vanasse GJ. Prevalence of 25-hydroxyvitamin D deficiency in subgroups of elderly persons with anemia: association with anemia of inflammation. Blood 2011;117:2800-6.
27. Sim JJ, Lac PT, Liu IL, Meguerditchian SO, Kumar VA, Kujubu DA, et al. Vitamin D deficiency and anemia: a cross-sectional study. Ann Hematol 2010;89:447-52.
28. Lee JA, Hwang JS, Hwang IT, Kim DH, Seo J-H, Lim JS. Low vitamin D levels are associated with both iron deficiency and anemia in children and adolescents. Pediatr Hematol Oncol 2015;32:2:99-108.
29. Thomas CE, Guillet R, Queenan RA. Vitamin D status is inversely associated with anemia and serumerythropoietin during pregnancy. Am J Clin Nutr 2015;102:1088-95.
30. Meguro S, Tomita M, Katsuki T, Kato K, Oh H, Ainai A, et al. Plasma 25-hydroxyvitamin d is independently associated with hemoglobin concentration in male subjects with type 2 diabetes mellitus. Int J Endocrinol 2011;2011:362981.
31. Zittermann A, Jungvogel A, Prokop S, Kuhn J, Dreier J, Fuchs U, et al. Vitamin D deficiency is an independent predictor of anemia in end-stage heart failure. Clin Res Cardiol 2011;100:781-8.
32. Ganz T, Nemeth E. Hepcidin and iron homeostasis. Biochim Biophys Acta 2012;1823:1434-43.
33. Carvalho C, Isakova T, Collerone G, et al. Hepcidin and disordered mineral metabolism in chronic kidney disease. Clin Nephrol 2011;76:90-8.
34. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81.

The European Research Journal 2020;6(3):238-247 Original Article

DOI: 10.18621/eurj.586551 Pscyhiatry

The effect of electroconvulsive therapy on hematologic inflammatory markers in schizophrenia in association with type of antipsychotic medication

Sinay Önen, İbrahim Taymur

Department of Pscyhiatry, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

ABSTRACT

Objectives: In recent years there has been an increased interest on the role of inflammation in the pathophysiology of schizophrenia and a search for readily applicable prognostic markers. The impact of electroconvulsive therapy (ECT) on inflammatory function in schizophrenia is still unclear. The aim of this retrospective study is to compare pre- and post-ECT values of red cell distribution width (RDW), mean platelet volume (MPV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) which are considered to be inflammatory markers, and to discuss the findings in context of neuroinflammatory ethiology of schizophrenia.

Methods: Inpatient files were reviewed via complete blood count (CBC), sociodemographic and clinical characteristics (e.g. gender, age, Body Mass Index (BMI), type of psychotropic medication). A total of 58 schizophrenic patients who underwent ECT were were compared in terms of pre- and post-ECT values of RDW, MPV, MCH, MCHC, NLR and PLR in association with type of psychotropic medication.

Results: It was found that MPV, RDW, MCH and MCHC levels significantly decreased after ECT ($p < 0.05$), but no significant difference was found in terms of NLR and PLR ($p > 0.05$). When compared according to the type of psychotropic medication during ECT, MPV and MCHC were decreased after ECT in both typicaland atypical antipsychoticintervention groups ($p < 0.05$). ECT-related inflammatory marker changes were more likely to be associated with atypical antipsychotic medication use during ECT.

Conclusions: Our results indicate that recurrent ECT sessions caused a change in the function of the immune system which might be considered to explain the therapeutic effects of ECT in schizophrenia.

Keywords: Electroconvulsive therapy, schizophrenia, inflammatory markers, antipsychotic medication, immune system

Schizophrenia is a severe, complex and multifactorial disorder with well-defined symptoms and a lifelong course causing disability. Increasing evidence suggests that immunological and inflammatory mechanisms play important roles in the pathophysiology of schizophrenia. Various immune alterations, such as increased frequency of activated lymphocytes [1] and abnormal levels of inflammatory cytokines [2, 3] have been observed in schizophrenic patients. Previous studies have demonstrated an association between elevated plasma inflammatory biomarkers and increased risk of schizophrenia [4, 5]. It had been suggested that the relationship between the long duration of disease, therapy resistance and high pro-inflammatory cy-

Received: ***July 3, 2019;*** *Accepted:* ***July 24, 2019;*** *Published Online:* ***February 15, 2020***

How to cite this article: *Önen S, Taymur İ. The effect of electroconvulsive therapy on hematologic inflammatory markers in schizophrenia in association with type of antipsychotic medication. Eur Res J 2020;6(3):238-247. DOI: 10.18621/eurj.586551*

Address for correspondence: *Sinan Önen, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Psychiatry, Mimar Sinan Mh., Emniyet Cd., 16310 Yıldırım, Bursa, Turkey. E-mail: sinayonen@hotmail.com, Fax: +90 224 366 0416*

e-ISSN: 2149-3189

tokine levels indicatedistinct immune processes might be taking place in different stages of schizophrenia [6]. Previous researches which demonstrated that mean platelet volume, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and red blood cell distribution width are correlated with inflammation in chronic diseases (such as cardiovascular diseases, chronic nephropathies, neoplasms, cerebrovascular diseases and autoimmune diseases), and that they may have valuable potential to evaluate the inflammation in these diseases [7-9]; the relationship between these hematologic parameters and immune dysfunction in schizophrenia is still unclear.

The neutrophil-to-lymphocyte ratio (NLR) has been suggested as a new indicator of low-grade inflammation and a predictor of clinical outcomes in neuroimmune disorders [10, 11]. NLR is previously been studied in major depressive disorder and bipolar disorder and higher NLR levels are detected to be correlated with the severity of MDD which is presented as evidence supporting the inflammatory hypothesis of MDD [12-15]. Cytokine abnormalities and other markers of immune dysfunction were severally identified in schizophrenic patients; but any credible correlation could not be demonstrated between the magnitude of the inflammatory process and the severity of schizophrenia [16]. Previous findings of limited number of studies demonstratedelevated NLR levels in non-obese patients with schizophrenia individuals and a statistically significant positive relationship between PANSS total scores with NLR [17, 18]. Also, platelet-to-lymphocyte ratio (PLR) is thought to be better than NLR for determining the severity of inflammation [19].

Electroconvulsive therapy (ECT), a procedure which provide faster therapeutic effects, is used for managing the patients with psychiatric disorders, such as major depressive disorder and refractory psychiatric disorders, in acute critical conditions, such as suicidal attempt or severe mania [20, 21]. Despite this range of action, the mechanisms by which ECT exerts its beneficial effects remain largely unknown. In a recent study of Kruse *et al*. [22], the levels of CRP, Interleukin-6 (IL-6), Interleukin-8 (IL-8) and tumor necrosis factor alpha (TNF-α)in 29 patients with treatment resistant depression were compared before ECT treatment and after second session of ECT; and the researchers suggested that acute changes in IL-6 and CRP had not been related to the alteration of depressive symptom severity over the course of ECT. Recently, Asoğlu *et al*. [23] investigated the effects of ECT on hematological parameters and reported a significant increase in MCH and no difference in MCHC, MPV and RDW after repetitive ECT in 25 patients diagnosed with schizophrenia, bipolar disorder and unipolar depression. There is compelling evidence that ECT is closely related to an enhanced innate neuroinflammatory as well as hematogenous immune response. For this reason, it is clear that studies to be done in this area may contribute to explain the mechanisms of ECT's therapeutic effect.

The aim of this retrospective study was to compare hematologic inflammatory markers (NLR, PLR, MPV, RDW, MCH and MCHC), before and after ECT, which is considered to have mediating roles on the therapeutic effects of ECT; and to discuss in context of neuroinflammatory ethiology of schizophrenia in the light of recent studies.

METHODS

Study population

This retrospective study was conducted at Bursa Yüksek İhtisas Training and Research Hospital Psychiatric Inpatient Unit. The study protocol was approved by local Ethics Committee (approval number: 2011-KAEK-25 2018/06-09). Data regarding age, gender, duration of disease, psychiatric diagnosis, indication of ECT, treatment status, type of psychotropic medication before and during hospitalization were collected from the hospital records. A total of 159 patients who had been hospitalized and had been applied ECT between April 2016 and June 2018 were recruited. Ninety-five patients, between 18 and 65 years of age, diagnosed with 'Schizophrenia Spectrum and Other Psychotic Disorders' according to DSM-5 criteria and underwent ECT during hospitalization were included in the study. All inpatient files were reviewed via complete blood count (CBC), sociodemographic and clinical characteristics such as gender, age, body mass index (BMI), duration of disease, previous history of medication, accompanying physical disease (hematological, cardiovascular, liver, rheumatic, etc.). Patients receiving any anti-inflammatory treatment

(non-steroid anti-inflammatory drug, corticosteroid or other anti-inflammatory drug) and having a history of coronary artery disease/myocardial infarction/heart valve disease, pulmonary disease, rheumatic disease, liver disease, neurological deficit, mental retardation, autism, iron deficiency anemia, bone marrow disease, kidney disease, alcohol and substance use, antiplatelet-anticoagulant drug use, clozapine use and also morbid obesity, pregnancy and acute infection during hospitalization period were excluded due to the risk of these affecting blood values in association with inflammation. Thus, 16 patients were excluded from the study because of the above comorbid conditions. Twentyone patients, whose post-ECT CBC results had not been available in the files, were also excluded from the study.

Data collection

Thus, a total of 58 schizophrenic patients (27 females and 31 males) were enrolled in the study. All patients had been initiated on psychotropic medication on the admission, which had not been altered during ECT procedure. Antipsychotic prescription data before hospitalization and during ECT intervention were also noted; antipsychotic prescription was further coded as typical (TAP), atypical (AAP) and combined typical-atypical (CAP) to examine for differences in hematologic values.

The patients underwent ECT procedure with a MECTA spECTrum 5000 ECT device, 3 times a week. The effective duration of seizure was determined to be at least 20 seconds. ECT was administered in the morning after an overnight fasting. Moreover, intravenous propofol and rocuronium bromide were administered to all patients in order to induce anesthesia and muscle relaxation. Blood samples being taken the day before the first session of ECT (pre-ECT) and the day after the 7th session of ECT (post-ECT) were extracted from the laboratory files to exclude bias due to different number of ECT sessions. The following parameters were reviewed from the inpatient laboratory files for all the subjects: Red cell distribution width (RDW), mean platelet volume (MPV), mean cell hemoglobin (MCH) and mean cell hemoglobin concentration (MCHC). The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The platelet-to-lymphocyte ratio (PLR) was calculated by dividing the absolute platelet count by the absolute lymphocyte count.

Statistical Analysis

Statistical Package for Social Sciences (SPSS v22, Chicago, IL, U.S.A.) programme for Windows was used. Descriptive parameters are expressed as mean, standard deviation or percentage. After performing Kolmogorov-Smirnov test the distribution normality of the quantitative variables, independent t-test was used for the normally distributed variables and Kruskal-Wallis and Wilcoxon test was used for the non-normally distributed variables. The significance level was set as $p < 0.05$.

RESULTS

A total of 58 schizophrenic patients (27 females and 31 males) were evaluated in this study. The mean age of the study group was 39.43 ± 10.43 years. The mean duration of disease was 12.98 ± 8.51 years. Of the 58 patients, 44.8% of them (n = 26) had been

Table 1. Demographic characteristics of the schizophrenic patients (n = 58)

Characteristics	Data
Age (years)	39.43 ± 10.43
Duration of disease (years)	12.98 ± 8.51
BMI (kg/m^2)	26.96 ± 3.73
Gender	
Female	27 (%46.6)
Male	31 (%53.4)
Regular psychotropic medication before hospitalization	
Yes	26 (44.8%)
No	32 (55.2%)
Indication of ECT	
Treatment resistance	42 (72.4%)
Refusal of oral intake	6 (10.3%)
Severe agitation	4 (6.9%)
Suicidal ideation	3 (5.2%)
Catatonic symptoms	3 (5.2%)

Data are shown as as mean ± standart deviation or n (%). BMI = Body mass index, ECT = Electroconvulsive therapy

Table 2. Comparison of pre-ECT and post-ECT of hematological inflammatory markers

		Mean ± SD	*p value*
PLR	Pre-ECT	116.40 ± 47.36	0.421
	Post-ECT	119.46 ± 41.54	
NLR	Pre-ECT	2.50 ± 1.11	0.769
	Post-ECT	2.72 ± 1.70	
MPV (fL)	Pre-ECT	8.51 ± 0.87	0.000**
	Post-ECT	8.04 ± 0.81	
RDW (%)	Pre-ECT	13.40 ± 1.43	0.004*
	Post-ECT	13.01 ± 1.10	
MCH (pg)	Pre-ECT	28.79 ± 2.07	0.031*
	Post-ECT	28.48 ± 1.69	
MCHC (g/dL)	Pre-ECT	33.28 ± 0.74	0.003*
	Post-ECT	33.03 ± 0.82	

Wilcoxon Signed Rank Test was used. ECT = Electroconvulsive therapy, Pre-ECT = Before electroconvulsive therapy, Post-ECT = After electroconvulsive therapy, PLR = Platelet-to-lymphocyte ratio, NLR = Neutrophil-to-lymphocyte ratio, MPV = Mean platelet volume, RDW = Red cell distribution width, MCH = Mean cell hemoglobin, MCHC = Mean cell hemoglobin concentration, SD: standard deviation

receiving regular psychotropic medication before hospitalization. Of these 26 patients, 10 were having typical (TAP), 15 were having atypical (AAP), 9 were having combined typical and atypical antipsychotic (CAP) medication. None of the patients were using clozapine before hospitalization. According to ECT indications; 72.4% (n = 42) of the patients were underwent ECT for treatment resistance; 10.3% (n = 6) for refusal of oral intake; 6.9% (n = 4) for severe agitation, 5.2% (n = 3) for suicidal ideation and 5.2% (n = 3) for catatonic symptoms. The mean BMI of the study group was 26.96 ± 3.73 kg/m2 on the admission. Socio-demographic and clinical characteristics of the patient group are given in Table 1. According to the comparison of inflammatory markers; there were statistically significant difference between pre-ECT and post-ECT measures of MPV, RDW, MCH and MCHC ($p < 0.001$, $p = 0.004$, $p = 0.031$ and $p = 0.003$, respectively); but no significant difference was found in terms of NLR and PLR ($p = 0.769$ and $p = 0.421$,

Table 3. Inflammatory markers according to type of psychotropic medication before ECT

	TAP (n = 10)	AAP (n = 15)	CAP (n = 9)	*p value*
PLR	113.15 ± 42.75	126.59 ± 58.2	112.47 ± 20.33	0.83
NLR	2.16 ± 0.74	2.78 ± 1.41	2.56 ± 0.77	0.47
MPV (fL)	7.54 ± 0.58	9.30 ± 0.49	8.16 ± 0.48	0.000**
RDW (%)	13.58 ± 1.58	13.62 ± 1.22	13.77 ± 2.01	0.91
MCH (pg)	28.99 ± 1.59	28.42 ± 3.08	27.82 ± 1.88	0.38
MCHC (g/dL)	33.23 ± 0.47	33.02 ± 0.89	33.23 ± 0.84	0.80

Data are shown as mean ± standart deviation. Kruskal Wallis Test was used. TAP = typical antipsychotic, AAP = atypical antipsychotic, CAP = combinedtypical and atypical antipsychotic, PLR = platelet-to-lymphocyte ratio, NLR = neutrophil-to-lymphocyte ratio, MPV = mean platelet volume, RDW = red cell distribution width, MCH = mean cell hemoglobin, MCHC = mean cell hemoglobin concentration, ECT = electroconvulsive therapy

Table 4. Inflammatory markers before and after ECT procedure according to type of psychotropic medication during hospitalization

		TAP	*p value*	AAP	*p value*
PLR	Pre-ECT	108.69 ± 36.78	0.411	124.66 ± 56.08	0.716
	Post-ECT	114.47 ± 37.47		124.81 ± 45.57	
NLR	Pre-ECT	2.37 ± 0.91	0.400	2.62 ± 1.30	0.665
	Post-ECT	2.88 ± 2.01		2.55 ± 1.30	
MPV (fL)	Pre-ECT	8.26 ± 0.94	**< 0.001**	8.77 ± 0.70	**< 0.001**
	Post-ECT	7.96 ± 0.96		8.12 ± 0.62	
RDW (%)	Pre-ECT	13.43 ± 1.37	0.120	13.37 ± 1.52	0.114
	Post-ECT	12.94 ± 0.90		13.10 ± 1.30	
MCH (pg)	Pre-ECT	28.74 ± 2.43	0.420	28.84 ± 1.64	0.367
	Post-ECT	28.32 ± 1.81		28.66 ± 1.57	
MCHC (g/dL)	Pre-ECT	33.34 ± 0.85	**0.031**	33.23 ± 0.62	**0.032**
	Post-ECT	33.02 ± 0.89		33.04 ± 0.75	

Data are shown as mean ± standart deviation. Wilcoxon Signed Rank Test was used. TAP = typical antipsychotic, AAP = atypical antipsychotic, ECT = electroconvulsive therapy, Pre-ECT = Before electroconvulsive therapy, Post-ECT = After electroconvulsive therapy, PLR = platelet-to-lymphocyte ratio, NLR= neutrophil-to-lymphocyte ratio, MPV = mean platelet volume, RDW = red cell distribution width, MCH = mean cell hemoglobin, MCHC = mean cell hemoglobin concentration

respectively). It was found that MPV, RDW, MCH and MCHC levels significantly decreased after 7 sessions of ECT (Table 2).

NLR, PLR, MPV, RDW, MCH and MCHC values were compared according to the type of psychotropic medication before hospitalization. Only MPV was found to be significantly different between three groups (TAP, AAP and CAP) ($p < 0.001$).The mean MPV was 7.54 ± 0.58 in patients using TAP (n = 10); 9.3 ± 0.49 in patients using AAP (n = 15) and 8.16 ± 0.48 in patients using CAP (n = 9) (Table 3).

The study parameters were also compared according to the type of psychotropic medication during ECT intervention. Of the total 58 patients, 30 of them was initiated on TAP and 25 of them was initiated on AAP (except for clozapine) on the admission; which had not been altered during ECT procedure. None of the patients underwent combined antipsychotic medication during ECT. There were statistically significant difference between pre-ECT and post-ECT values of MPV and MCHC in the both TAP ($p < 0.001$ and p = 0.031, respectively) and AAP groups ($p < 0.001$ and $p = 0.032$, respectively). Both MPV and MCHC were decreased after ECT in both medication groups. No significant difference was found in terms of NLR, PLR, RDW and MCH values in both groups (Table 4).

Since MPV changes before and after ECT were significant in both atypical and typical antipsychotic use during ECT and MPV was normally distributed, Independent t-test was done to examine which MPV change is more significant between the different

Table 5. Change in MPV according to type of psychotropic medication during ECT procedure

MPV change	Mean ± SD	Mean difference	*p value*	*df*	*t*	95% CI	
						Lower	Upper
TAP (%)	3.57 ± 4.68	-3.763	**0.004**	56	-2.998	-6.278	-1.248
AAP (%)	7.33 ± 4.87						

Independent t-test was used. TAP = typical antipsychotic, AAP = atypical antipsychotic, MPV = mean platelet volume, ECT = electroconvulsive therapy, SD = standard deviation, CI = confident interval,

antipsychotic types. Mean MPV change was 3.57 ± 4.68 % in TAP group and 7.33 ± 4.87 % in AAP group (t = -2.998, df = 56, p = 0.004) (Table 5).

DISCUSSION

To the best of our knowledge, this is the first study examining the effects of ECT on hematologic inflammatory markers as NLR, PLR, MPV, RDW, MCH and MCHC with regard to its anti-inflammatory effects in schizophrenia. The present study mainly suggested that MPV, RDW, MCH and MCHC were decreased but NLR and PLR did not differ after ECT. Also, it is proposed that the mean MPV values differ in schizophrenicpatients according to the type of medication. In contrast, MPV and MCHC were found to be differed after ECT independently of type of antipsychotic medication.

Animal studies have demonstrated that electroconvulsive seizures induce several changes in neurotrophin and immune signaling, both in the central nervous system (CNS)and in peripheral tissues. Fluitman *et al*. [24] showed that acute ECT (15-30 min.after the electrostimulus) induces a leukocytosis in MDD patients, driven by significantincreases in absolute numbers of granulocytes, monocytes and natural killer cells. A similar leukocyte pattern of polymorphonuclear leukocytosis and relative lymphopeniawas observed 2 hour after a single ECT in a previous study[25].

The abnormalities of the immune system seen in schizophrenia and related psychosis are varied and overlapping, and involve many immune components [26]. Thus, many current studies have inadequately accounted for confounding factors such as body mass, smoking, and medication to fully understand the role of inflammation and immunity in neuropsychiatric disorders. In this study we also evaluated some factors such as duration of disease and type of psychotrop medication before and during ECT intervention to exclude partially their confounding effects.

It has been reported that obesity is associated with a low-grade inflammatory process in the white adipose tissue (WAT) [27, 28]. Increased mass of adipose tissue simultaneously activates the inflammatory process in WAT itself, in the liver and in immune cells [29]. In our study the mean BMI of the schizophrenia group was less than obesity range (< 30 kg/m^2) on the admission and thus, the confounding effect of obesity on inflammatory changes was ensured.

A meta-analysis of 26 cross-sectional or longitudinal studies demonstrated that increased levels of C-reactive protein (CRP) in schizophrenic patients was parallel to the severity of positive symptoms but not associated with the initiation of antipsychotic medication; and the researchers suggested that CRP might be a marker of systemic low-grade inflammation [30]. The NLR can be derived from the white blood cell count, and is inexpensive, replicable and also it has been found to be significantly correlated with CRP [31]. It has been suggested as a new indicator of low-grade inflammation and a predictor of clinical outcomes inneuroimmune disorders [10, 11]. Previously, NLR is found to be higher in patients with MDD, bipolar disorder and schizophrenia[14, 17, 32-34]. Özdin *et al*. [14] have shown that PLR values like NLR are higher in schizophrenia patients than healthy controls and bipolar disorder patients, and authors have suggested that the sefindings support the imflammatory hypothesis of schizophrenia and bipolar disorder. However, to date one study has been encountered in the literature investigating the effect of ECT on NLR and in this study it is noted that no significant difference was found in NLR after repeated ECT treatments in 61 patients with schizophrenia, bipolar disorder and depression [35]. The authors argued that the use of psychotropic drugs has not been evaluated and the few number of patients in the subgroups according to the diagnosis may have affected the results of the study. Unlike previous studies, the type of antipsychotic treatment before hospitalization and during ECT was also assessed in our study. Our results showed that antipsychotic treatment both before and during ECT treatment did not cause any significant changes in NLR after ECT intervention. Some previous data suggest that cytokine levels, including IL-6, are associated with severity and duration of schizophrenia and antipsychotic therapy [26, 36, 37].As the vast majority of patients indication of ECT were treatment resistance and the mean duration of disease was 12.98 ± 8.51 years; so the difficulty of suppressing the inflammatory response by somatic therapies in patients with long duration of schizophrenia and treatment-resistance might be the

reason why NLR and PLR did not altered with ECT in our study.

Wysokinski and Szczepocka [38] examined 1243 patients with schizophrenia and showed a significantly lower PLT count and significantly higher MPV value compared with bipolar disorder and unipolar depressive patients. In a study of Lee *et al*. [39], which was carried out with 100 patients who were initiated on clozapine, the researchers demonstrated higher MPV in patients with schizophrenia, which was unaltered after 1 year of clozapine treatment. Except for the recent study of Asoğlu *et al*. [23], that could not found any significant difference between pre- and post-ECT MPV values in schizophrenic patients, there were no studies evaluating MPV levels in patients underwent ECT in the literature. Our results demonstrated that mean MPV was higher in patients using atypical antipsychotic medication than typical antipsychotic medication on the admission. When compared according to the type of antipsychotic drug used during ECT, MPV was found to be decreased after ECT in patients receiving both typical and atypical antipsychotic treatment in our study. Furthermore, univariate analysis showed that MPV was reduced by 7.33% in patients underwent atypical antipsychotic medication, while it was reduced by 3.57% in patients underwent typical antipsychotic medication during ECT. Considering the fact that the mean MPV values were higher in patients using atypicalantipsychotics before hospitalization and more MPV reduction was observed in patient sunder went atypical antipsychotic medication after ECT, it can be concluded that ECT-related inflammatory marker changes were more likely to be associated with atypical antipsychotic medication use. We suppose that this is one of the most important finding that differ our study from previous studies.

The relationship between inflammation and anemia in some disease is well described and it has been shown that inflammation enforce both direct and indirect effects on erythropoiesis [40]. Ayyildiz *et al*. [41] found higher RDW in 518 schizophrenic patients than healthy controls in their retrospective study and suggested that RDW might be a helpful diagnostic and prognostic marker of schizophrenia with potential utility in risk estimation and treatment monitoring. Another study with a smaller sample comparing MPV, RDW and vitamin B12 levels in schizophrenic patients and healthy controls claimed that higher RDW and MPV is associated with the inflammatory hypothesis of schizophrenia [42]. According to our study results, like MPV, RDW is also significantly decreased after ECT.

Huang and Hu [43] found decreased levels of MCHC in acute myocardial infarction (AMI) and speculated that similar to RDW, MCHC can be regarded asan inflammatory marker and thus can affect the prognosis after AMI. Ayyildiz *et al*. [41] determined higher MCH and lower MCHC in schizophrenic patients compared to healthy controls.When the literature was reviewed, only one study could be found assessing hematologic differences in schizophrenic patients after ECT. In the same study Asoglu *et al*. [23] reported a significant increase in MCH and no difference in MCHC, MPV and RDW after repetitive ECT in 25 patients diagnosed with schizophrenia, bipolar disorder and unipolar depression. In our study we determined a significant decrease in both MCHC and MCH after ECT, which are inconsistent with the previous relatively smaller sample sized study findings. It can be asserted that our findings are more representative due to the higher number of schizophrenic patients included. There was no difference in MCH and MCHC according to the type of medication before hospitalization. But when all patients were grouped due to their type of medication during ECT, only MCHC showed significant change between pre- and post-ECT measures. It can be speculated that MCHC might be considered as a better indicator of inflammatory response than MCH according to our results.

For a long time it has been known that antipsychotic drugs have immunmodulatory effects [44]. It has been asserted that antipsychotic agents might exert varying effects on immune system mediated by their effect on weight gain and increased adiposity [44]. Previous studies showed that both atypical and typical antipsychotic agents stimulate the production of anti-inflammatory cytokines and suppress the production of pro-inflammatory cytokines [45]. Antipsychotic-naive first episode psychosis and acute psychotic relapse are also found to be associated with increased serum pro-inflammatory cytokine levels and decreased anti-inflammatory cytokine levels, which are returned

to previous serum concentrations after remission of symptoms with antipsychotic treatment [36, 46]. Semiz *et al*. [47] ascertained that MPV levels are influenced by both atypical antipsychotics and schizophrenia itself. According to our findings, only MPV and MCHC values were decreased after ECT in both groups of schizophrenic patients having TAP or AAP treatment, but the mean MPV change was more in AAP group. Thus, it can be speculated that ECT may have anti-inflammatory effects by decreasing MPV levels and this effect is more prominent in patients having atypical antipsychotic treatment.

Propofol is one of the most widely used, safe intravenous anesthetic agent with minimal side effects [48] which has been shown to have anti-inflammatory effects by inhibiting neutrophil functions and the release of pro-inflammatory cytokines [49, 50]. In the literature, no evidence could be found investigating the impact of rocuronium bromide on inflammatory markers. Although there are some data on the short-term anti-inflammatory effects of propofol [51], we consider that the evaluation of hematologic inflammatory parameters a day after the last session of ECT anesthesia provide support toexclude the confounding anti-inflammatory effects of propofol on our hematological variables.

Our study has some strengths but as well as a number of limitations. The most important limitation of this study was the retrospective file screening design and therefore the relation with the clinical response could not be evaluated. CRP was not routinely evaluated before ECT; so, we could not be able to assess CRP levels due to the retrospective design of the study. The fact that chlorpromazine equivalent antipsychotic drug doses were not specified is another limitation of our study. In addition, pre-ECT hematologic parameters of patients were not compared with a healthy control group. Another limitation is that accompanying depressive symptoms, which might be an important potential confounder on either ECT and inflammation, and the severity of psychotic symptoms before and after ECT was not measured with clinical evaluation scales.

Although there are small sample studies evaluating some inflammatory markers in patients with major depression, bipolar disorder and schizophrenia who had undergone ECT [22, 23], our study is the first in the literature that extensively handle the effect of ECT on hematologic inflammatory markers in patients with schizophrenia: (1) The evaluation of a wide range of indications for ECT, (2) the fact that only schizophrenic patients were included in this study, (3) the assesment of type of psychotropic drug use before and during ECT, (4) exclusion of risk factors that affect hematologic parameters (like clozapine use and obesity), and (5) the fact that pre- and post-ECT blood samples have been collected within certain time, are the strengths of this study. We suggest that the larger sample size, evaluation of a wider hematologic profile and research of a longer-term effects of ECT on these easily applicable hematologic parameters makes our study different from previous studies and provide a distinct perspective on the immunological effects of ECT.

CONCLUSION

ECT is one of the oldest and most effective biological treatment methods in psychiatry which unfortunately lose its popularity from time to time. In the literature there is limited number of studies that examine the effect of ECT on the immune system. Previous researches assessing the effects of ECT on inflammatory response are mainly had focused on changes in anti-inflammatory and pro-inflammatory cytokine levels, but unfortunately cytokine levels do not appear to be cost-effective markers in everyday practice. It is obvious that inflammatory markers that are easier and faster to implement, compatible with clinical features and predicting prognostic factors are needed.

In conclusion, NLR, PLR, RDW, MPV, MCH and MCHC, which are easy to apply and inexpensive inflammatory markers, were evaluated before and after ECT in the present study. Both MPV and RDW levels in schizophrenia patients were found to be decreased after 7 sessions of ECT treatment. According to our results, it can be affirmed that recurrent ECT sessions caused a change in the function of the immune system. This finding supports the hypothesis of alteration in the immune system, which is asserted to explain the mechanism of action of ECT. Because of the fact that all of 58 patients were receiving psychotropic medication during ECT, it seems to be difficult to claim that the change in

hematologic parameters are due to ECT intervention alone. In order to obtain more robust evidence about the effect of ECT on hematologic inflammatory markers further researches (1) carried out with patients who had the first psychotic episode and did not receive additional psychotropic medication, (2) excluded confounding factors such as smoking and obesity besides drug use, (3) evaluated other immunological markers, like cytokines, with inflammatory markers and (4) with wider patient samples are required to be conducted. There is a need of scope for new research in schizophrenia over the coming years, encompassing immune, genetic, microbiological, and other biomarkers.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Nikkilä HV, Müller K, Ahokas A, Rimón R, Andersson LC. Increased frequency of activated lymphocytes in the cerebrospinal fluid of patients with acute schizophrenia. Schizophr Res 2001;49:99-105.
2. Potvin S, Stip E, Sepehry AA, Gendron A, Bah R, Kouassi E, et al. Inflammatory cytokine alterations in schizophrenia: a systematic quantitative review. Biol Psychiatry 2008;63:801-8.
3. Müller N. The role of anti-inflammatory treatment in psychiatric disorders. Psychiatr Danub 2013;25:292-8.
4. Benros M, Nielsen P, Nordentoft M, Eaton W, Dalton S, Mortensen P. Autoimmune diseases and severe infections as risk factors for schizophrenia: a 30-year population-based register study. Am J Psychiatry 2011;168:1303-10.
5. Wium-Andersen MK, Orsted DD, Nordestgaard BG. Elevated C-reactive protein associated with late- and very-late- onset schizophrenia in the general population: a prospective study. Schizophrenia Bull 2014;40:1117-27.
6. Müller N, Schwarz MJ. Immune system and schizophrenia. Curr Immunol Rev 2010;6:213-20.
7. Kuyumcu ME, Yesil Y, Ozturk ZA, Kizilarslanoglu C, Etgül S, Halil M, et al. The evaluation of neutrophil-lymphocyte ratio in Alzheimer's disease. Dement Geriatr Cogn Disord 2012;34:69-74.
8. Balta S, Demirkol S, Kucuk U. The platelet lymphocyte ratio may be useful inflammatory indicator in clinical practice. Hemodial Int 2013;17:668-9.
9. Kopuz A, Turan V, Ozcan A, Kopuz Y, Toz E, Kurt S. A novel marker for the assessment of the treatment result in pelvic inflammatory disease. Minerva Ginecol 2016;68:117-23.
10. Akıl E, Bulut A, Kaplan I, Özdemir HH, Arslan D, Aluçlu MU. The increase of carcinoembryonic antigen (CEA), high-sensitivity C-reactive protein, and neutrophil/lymphocyte ratio in Parkinson's disease. Neurol Sci 2015;36:423-8.
11. Rembach A, Watt AD, Wilson WJ, Rainey-Smith S, Ellis KA, Rowe CC, et al. An increased neutrophil-lymphocyte ratio in Alzheimer's disease is a function of age and is weakly correlated with neocortical amyloid accumulation. J Neuroimmunol 2014;273:65-71.
12. Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. Psychiatry Res 2015;228:925-7.
13. Gündüz N, Timur Ö, Erzincan E, Turgut C, Turan H, Akbey ZY. Evaluation of mean platelet volume, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and red cell distribution width in patients with diagnosis of major depressive disorder. Med Med J 2017;32:230-7.
14. Özdin S, Sarisoy G, Böke Ö. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients - a retrospective file review. Nord J Psychiatry 2017;71:509-12.
15. Aykut DS, Arslan FC, Karagüzel EÖ, Aral G, Karakullukçu S. The relationship between neutrophil-lymphocyte, platelet–lymphocyte ratio and cognitive functions in bipolar disorder. Nord J Psychiatry 2018;72:119-23.
16. Manu P, Correll CU, Wampers M, Mitchell AJ, Probst M, Vancampfort D, et al. Markers of inflammation in schizophrenia: association vs. causation. World Psychiatry 2014;13:189-92.
17. Semiz M, Yildirim O, Canan F, Demir S, Hasbek E, Tuman TC, et al. Elevated neutrophil/lymphocyte ratio in patients with schizophrenia. Psychiatr Danub 2014;26:220-5.
18. Kulaksizoglu B, Kulaksizoglu S. Relationship between neutrophil/lymphocyte ratio with oxidative stress and psychopathology in patients with schizophrenia. Neuropsychiatr Dis Treat 2016;12:1999-2005.
19. Turkmen K, Erdur FM, Ozcicek F, Ozcicek A, Akbas EM, Ozbicer A, et al. Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients. Hemodial Int 2013;17:391-6.
20. Keshtkar M, Ghanizadeh A, Firoozabadi A. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for the treatment of major depressive disorder, a randomized controlled clinical trial. J ECT 2011;27:310-4.
21. Jahangard, L, Haghighi M, Bigdelou G, Bajoghli H, Brand S. Comparing efficacy of ECT with and without concurrent sodium valproate therapy in manic patients. J ECT 2012;28:118-23.
22. Kruse JL, Congdon E, Olmstead R, Njau S, Breen EC, Narr KL, et al. Inflammation and improvement of depression following electroconvulsive therapy in treatment-resistant depression. J Clin Psychiatry 2018;79:17m11597.
23. Asoğlu M, Göbelek M, Karka İ, Pirinççioglu F, Çelik H, Ay H, et al. Effect of electroconvulsive therapy on hematological

parameters. Bezmialem Science 2018;6:130-3.
24. Fluitman SB, Heijnen CJ, Denys DA, Nolen WA, Balk FJ, Westenberg HG. Electroconvulsive therapy has acute immunological and neuroendocrine effects in patients with major depressive disorder. J Affect Disord 2011;131:388-92.
25. Chaturvedi S, Chadda RK, Rusia U, Jain N. Effect of electroconvulsive therapy on hematological parameters. Psychiatry Res 2001;104:265-8.
26. Khandaker GM, Cousins L, Deakin J, Lennox BR, Yolken R, Jones PB. Inflammation and immunity in schizophrenia: implications for pathophysiology and treatment. Lancet Psychiatry. 2015;2:258-70.
27. Patel PS, Buras ED, Balasubramanyam A. The role of the immune system in obesity and insulin resistance. J Obes 2013;2013:616193.
28. Rodríguez-Hernández H, Simental-Mendía LE, Rodríguez-Ramírez G, Reyes Romero MA. Obesity and inflammation: epidemiology, risk factors andmarkers of inflammation. Int J Endocrinol 2013;2013:678159.
29. Balistreri CR, Caruso C, Candore G. The role of adipose tissue and adipokines in obesity-related inflammatory diseases. Mediators Inflamm 2010;2010:802078.
30. Fernandes B, Steiner J, Bernstein HG, Dodd S, Pasco JA, Dean OM, et al. C-reactive protein is increased in schizophrenia but is not altered by antipsychotics: meta-analysis and implications. Mol Psychiatry 2016;21:554-64.
31. Kweon OJ, Lee MK, Kim HJ, Chung JW, Choi SH, Kim HR. Neutropenia and neutrophil-tolymphocyte ratio in a healthy Korean population: race and sex should be considered. Int J Lab Hematol 2016;38:308-18.
32. Çakır U, Tuman TC, Yıldırım O. Increased neutrophil/lymphoctye ratio in patients with bipolar disorder: a preliminary study. Psychiatr Danub 2015;27:180-4.
33. Kayhan F, Gündüz S, Ersoy SA, Kandeger A, Annagür BB. Relationships of neutrophil–lymphocyte andplatelet–lymphocyte ratios with the severity of major depression. Psychiatry Res 2017;247:332-5.
34. Mayda H, Ahsen A, Bagcıoglu E, Öztürk A, Bahçeci B, Soyuçok E, et al. Effect of increased neutrophil-to-lymphocyte ratio (NLR) and decreased mean platelet volume (MPV) values on inflammation in acute mania. Arch Neuropsychiatry 2016;53:317-20.
35. Canan F, Kürklü N, Geçici Ö, Kuloglu M. The effect of electroconvulsive therapy on neutrophyl/lymphocyte ratio. JMOOD 2016;6:1-6.
36. Miller BJ, Buckley P, Seabolt W, Mellor A, Kirkpatrick B. Meta-analysis of cytokine alterations in schizophrenia: clinical status and antipsychotic effects. Biol Psychiatry 2011;70:663-71.
37. de Witte L, Tomasik J, Schwarz E, Guest PC, Rahmoune H, Kahn RS, et al. Cytokine alterations in first-episode schizophrenia patients before and after antipsychotic treatment. Schizophr Res 2014;154:23-9.
38. Wysokinski A, Szczepocka E. Platelet parameters (PLT, MPV, P-LCR) in patients with schizophrenia, unipolar depression and bipolar disorder. Psychiatry Res 2016;237:238-45.
39. Lee J, Powell V, Remington G. Mean platelet volume in schizophrenia unaltered after 1 year of clozapine exposure. Schizophr Res 2014;157:134-6.
40. Ma J, Dou Y, Zhang H, Thijssen SW, Kuntsevich V, Ouellet G, et al. Correlation between inflammatory biomarkers and red blood cell life span in chronic hemodialysis patients. Blood Purif 2017;43:200-5.
41. Ayyildiz H, Karabulut N, Kalayci M. Relationship between red blood cell distribution width and schizophrenia. Int J Med Biochem 2018;1:15-9.
42. Asoglu M, Aslan M, Canbolat O, Imre O, Savik E, Kivrak Y, et al. Red cell distribution width, mean platelet volume and vitamin B12 levels in patients with schizophrenia: an observational study. Int J Clin Exp Med 2016;9:16629-36.
43. Huang YL, Hu ZD. Lower mean corpuscular hemoglobin concentration is associated with poorer outcomes in intensive care unit admitted patients with acute myocardial infarction. Ann Transl Med 2016;4:190.
44. Balõtšev R, Haring L, Koido K, Leping V, Kriisa K, Zilmer M, et al. Antipsychotic treatment is associated with inflammatory and metabolic biomarkers alterations among first-episode psychosis patients: A 7-month follow-up study. Early Interv Psychiatry 2019;13:101-9.
45. Maes M, Bocchio CL, Bignotti S, Battisa TG, Pioli R, Boin F, et al. Effects of atypical antipsychotics on the inflammatory response system in schizophrenic patients resistant to treatment with typical neuroleptics. Eur Neuropsychopharmacol 2000;10:119-24.
46. Upthegrove R, Manzanares-Teson N, Barnes NM. Cytokine function in medication-naive first episode psychosis: a systematic review and meta-analysis. Schizophr Res 2014;155:101-8.
47. Semiz M, Yucel H, Kavakci O, Yildirim O, Zorlu A, Yilmaz MB, et al. Atypical antipsychotic use is an independent predictor for the increased mean platelet volume in patients with schizophrenia: a preliminary study. J Res Med Sci 2013;18:561-6.
48. Celebioglu B, Yigit H, Rezaki M, Ercelen O, Kayatekin S. Anesthesia in electroconvulsive therapy. Ann Saudi Med 1999;19:144-6.
49. Zhou R, Yang Z, Tang X, Tan Y, Wu X, Liu F. Propofol protects against focal cerebral ıschemia via inhibition of microglia-mediated proinflammatory cytokines in a rat model of experimental stroke. PLoS ONE 2013;8:e82729.
50. Samir A, Gandreti N, Madhere M, Khan A, Brown M, Loomba V. Anti-inflammatory effects of propofol during cardiopulmonary bypass: A pilot study. Ann Card Anaesth 2015;18:495-501.
51. Markovic-Bozic J, Karpe B, Potocnik I, Jerin A, Vranic A, Novak-Jankovic V. Effect of propofol and sevoflurane on the inflammatory response of patients undergoing craniotomy. BMC Anesthesiol 2016;16:18.

The European Research Journal 2020;6(3):248-256 Review

DOI: 10.18621/eurj.519115 *Psychology*

Terminal cancer in Northeast India: an analytical study on its rapid growth, causes, and solutions

Suantak Demkhosei Vaiphei, Devendra Singh Sisodia

Department of Psychology, Bhupal Noble's University, Udaipur, India

ABSTRACT

The underlying aim of the study is to investigate the reasons behinds the rapid growths of cancer populations and the cancer mortality rates in the Northeastern States of the country. The current study is an analytical study on the collected data and reports of the following reliable sources: The Population-Based Cancer Registries' Data of the Central and State Governments, the data from National Cancer Registry and Regional Cancer Centers, National Family Health Survey of India (NFHS-3), National Institute of Cancer Prevention and Research, and Indian Council of Medical Research. The study will be specific to the reasons behind the rapid growths, causes, and solutions in the Northeastern regions of the country. The study also utilized the available journals database, along with World Health Organization database. The researcher also access to the government's data and hospitals documents on cancer statistics and their reports. By eliminating the usages of tobacco, cigarettes, chewing, and bitternuts with hygenic environment, the rates of oral lip, breast, mouth, cervical, head and neck, and the nasopharyngeal cancer can successfully be reduces into at least 40-50% in Northeast region, as per the researcher findings. The urgent need of the regions is to develop social awareness on the causes of cancer. Gearing up for health awareness and strengthening the health care team at the community level by addressing the cancer preventive measures in the Northeast region will effectively decreases the growing cancerpopulations of cancer/terminal illness.

Keywords: Cancer, terminal illness, awareness, terminal deaths, early detection

The increasing of the modern technologies requires the setting up of multiple factories and industries that produce smokes and chemicals, which polluted the air, water, and the environment resulting in putting lives in dreaded conditions. In fact, the coming of the modern era and the modern lifestyle gives birth to numerous deadly diseases like cancer and its related diseases, which increasingly takes the lives of many in the Northeast regions of the country. The cold-blooded killer 'cancer' becomes the major public health concern in Northeast region in particular and India as a whole in India today. Among all the problems existed across the world, the problems or the issues associated with cancer or terminal illness becomes the worldwide phenomenon that produces several unwanted worst experiences. Human polluting the water, soil, and the air continued and the global burden of cancer affected populations rapidly increasing year after year. Unfortunately, the Northeast States of India turns out to be the world most densely cancer populated regions. The reason behind the rapidly increasing of cancer illness and its mortality rates in these regions were generally people lack of awareness on cancerous factors, no proper preventive measures,

Received: *January 29, 2019;* ***Accepted:*** *July 6, 2019;* ***Published Online:*** *February 1, 2020*

How to cite this article: *Vaiphei SD, Sisodia DS. Terminal cancer in Northeast India: an analytical study on its rapid growth, causes, and solutions. Eur Res J 2020;6(3):248-256. DOI: 10.18621/eurj.519115*

Address for correspondence: *Suantak Demkhosei Vaiphei, Research Scholar, Bhupal Noble's University, Department of Psychology, Udaipur, India*
E-mail: gdsuantak@yahoo.com

e-ISSN: 2149-3189

and the late detection of the symptoms at the advanced stages when cure is not possible. Thus, concerning the helplessness conditions of the people of Northeast in general, the current analytical study has been forms with an aim to spread awareness on the cold-blooded killer cancer. The study focus mainly on the current cancer situations and the underlying causes of cancer in the North Eastern regions of the country. The study also includes the essential preventive strategies and the treatment policy when it comes to its terminal stages.

CURRENT SITUATIONS OF CANCER ILLNESS IN NORTHEAST INDIA

In the definitions of World Health Organization, cancer or terminal illness is the uncontrolled growth of deadly cells with unstoppable spreads, which destroys every portion of human body organs one after another. Once the deadly cells increase and affected the patient's startlosing the functioning of his/her body sites that usually leads to a paralyses condition. These deadly cancer cells expanded through invading the surrounding tissues and spreads to other parts of the body by metastasis leading to 8.2 million global deaths a year at present. In which India becomes the world top contributor to cancer mortality rates with around 556,400 terminal deaths per year as per World Health Organization [1]. The modern India turn out to be a cancer hub with 2.5 million cancer-affected people (Table 1), which would be expect to increases by 50% in 2020, if no immediate action plan had been done by the governmental and non-governmental agencies. A premature death through non-communicable diseases is the leading causes of deaths in India like cardiovascular ailments, chronic respiratory problems, and diabetes [2]. Unfortunately, the Northeastern regions become the largest contributors to cancer illness and its mortality rates in the country.

The cervical and stomach cancer symptoms populations in Mizoram alone is equal with the total numbers of cancer affected populations of Japan, and is the highest cancer populated region in the world [3]. At present, Aizawl in the State of Mizoram and Papumpare District of Arunachal Pradesh has the highest age adjusted cancer incidences in the country. In which 271 men in 100,000 populations in Aizawl were with Cancer illness, and 249 cancer patients in 100,000 populations in Papumare town of Arunachal Pradesh. The third highest cancer population in the country is in Karum district of Assam with 206 cancer patients in 100,000 populations [4]. In Mizoram and Tripura, the cervical cancer is the leading cancer symptoms, while in the State of Nagaland and Meghalaya, tongue, mouth, stomach, and gall bladder were the leading cancer symptoms. While in Manipur cervical, oral, lip, mouth, pharyngeal, head, and neck cancer were visible largely affecting people. Table 2 shows the five most common deadly cancer symptoms, its causes, and the numbers of terminal deaths in a year in India as a whole.

Looking at the present conditions, it is visible that Northeast in particular and India as a whole is fighting with the cold-blooded killer "Terminal Illness" in the most unsuccessful ways. Moreover, India at present is in critical conditions with rapid increasing of one-lakh cancer populations and with the minimal cancer care center, which is around only 300 regional cancer care centers thatare not enough even to treats the one thirds of the cancer populations. The India today had only 1000 oncologists, which is in the ratio of 1:2000 one oncologist per two thousand cancer patients. This constituted the underlying reason why modern India turned into a cancer hub and the fighting will continues as the numbers of affected patient's raises up every year [5, 6]. The following statistic is form to explain the details about of the current cancer status of India today:

In the latest statistical report of NICPR at present

Table 1. Current cancer statistic in India

No. of cancer affected	Yearly cancer registration	No. of deaths in a year	Common age of death (39-60 years)	Women	Men	Percentage
2.5 million	7 Lakh	556,400	395,400	195,300	200,100	71%

Adapted from NICPR statistical report on August 23, 2018.

Table 2. The five common cancer symptoms in Northeast and yearly terminal deaths [4]

	Cancer symptoms	Numbers of deaths per year	Main causes
1	Head & neck cancer	575,000	Alcohol, tobacco, and cigarettes
2	Breast cancer	522,000	Unhealthy lifestyle, genetic, and alcohol
3	Gall bladder cancer	230,000	Unhealthy lifestyle, genetic, and poor prevention
4	Cervical cancer	67,477	Human papilloma virus (HPV), birth control pills, smoking, and unhealthy sex
5	Oral cancer	45,800	Smoking, tobacco, alcohol, HPV, sunlight, and weak immune system

one woman dies of cervical cancer every 8 minutes and for every newly diagnosis with breast cancer one out of two women dies in India today. Moreover, around 2,500 died per day due to the consumptions of tobacco and bitternut. While smoking, which is the most common practices in India cause 1 in 5 death amongst men and 1 in 20 death amongst women, which constituted around 930,000 deaths in 2010 mainly because of smoking related issues in the country. In which the most productive age period could be highlights in the ages between 30-60 years [7], which need a special consideration and these ages grouped need to be targeted the most.

UNDERLYİNG CAUSES OF CANCER AND ITS DEADLY SYMPTOMS

The main cause of cancer is through the internal factors (inherited mutations, hormones, and immunes conditions) and external/ environment factors (tobacco, insufficient diet, unhealthy food, organism, and chemical with radiations) (Table 3). Among all these components for the causes of cancer and its deadly symptoms, there is a closed link between unhealthy food and insufficient diets with cancer disease as observed by many experts [2]. Unhealthy lifestyles with alcohol and smoking are the second most common cancerous factors leading to chronic disease, cardiovascular, lung, kidney, throat, esophagus, and breast cancer. The third common factor for the causes of cancer is visible in excessive consumptions of red meats and fish leading to heart and breast cancer [8]. Moreover, looking at the context of Northeast India at present, all the three main cancerous factors are the most common practices of the people like eating tobacco, unhealthy lifestyle,

Table 3. Cancerous factors in Northeast India

Factors for the causes of cancer and it's deadly symptoms				
Tobacco products	Excessive alcohol uses	Insufficient diets	Excessive cholesterols	Physical inactivity
Ultraviolet radiation	Virus & bacteria's	Ionizing radiation/ waves or particles	Uses of pesticides in cultivations	Excessive medical drugs
Solvents or unhealthy liquids components	Fibers or any mineral substances	Fine particles, dust & contaminants environment		Dioxins highly toxic components
Polycyclic aromatic hydrocarbon PAHs	Metals or coated with metals	Diesel exhaust particles	Toxin from fungi	Smoking & hookahs'
Vinyl chloride and benzedrine	Excessive meat's	Unhealthy drinking water	Chewing of bitternuts	Junk food

excessive consumptions of meats of any kind, and drinking alcohol to the maximum, which resulted in turning these tiny regions into a cancer hub. At present as per the National Tobacco Control Programme, Manipur has the highest age adjusted tobacco consumption in India, in which every second men and every third women were addicted with tobacco. Thus, becoming the highest burden of tobacco related cancer illness in the country like heart attack, lung diseases, and stroke, etc. The uses of tobacco causes 100% poor oral health with 90% of mouth cancer, 80% of lung cancer, 50% of all human cancers, 70% of lung diseases, and 60% of heart attacks. Unfortunately, Manipur stood in the world top for lung cancer, especially among the female population mainly due to the uses of tobacco, smoking, and the smoke produces by firewood in cooking [9]. As per the Global Adult Tobacco Survey, 54% of people in Manipur are addicted with tobacco of which 66.6% men and 41.8% women excessively use tobacco, resulting in causing premature terminal deaths to 100,000 people in a year [9, 10].

Another reason for the Northeast being the top cancer populated in the country is mainly due to people unawareness of cancerous components, its preventive measures, and the treatment policy. Due to the lack of awareness, people in these regions detect their cancer symptoms only when it comes to terminal stages (third or fourth stages), which is in the condition of impossible to cure. Late detection of cancer symptoms and late cancer diagnosis becomes the underlying reasons for failing to cure 80% of cancer illness in India today. However, early detections of the symptoms in its first stage there is 80% chances to cure. On the other hand, undergoing cancer diagnosis in the second stages could possibly have 60%, chances for cure, and in the third stage the cure possibility rates reduces down to 30%, but with the possibility of stage four of cancer within a short period of time. However, in the fourth stage, which is the terminal stage there is no chances to cure, rather to live with the pain symptoms for maximum life spends of 5-7 years [5, 6].

The causes of stomach and cervical cancer symptoms in Mizoram were mainly due to the consumptions of water filtrate tobacco "Tuibur," excessive drinking of alcohol, cigarette smoking, and bitternuts. While in Manipur, lung and oral cancer hugely affect the men and women populations, the reason being excessive uses of tobacco, smoking, hookah, and the consumption of local made alcohol. Another prevailing cancer symptom in Manipur is nasopharyngeal cancer, which is a malignant cells disease form in the tissues of the nasopharynx. The nasopharyngeal cancer (NPC) is the rarest type of cancer around the world; accept in the South East Asia, North Africa, and Arctic. The NPC is claims to be a Chinese origin, which is largely affecting the Northeast Indian states of Nagaland, Manipur, Mizoram, and to some extend to Meghalaya. The state of Nagaland has the highest age adjusted with 19.5/100,000, followed by the state of Manipur. The nasopharyngeal cancer is mainly causes by excessive eating of meat, fish, salted fish, uses of firewood in the house and other environmental related factors like the eating of bitternuts (Kuwa or Komkuwa) with or without tobacco products. Mostly the women populations in Manipur were mainly affects with nasopharyngeal cancer comparing to men. Moreover, within 15-20 years the nasopharyngeal affected women populations in Manipur will be increasing, if the uses of tobacco, bitternuts, and the uses of firewood in cooking are not being under-controlled [3, 11]. The table below will clearly shows the various factors that are responsible for the causes of cancer as a whole:

Moreover, apart from food habits, the population explosion, rapid industrialization, and genetics, which include mutations, hormonal and lack of immunity are also responsible for the rapid growth of terminal illness in the these regions. If proper awareness had not given to the people of Northeast, there is a possibility of increasing cancer populations to 19% in the next five years. In which women have more chances of affected with cancers than men in India, as per the findings of many. Moreover, the mortality rate of cancers in India is visible higher among the illiterate people groups in the rural areas of the country than the educated, and the maximum deaths in India are mainly due to poor prevention strategies and no proper diagnosis as a whole [12].

According to the latest NICRP reports, 122,844 women are diagnoses with cervical cancer every year out of which 67,477 women died from cervical cancer per year. In a population of 432.2 million women in India at present, those women who are at the age of

15 and above and or between 15-40 years are at risk of developing cervical cancer in India. The health scientists on the other hand, were not able to identify the processes of how the risk factors like genetic, hormonal, and environment factors works together to cause normal cells to become cancerous tumor for the cancer symptoms. Thus, cancer becomes the leading causes of deaths in India, with 2.5 million cancer populations, with 1 million cancer patients added every single year and it could be predicts that the numbers of cancer patients by 2025 would be increases by five fold in India [7, 8]. The rapid increasing rates of cancer in the country are mainly due to lifestyle risk factors like uses of tobacco, alcohol, low fiber in diet, increasing body weight, minimal physical activities, and the reproductive risk factors in regards to age at first pregnancy, and higher numbers of children breastfeeding's. Out of many cancer mortalities, the two leading deaths are from cervical cancer (HPV), hepatitis C (liver), and gastric H. Pylori (stomach). Moreover, in Northeast India genetic and environmental factors combine in making the region as the highest cancer populated in the country, the people on the other hand were highly unaware of the cancerous factors and its preventive measures [13].

SOLUTIONS AND PREVENTIVE MEASURES: TRADITIONAL APPROACH

Terminal deaths is the top causes of Death in India, and the Northeastern states of the country becomes the top contributors to cancer illness and its mortality rates. In the 2000, India was in Seventh position among the world cancer populated country, however the rapid increasing of cancer populations in the Northeast States like Mizoram, Arunachal, Assam, Manipur, Nagaland, and Meghalaya in 2007-2018 India successfully stood in world top cancer populated country, and the numbers of effected populations is visible increasing with 100,000 in a year. Looking at the cancerous factors only 5-10% the cancer is from genetics, in which the other 90-95% of the cancer and its related diseases are from hormonal and environment factors. Moreover, the 90% of the cancer and its related diseases can be effectively prevents through proper medical interventions in its early stages. Another 10% genetic cancerous symptoms can also be cure through early detection and immediate diagnosis. In short, cancer of any types is curable if detected in its early stages and through proper preventive measures [14]. The followings are the qualitative preventive measures in order to control the rapid growths of cancer in the Northeast Regions of the country [2, 8, 14, 15]: (1) Regular medical checked-up, though being in a healthy condition, negligees of regular medical checked-up is visible as the underlying reason for the rapid growths of cancer in Northeast in the past ten years; (2) Educating people with proper awareness strategies, offer effective public health concerned in the school, Church meetings, or organizing a social meeting for spreading cancer awareness; (3) Early detection of the symptom and early medical intervention, because when it comes to third and fourth stages there is no possibility for cure; (4) Public awareness on active physical activities, exercise at least for 30 minutes per day, the healthier a person is the cells in the body effectively fights against the invader virus and bacteria's. Regular exercise prevents oneself from colon and breast cancer too; (5) Minimizing the uses of alcohol products, smoking, tobacco, and chewing of bitternut products, which will minimized the risk of having lung, kidney, throat, esophagus, and breast cancer. It is better to develop a moderate ways of consuming with 2-3 glass per day, which will keep oneself away from heart attacked; (6) Immunization against hepatitis B virus to the infants of one to sixth months old without failed. Neglecting medical treatment in hepatitis B & C can causes chronic illness and liver cancer; (7) Developing healthy and safe sexual practices to avoid cancer genesis, unhealthy sexual practices can give birth to cancer cells; (8) Avoiding obesities, as being grossly fat or overweight have negative effects on health; (9) Developing healthy diets, a healthy diets has scientifically proven with numerous health benefits and reducing the risk from chronic diseases; (10) Reducing occupational and environmental exposures, as excessive exposures to chemical and its related heavy metals produces ill health. It also effected for the future offspring and produces toxicity; (11) Avoiding excessive consumption of red meats, salt and long preserved food. High consumptions of red meat, salt and preserved food leads to diabetes, breast cancer, and obesity; (12) Developing the habits of

eating fruits regularly, most fruits are less in calories, sodium, and fats. Fruits are the sources of essential nutrients like potassium, dietary fibers, vitamin C, and foliate (folic acid), which prevents deficiency, birth defect, and helps a person to growth with healthy blood pressure; (13) In order to have fair skins some avoid exposing to sunlight, wearing protective clothing during 10 am-4 pm and the excessive uses of sunscreen cream need to be avoid. Avoiding of exposing to sun or UV resulted in many women diagnoses with skin cancer. On the other hand, excessive exposing to sunlight or UV ray is also dangerous, especially for those having genetic cancerous symptoms; and (14) Immediate medical intervention on virus and bacterial infections, otherwise the bacteria diseases virus cells usually hide inside the cells and turning out to be a terminal virus. The increasing industrializations and urbanizations are visible as the two factors leading to new lifestyle of many Indians, which resulting in increasing the cancer affected populations in the country. Concerning the current polluted environment the burden of cancer incidences will gradually keep on increasing, as majorities of the Indians were not aware of cancerous preventive measures. The only ways to prevent the Indian men and women from the rapid growths of cancer and its deadly symptoms is to detect the symptoms at the early stages with immediate medical interventions. It is also important to prevent the water and the environment from polluted by industries and chemicals. However, it can only be possible only if the men and women in the rural areas were being educated on cancer awareness like preventive measures, and overall treatment policies, which needs multiple efforts from the government agencies and other non-governmental agencies. Through such awareness programs, men and women should realize the risk factor and to identify the symptom through screening by physical examination or by self-cancerous symptom examination, in which if the rick substances where found than certain carcinogenic substances need to be reduces or eliminated. Moreover, there are over 85,000 synthetic chemicals that were easily available in the market of the country today like cosmetic items to flame-retardants, plasticizers in water bottles to pesticides in fruits and vegetables' etc. In the findings of the researcher, 80% of the cancer patients in the country were associated with environment factors like exposes to contaminants, unhealthy lifestyle, food, and exposing to ionizing radiations. In the urban areas, the cleaning of contaminated drainages without any proper preventive measures, polluting the river to the maximum with many forms of chemical and eating those fishes from the river produces several cancerous symptoms. The using of polluted water from the factories or industries for agricultural farming also produces several cancerous components leading in rapid increasing of cancer populations through consuming theses agricultural products [2, 12, 14, 16]. Thus, maintaining healthy environment, healthy lifestyle, healthy food, proper diets, daily exercise, staying away from tobacco, and smoking, with decreasing alcohol consumptions can decreases the rates of cancer-affected populations in the Northeast India. Moreover, the common practices in the Northeast villages of using of the water, which were uses in deeping the hot metal or iron in the blacksmith for washing hand and leg need to be avoided, as it contains the component that is cancerous.

CANCER TREATMENT POLICY AND TERMINAL DIAGNOSIS

The World Health Organization proposed that the cancer patients need immediate access to the modern equipments like; 3D Conformal Radiation Therapy, Intensely Modulated and Therapy (IMRT), Image Guided Radiation (IGRT). the VMAT and Rapid Arc-Volumetric Modulated Arc Therapy (VMAT), Low Dose Rate Brachyntherapy (LDR), High Dose Rate Brachyntherapy (HRD), Deep Inspiration Breath Hold (using the goggles or snorkel technique), and Stereotactic Radiation Therapy [17[. However, in most of the cancer care centers in the North East regions of the country, the modern instruments for cancer treatments were not being utilizes in majority of the terminal diagnosis due to its unavailability. Failing the interventions of modern equipments in terminal diagnosis failed in treating the symptoms effectively in many cases. The higher rates or costly of medical treatments rates and medicines prices becomes the underlying reason for those living under poverty lines failed to undergo proper medical interventions in their cancer experiences, which resulted in experiencing the

worst and painful life experience for 5-7 years. Moreover, treatments like Breast Conserving Surgery, Mastectomy, Chemotherapy, Radiation Theory, and Scanning related treatments, which were the core treatments to cancer and terminal diagnosis, requires maximum amounts of money that the poor cancer affected people were remained helpless. The quality treatment plan and policy are the core components for successful cancer metastasis diagnosis, which is also visible ineffective to the minimal. The main emphasis of a cancer diagnosis is to cure the symptom of the cancer patient or to prolong the lives' of the patientthrough ensuring quality of life [15, 16, 18]. However, the greatest challenges in the cancer diagnosis in the Northeast region is the ensuring of the patient quality of life, which is not visible in the clinical practices of the country as a whole, and unnecessarily prolonging the patient lives with an aim to increases the numbers of days spend in the hospital ward for more bills. The patient's value and dignity were unconcern the most by the clinicians' and the patient undergoing treatment against their will/choices need to be rectifying immediately in the health care systems of the country as a whole.

The early detection and immediate treatment is the most effective way of cancer diagnosis to control the cancer metastasis and to deliver total cure. The medical intervention in stages one and two has higher possibilities rates to cure, which has around 80% cure possibilities in any cancer experiences. While detecting the cancer symptom and consulting the oncologists in stage three is visible in curtail conditions, having higher impossibility rates as the cancer metastasis accelerates in higher speeds from one body part to another. However, if the stage three patient being diagnosis by special medical team in a well to do clinical setting, it has around 60% possibility chances to cure. Though being cure in stage three does not guarantee a complete free from cancerous cells, there is a possibility of being in terminal stage after three to five months, as the cancer cells have the possibility of hiding under another cells that is hard to detect, resulting in leading one's life a disability-adjusted life years (DALY) [15, 16]. Nevertheless, the detection of the cancer symptoms in the fourth stage have no possible ways to cure by any means, which is term as the 'terminal stage' that is 100% impossible to cure in any clinical practices. Thus, resulting in leaving the patient with disability-adjusted life for five to seven years until the inevitable death strikes him/her.

These 5-7 years period of terminal experience is the most crucial moment for every terminal patients, which is also considers as the worst moment in a terminal experience with heartful of emotional sufferings and mindful of mental disharmony that needs special considerations to the most. The acknowledgment of the psycho-emotional symptoms alongside the treatments of physical pain is very essential in any terminal diagnosis in the clinical practices. However, at present India turns out to be the worst place to die or a place not to die. The reasons for unfruitfulness behind the undergoing cancer/terminal diagnosis in the existing cancer care centers in Northeast regions lies in the core emphasis is on the physical pain treatment alone. The psychological symptoms experiences by the cancer/terminal patients, which were produces due to their encounter with cancer were not acknowledge for a symptom that need to be treated in the clinical practices. Thus, failing to acknowledge and leaving the psycho-emotional symptoms untreated resulted in worsening the patient's conditions, and on the other hand, it makes the treatments of the patient physical pain symptom unfruitful due to the patient psycho-emotional not in well-being. Well being of the whole body or healthy living requires a psycho-emotional well-being to the most; a psychological well-being can give positive responses to physical pain treatment to the maximum. In India as a whole, the clinicians tend to forgot that even when cure is not possible in terminal diagnosis, there is a possibility of delivering healing as an alternative to cure. However, only through a person centered meaning making psychotherapy in the clinical practices. The psychological self-reflective and life review therapeutic approach in terminal diagnosis can make oneself aware that he/she is still in the condition of limitless achievements. Which will in turn helps the patient to recreate his/her life goals, and set new life goal that could be achieved in a due time, also able to make beautiful memories with his/her loved ones and deliver quality of life. Above all, it will make dying as normal as birth, which will deliver peaceful and meaningful death [19]. Thus, in terminal diagnosis, healing can be delivers as an alternative to cure, even

when total cure is not possible in the clinical practices. However, sadly, in the clinical practices of the Northeast region and India as a whole, the clinicians alone are the core medical team in the cancer/terminal diagnosis, in the absences of professional clinical psychologists and clinical social workers. The terminal diagnosis requires a multidisciplinary team to deliver quality of life and quality end-of-life care. The clinicians were responsible for treated the physical pain symptoms related, while the clinical psychologists and clinical social workers were responsible for the patient psycho-emotional suffering treatments, which the trained medical doctors or nurses cannot handles in the clinical practices.

CHALLENGES AND CONCLUSION

Looking at the present conditions of Northeast regions of the country, cancer affected people and its mortality rates is visible rapidly increasing mainly due to people unawareness on the causes of cancerous, treatment policy, unhealthy lifestyles, and unhealthy food consumptions with no proper preventive measures interventions. Moreover, though densely populated with cancer illness, the cancer care centers in the regions are minimal, and some places in these regions are being cut-off from good transportations and communication systems. Thus, majority of the cancer patients in those areas have no choice, but to live with the cancer symptoms with unbearable physical pain and mental disharmony. Majority of the cancer patient in Northeast regions failed to maintain their diets, in which proper dietary is the core for successful diagnosis. The uses of tobacco, cigarettes, bitternuts were visible the common causes of cancer in Northeast India, in which eliminating the usages of tobacco, cigarettes and chewing of bitternuts can successfully reduces the rates of oral lip, breast, mouth, cervical, head and neck, and the nasopharyngeal (NPC) cancer into at least 40-50% in North East region, as per the researcher findings.

Another urgent need of the regions is to develop social awareness on the causes of cancer, and treatment policies by educating the Northeast people mainly those leaving in the rural areas of the region. Gearing up for health awareness and strengthening the health care team at the community level by addressing the cancer preventive measures in the NE region will effectively decreases the growing cancer populations. It is also important to maximize the numbers of the regional cancer care centers and the government increasing the funding amounts for cancer awareness and treatments in the rural areas. As stated by many researches, the government agencies, non-governmental organizations and the present media can plays a major in maximizing the level of cancer awareness among the public, especially in the rural undeveloped or uneducated areas. Moreover, those local celebrities and well-known figures involvements in promoting cancer awareness, the awareness effective rates will be visible hugely. Hygienic living by maintaining the surrounding need and clean can helps in controlling the rapid growths of cancer populations in these regions more effectively. The community leaders organizing several seminars on cultural related cancer awareness programs in each community or within the tribes would enhances people understanding on the causes of cancerous related illness, preventive measures, and treatment policies in a better way. On the other hand, the mobile mammography units in Northeast India can effectively reduces several barriers to breast and its related cancers among the Northeast women, if they can set their target to the interior villages and unreached areas. On the other hand, many studies proposes that the present conditions of the mobile mammography in the Northeastern states need to be updates with appropriate equipments and infrastructures, with maintaining quality resources for better functioning in the regions. Since, most of the cancer mortality in India as a whole occurs between 30-69 ages, these ages group need special considerations by the mobile mammography units and other cancer care agencies in Northeast regions. Moreover, the rural undeveloped areas in Northeast states should be the targets of every organizations working in cancer awareness programs, as 80% of cancer mortality are from the rural areas due to lack of awareness. Thus, at present the main causes of the rapid increasing of cancer in Northeast India are people unawareness of the cancerous symptoms, late detection of the cancerous symptom with late medical interventions, and most importantly lack of cancer treatment centers in the regions. It is high time for the Northeast people to take up necessary steps to fight against the cold-blooded killer, and better late than

never is the need of the hour. In the battle of cancer/terminal illness fighting back and defending people is the only option that the Northeast people had. For the love of humanity let the terminal diagnosis, acknowledge the psycho-emotional sufferings of the patient alongside the physical pain symptoms to deliver a whole person or total healing treatment in the clinical practices.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. World Health Organization. Global action against cancer 2018. Available at http://www.who.int/cancer/media/GlobalActionCancerEnglfull.pdf? Accessed 25th September, 2018.
2. Ingole SP, Kakde AU, Bonde PB. A review on statistics of cancer in India. IOSR J Environ Sci Toxicol Food Technol 2016;10:107-16.
3. Singh TT. Cancer scenario in Northeast India. Available at http://www.epao.net/epsubpageExtractor.asp?src+education.Health_Issue.Scenario_in_Northeast_India. Accessed October 25, 2018.
4. NICPR-ICMR. Cancer hits more women in India than men, but more men to die. Available at http://www.nicpr.res.in/images/imp ban.png2017. Accessed December 4, 2018.
5. Deccan Chronicle. (Sept. 12, 2018). Cancer kills 10 million in India. Available at https://www.deccanchronicle.com/lifestyle/health-and-wellbeing/120918/cancer-to-kill 10-mn- in-2018 -despite-better-prevention.html Accessed 30th September, 2018.
6. Sreedevi A, Javed R, Dinesh A. Epidemiology of cervical cancer with special focus on India. Int J Womens Health 2015;7:405-14.
7. NICPR (August 23, 2018). Cancer statistic in India. Available at http://cancerinindia.org.in/statistics/. Accessed 3rd December, 2018.
8. Cherian V. Cancer prevention and control in India. 50 years of cancer control in India 2016. Available at https://mohfw.gov.in/sites/default/files/Cancer%20Prevention%20And%20Control%20In%20India.pdf. (Accessed 27th September, 2018.
9. National Tobacco Control Programme. Manipur has the highest tobacco consumption in India. Retrieved from https://www.ifp.co.in/page /items/8126/8126-manipur-has-the-highest-tobacco-consumption-in-india/. Accessed 1st November, 2018.
10. Global Adult Tobacco Survey. India 2016-2017/Report. Available at http://www.indiaenvironmentportal.org.in/files/file/GATS_.pdf. Accessed 1st November, 2018.
11. Kataki AC, Simons MJ, Das AK, Sharma K, Mehra NK. Nasopharyngeal carcinoma in the Northeastern states of India. Chin J Cancer 2011;30:106-13.
12. Bhattacharjee A, Chakraborty A, Purkaystha P. Prevalence of head and neck cancers in the North East -An Institutional Study. Indian J Otolaryngol Head Neck Surg 2006;58:15-9.
13. Preeet D. Cancer – A Looming Threat In The North East. The Shillong Times. Available at http://www.theshillongtimes.com/2016/07/26/cancer-a-looming-threat-in-the-north-east/. Acessed 30th October, 2018.
14. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, et al. Cancer is a preventable disease that requires major lifestyle changes. J Pharm Res 2008;25:2079-116.
15. Dikshit R, Gupta PC, Ramasundarahettige C, Gajalakshmi V, Aleksandrowicz L, Badwe R, et al.; Million Death Study Collaborators. Cancer mortality in India: a nationally representative survey. Lancet 2012;379:1807-16.
16. Murthy NS, Chaudhry K, Nadayil D, Agarwal UK, Saxena S. Changing trends in incidence of breast cancer: Indian scenario. Indian J Cancer 2009;46:73-4.
17. World Health Organization. WHO list of priority medical devices for cancer management: WHO Medical Device Technical Series 2017. Available at http://apps.who.int/iris/bitstream/handle/10665/255262/9789241565462eng.pdf;jsessiond=4A6BE3B164041D129A49E2F006282717?sequence=1. Accessed 8th December, 2018.
18. Sharma TD, Sinam N, Singh TT, Devi RP, Sarma R, Bhaumik A, et al. Evaluation of socio-demographic profile of patients with cervical cancer at regional cancer centre in Manipur. Indian J Appl Res 2017;7:701-4.
19. Vaiphei SD, Sisodia DS. Existential psychotherapeutic intervention in the end-of-life and positive outcomesagn: an overview. J Indian Health Psychol 2018;13:20-34.

The European Research Journal 2020;6(3):257-259 Case Report

DOI: 10.18621/eurj.477636 *Orthopedics and Traumatology*

Giant anterior cruciate ligament lesion with destruction: operative management

Levent Bayam[1], Alauddin Kochai[1], Ahmet Can Erdem[2], Fatma Bayam[3], Mehmet Erdem[1]

[1]*Department of Orthopedics and Traumatology, Sakarya University School of Medicine, Sakarya, Turkey*
[2]*Department of Orthopedics and Traumatology, Bezmialem University School of Medicine, İstanbul, Turkey*
[3]*Department of Radiology, Aintree University Hospital NHS Foundation Trust, Liverpool, United Kingdom*

ABSTRACT

Objectives: We present a case report of an unusual giant lesion of anterior cruciate ligament (ACL) causing destruction and requiring reconstruction of ACL. A case report of a 32-year-old male patient presented to orthopedics outpatient clinic with 2 years history of right knee instability and clicking symptoms with no history of an obvious injury. Magneric resonance imaging showed a giant lesion occupying all ACL structure in the knee with 30×15×15 mm dimensions. The patient had an arthroscopy and it showed destruction of ACL, which required ACL reconstruction in the same sitting. Biopsy results showed a chronic non-specific inflammatory synovial epithelial tissue with increased vascularity and thickened wall vessels.

Keywords: Anterior cruciate ligament (ACL) lesion, ACL reconstruction, ACL ganglion

Although the anterior cruciate ligament (ACL) lesions are rare, there have been some case reports and studies on ganglion cysts in the literature [1, 2-4]. The cysts are mostly managed conservatively or draining, however, it may very rarely require further management such as ACL reconstruction. The absence of ACL reconstruction as treatment option for these cases is probably due to its rarity. We would like to emphasise that in case of nonfunctional ACL due to its destruction, ACL reconstruction could be the choice of treatment.

CASE PRESENTATION

We present an unusual giant lesion of ACL causing destruction and requiring reconstruction of ACL. A 32-year-old male patient presented to orthopaedic outpatient clinic with 2 years history of right knee instability and clicking symptoms with no history of an obvious injury.

The patient started to get a recent increase in pain even in rest and night time. The patient could not recall any trauma or incident before the change of symptoms and he did not de scribe any particular sport activities. The patient described a rather generalised knee pain than sharp pain without any swelling or sensation problem. His other symptoms were decreased flexion and difficulty in scouting. On examination, there was no effusion and no particular tenderness. Flexion of the knee decreased to 80 degree with pain. McMurray's test was negative and Lachman'stest showed slight laxity comparing to contra-lateralside.

Magneric resonance imaging showed a giant lesion occupying all ACL structure in the knee with 30×15×15 mm dimensions (Fig. 1). The patient had an arthroscopy and it showed destruction of ACL,

***Received:** November 2, 2018; **Accepted:** March 1, 2019; **Published Online:** January 20, 2020*

***How to cite this article:** Bayam L, Kochai A, Erdem AC, Bayam F, Erdem M. Giant anterior cruciate ligament lesion with destruction: operative management. Eur Res J 2020;6(3):257-259. DOI: 10.18621/eurj.477636*

***Address for correspondence:** Levent Bayam, MD., Assistant Professor, Sakarya University School of Medicine, Sakarya Training and Research Hospital, Department of Orthopedics and Traumatology, Sakarya, Turkey. E-mail: levbayam@hotmail.co.uk*

e-ISSN: 2149-3189

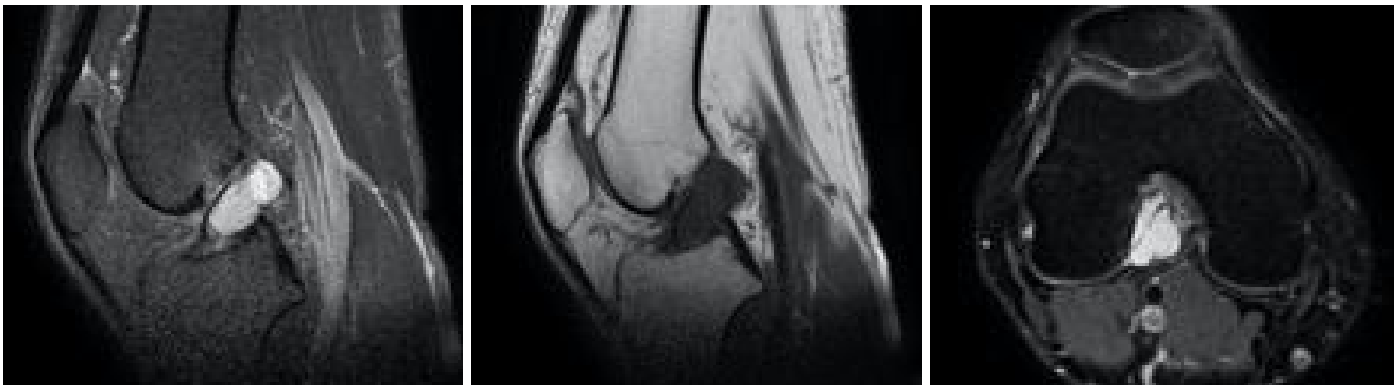


Fig. 1. T2 sagittal, T1 sagittal MR scan views of knee and T2 axial view.

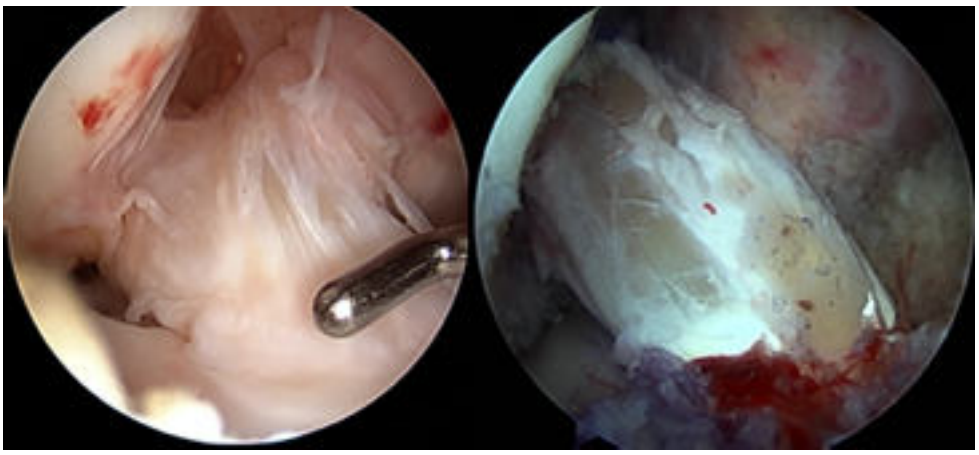


Fig. 2. Arthroscopic view preoperative and postoperative (ACL reconstruction).

which required ACL reconstruction in the same sitting (Fig. 2). Biopsy results showed a chronic non-specific inflammatory synovial epithelial tissue with increased vascularity and thickened wall vessels (Fig. 3).

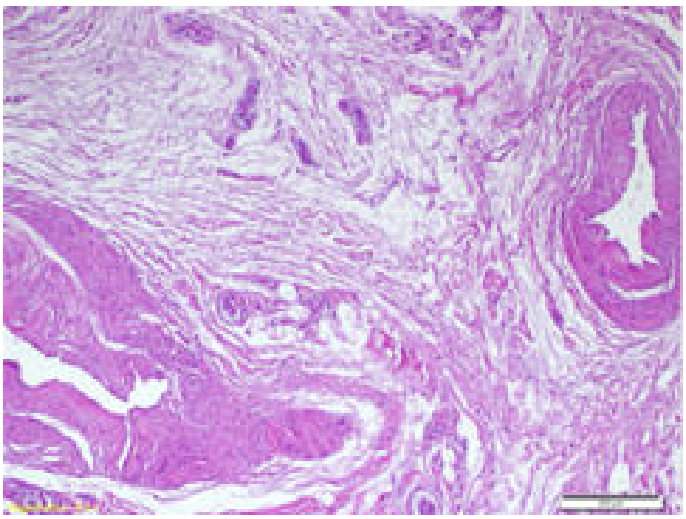


Fig. 3. Histopathology slide of the lesion.

DISCUSSION

Although the ACL lesions are rare, there have been some case reports and studies on ganglion cysts in the literature [1, 2-4]. The cyst are mostly managed conservatively or draining, however, it may very rarely require further management such as ACL reconstruction. Although biopsy results of our case showed increased vascularity with query of haemangioma, MR scan and arthroscopy findings confirmed ganglion cyst clinically. Synovial haemangiomais also very rare intra-articular benign tumour, which may arise from any synovium-lined surface [5].

Ganglion cysts are common around the joints and particularly around wrist but those are less common around the knee and if so, mostly associated with capsule or meniscus. Rarely, they can be associated with ACL and there are few publications about it [1, 3, 6]. Patients may present with symptoms pain, swelling, decreased flexion with or without previous

injuries or they could be asymptomatic with incidental findings of radiological diagnostic images. Common clinical findings include tenderness on palpation, decreased range of motion, swelling and joint effusion [2, 3]. If the cyst is large enough, it may mechanically obstruct the knee during motion.

According to Plotkin *et al*. [3], if the cysts anterior to the ACL, they tend to limit extension, whilst the cysts posterior to the ACL may limit flexion. Even for symptomatic patients, history and physical exam alone are not enough to make the diagnosis. Magneric resonance imaging is the choice of investigation for further evaluation and diagnosis [2, 3].

The irritation or trauma to the synovium covering the ACL may initiate the release of hyaluronic acid and the production of mucin, which may lead to ganglion formation. Cysts associated with the ACL tend to be fusiform and oriented parallel to its fibres [3]. For the management of ACL cysts, there are few options described in the literature such as functional treatment, computed tomographic scan or ultrasound-guided aspiration [2-4].

Surgical treatment includes arthroscopic excision or resection and debridement [4]. ACL reconstruction is not described in the literature as a treatment option, however, association with ACL tears was explained [3]. The absence of ACL reconstruction as treatment option for these cases is probably due to its rarity.

CONCLUSION

The lesion of our case was an ACL ganglion cyst clinically with additional comments of increased vascularity from histopathology. There may be a question arising from this case on what caused the destruction of ACL. Nevertheless, we would like to emphasise that in case of nonfunctional ACL due to its destruction, ACL reconstruction could be the choice of treatment.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' contributions

All the authors had contributions to the case report. LB = collected the data and analysed and written up. AC and ACE = had contribution to the literature review and discussions. FB = had contribution to diagnostic features and interpretation of data. ME = was the main surgeon of the case, involved at all the stages. All the authors are conversant with the content and agreed with the final version.

REFERENCES

1. Sonnery-Cottet B, Guimarães TM, Daggett M, Pic JB, Kajetanek C, de Padua VB, et al. Anterior cruciate ligament ganglion cyst treated under computed tomography - Guided aspiration in a professional soccer player. Orthop J Sports Med 2016;4:2325967116644585.
2. Parish EN, Dixon P, Cross MJ. Ganglion cysts of the anterior cruciate ligament: a series of 15 cases. Arthroscopy 2005;21:445-7.
3. Plotkin B, Agarwal VK, Varma R. Ganglion cyst of the anterior cruciate ligament. Radiol Case Rep 2009;4:309.
4. Su Y, Bai L. [Diagnosis and treatment of anterior cruciate ligament cysts]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi 2011;25:650-2 [Article in Chinese]
5. Tzurbakis M, Mouzopoulos G, Morakis E, Nikolaras G, Georgilas I. Intra-articular knee haemangioma originating from the anterior cruciate ligament: a case report. J Med Case Rep 2008;2:254.
6. Drosos GI, Pozo JL. Large extrasynovial intracapsular ganglia of the knee: a report of 3 cases. Arthroscopy 2005;21:1362-5.

The European Research Journal 2020;6(3):260-264 Case Report

DOI: 10.18621/eurj.510830 *Pathology & Otorhinolaryngology*

Sinonasal sarcoidosis: a case report

Selma Erdoğan Düzcü[1], Serap Köybaşı Şanal[2]

[1]Department of Pathology, Bolu Abant İzzet Baysal University School of Medicine, İzzet Baysal Training and Research Hospital, Bolu, Turkey
[2]Department of Otorhinolaryngology, Bolu Abant İzzet Baysal University School of Medicine, İzzet Baysal Training and Research Hospital, Bolu, Turkey

ABSTRACT

Objectives: Sarcoidosis is an idiopathic and multisystemic chronic disease characterized by non-caseating granulomas. Sinonasal sarcoidosis may be seen in an isolated form or related to a multisystemic disease. A 48-year-old female patient visited the otolaryngology department with complaints of headache and nasal obstruction for two years. The physical examination revealed a saddling on the nose, and crusted fragile mucosa was observed bilaterally in nasal endoscopy. Paranasal CT showed invasion of the right orbita. In chest X-ray, there was bilateral hilar enlargement, and lung biopsy revealed non-caseating granulomas. A bilateral endoscopic sinus surgery was applied to the patient. Upon histopathological demonstration of multiple non-caseating granulomas in the specimen, the diagnosis of sinonasal sarcoidosis was made. The patient responded well to the following steroid treatment. Although rare, sarcoidosis should be taken into consideration in differential diagnosis of sinonasal diseases.

Keywords: sarcoidosis, sinonasal involvement, non-caseating granulomas

Sarcoidosis is an idiopathic and multisystemic chronic disease characterized by non-caseating granulomas [1, 2]. The primary site of involvement is the lung [3]. It mostly affects young and middle-aged women [4].

The pathological background of sarcoidosis is not clear. It is thought to be triggered by an oligoclonal CD4 positive T cell response to an unknown antigen with the effects of environmental factors (e.g. bacteria, viruses, fungi, bugs, inorganic particles) [5, 6].

Sinonasal sarcoidosis may be seen in an isolated form or related to a multisystemic disease [2]. Nasal localization constitutes less than 2% of cases and is rare [7]. A case of nasal sarcoidosis alongside systemic attachment was first reported by Boeck in 1905 [2]. Its otorhinolaryngologic signs and symptoms are not specific and are similar to the signs of other more common diseases [9]. The most common symptom is nasal obstruction [4]. The diagnosis of sarcoidosis is made through clinical, radiologic and histologic examinations together [7].

The aim of this case presentation is to report the clinicopathologic characteristics of a sinonasal sarcoidosis case as a part of a multisystemic disease.

CASE PRESENTATION

A 48-year-old female patient admitted the otolaryngology department with complaints of nasal obstruction and headache for two years. The patient's medical history revealed neither allergies nor usage of

Received: ***January 9, 2019;*** *Accepted:* ***May 18, 2019;*** *Published Online:* ***January 27, 2020***

How to cite this article: *Erdoğan Düzcü S, Köybaşı Şanal S. Sinonasal sarcoidosis: a case report. Eur Res J 2020;6(3):260-264. DOI: 10.18621/eurj.510830*

Address for correspondence: *Selma Erdoğan Düzcü, MD., Bolu Abant İzzet Baysal University School of Medicine, İzzet Baysal Training and Research Hospital, Department of Pathology, Bolu, Turkey. E-mail: serdoganduzcu@hotmail.com*

e-ISSN: 2149-3189

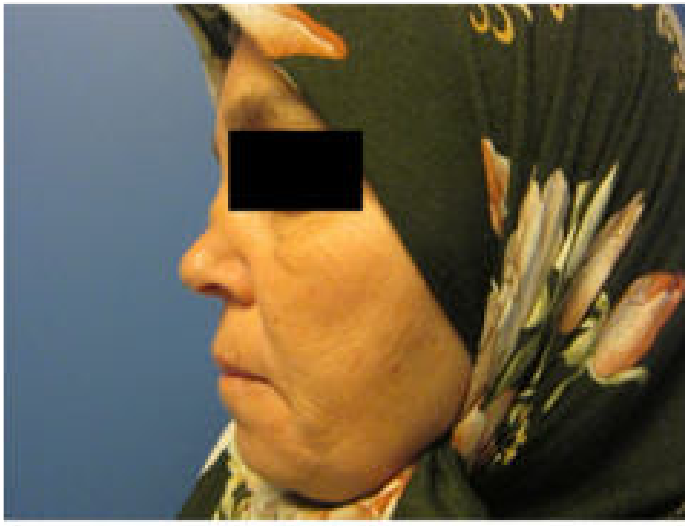


Fig. 1. Saddle nose appearance.

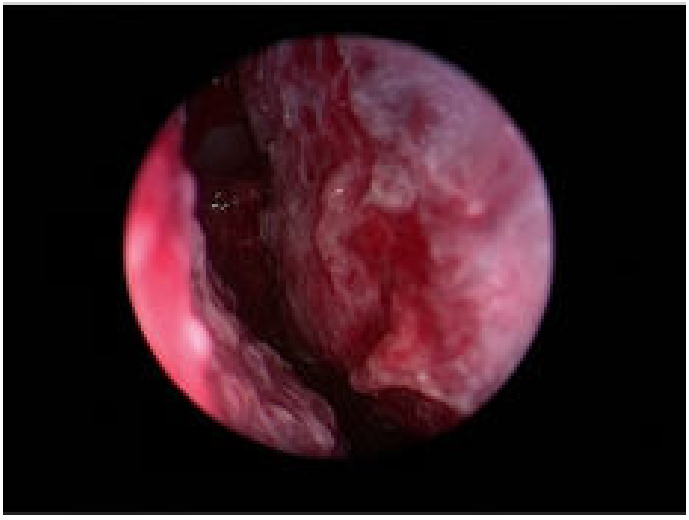


Fig. 2. In the endoscopic examination of the nose, the nostrils were full of granular tissue.

alcohol or tobacco.

The external nose had a saddle nose appearance (Fig. 1). In the endoscopic examination of the nose, the bilateral nose, septum, nasal lateral wall, inferior concha mucosa had crusted granular and fragile appearance. The nostrils were full of granular tissue. The right middle concha was eroded (Fig. 2).

Paranasal CT revealed soft tissue density in both anterior and posterior ethmoidal cells and the maxillary sinuses. The lamina papyracea was observed to be eroded, and the medial rectus muscle was compressed. A bilateral functional endoscopic sinus surgery (FESS) was planned. In the preoperative work up, a pulmonology consultation was performed because of bilateral hilar enlargement. Thorax CT showed bilateral hilar, mediastinal lymphadenopathy and nodular opacity. Non-caseating granulomas were diagnosed via lungbiopsy that was taken endobronchially at an external medical center.

A bilateral functional endoscopic sinus surgery was applied both to get a histopathological diagnosis and avoid any possible orbital complication of the disease such as diplopia. The granulomatous tissue that filled the nasal cavity and obliterated the bilateral posteroanterior ethmoidal cells and the maxillary sinuses was removed. The right lamina papyracea was

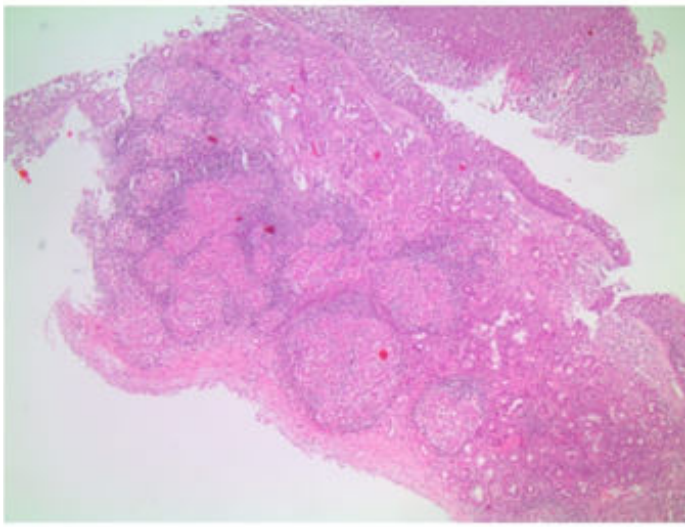


Fig. 3. The view of granulomas under the respiratory epithelium (H-E staining, ×40).

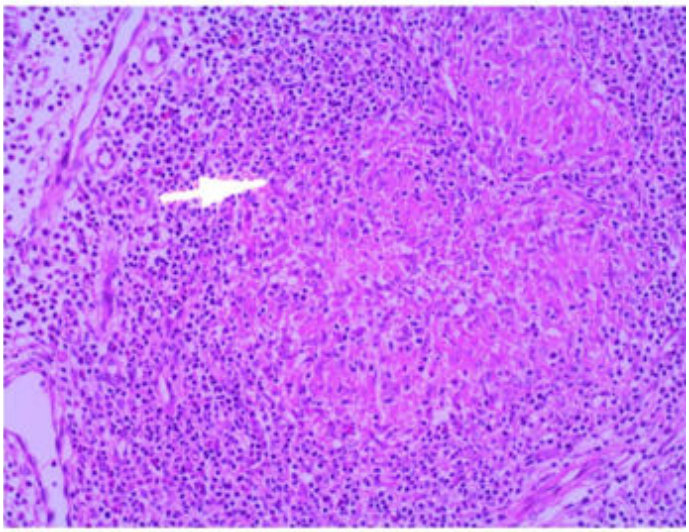


Fig. 4. The granuloma was composed of epitheloid histiocytes, mature mononuclear cells (lymphocytes)(H-E staining, ×200).

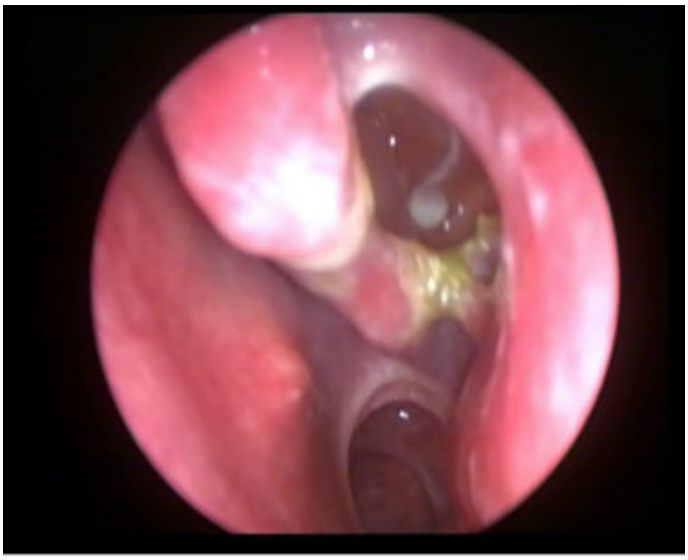


Fig. 2. In the endoscopic examination of the nose, the nostrils were full of granular tissue.

observed to be eroded, and the pressure over the right orbita was released. Repairing the saddle nose deformity was postponed to another operation after the histological diagnosis and medical treatment.

In the microscopic examination performed in the pathology department, mature mononuclear cells (lymphocytes), epithelioid histiocytes and Langhans-type multinuclear giant cell multiple granuloma structures were observed. No caseification necrosis or suppurative necrosis was seen in the granulomas [Figs. 3 and 4]. Since the observation of a non-caseating granulomatous inflammation suggested sarcoidosis, a differential diagnosis was required. Although the absence of caseification made the diagnosis of tuberculosis less likely, an additional EZN (Ehrlich-Ziehl-Neelsen) staining was applied, and no mycobacteria were observed. No staining was observed with the PAS histochemical stain, which is applied for fungi, either. Combining these histopathological findings with the clinical presentation, a diagnosis of sarcoidosis was made. The patient received steroid treatment starting with 40 mg per day and tapering the dose in weeks. The bilateral hilar enlargement was observed to respond well.

In the ENT evaluation, the complaints of the patient were completely relieved. In the endoscopic nasal examination, granular whitish mucosa was seen to turn into a normal appearance in color and nature, with tiny polypoid structures observed in the ethmoidectomy cavities (Fig. 5).

DISCUSSION

Sarcoidosis is a complex disorder in which head and neck involvement may be observed in 10-15% of the cases; however, sinonasal involvement is reported in about only 1% of cases of sarcoidosis [10]. Sarcoidosis may involve both the mucosa and cartilaginous and bony structures beneath the mucosa in the nose and the paranasal sinuses. Despite the presence of clinical findings, imaging and tissue diagnosis are needed for confirmation of the disease. It is important to understand and differentiate sarcoidosis as it may involve vital structures in this area [11].

Sinonasal sarcoidosis most often attaches to the septum mucosa and the inferior turbinate. In some patients, nasal bone lesions may also be seen. Sinonasal sarcoidosis may be clinically classified as atrophic, hypertrophic, destructive and nasally widening [12]. In our case, it could be accepted to be both hypertrophic and destructive.

In some cases, as in ours, nasal involvement may be the first sign followed by pulmonary disease [4]. A tissue biopsy is necessary to ascertain the diagnosis [4]. The observation of opacification and the presence of non-caseating granuloma are important in its discrimination from other granulomatous diseases [13]. Beside non-caseating granuloma structures, hyaline fibrosis and necrosis may also be seen in the histopathology [4]. In our case, focal necrosis was also present. In sarcoid granuloma, wide, pale epithelioid histiocytes with oval nuclei are observed, and T lymphocytes may be seen to surround the histiocytes [14]. Additionally, multinuclear Langhans-type giant cells may be observed [6, 10]. The giant cells seen in sarcoidosis may be larger than the giant cells seen in tuberculosis, and they may have more nuclei [6]. In the giant cells, intracytoplasmic inclusion objects known as asteroid and Schaumann bodies may be found [6].

Differential diagnosis of sinonasal sarcoidosis includes Wegener granulomatosis, fungal infections, foreign body reactions and lymphoma [14]. In the histopathology of Wegener granulomatosis, the presence of leukocytoclastic vasculitis or necrotizing granulomas help differentiate the disease [13]. In James *et al.*'s [8]retrospective analysis with 1686 patients, 8.3% patients were noted non-pulmonary

sarcoidosis with biopsy proven. Among the 1944 different sinus surgery materials Van der Boer *et al*. [15] reported, only 3 patients were reported to have sarcoidosis. Since the suspicion of clinical sarcoidosis was supported with pathological examination, the necessity of FESS was stressed [15]. Our patient had both septal and paranasal sinus involvement. Braun *et al*. [2] reported 15 (8 male, 7 female)sinonasal sarcoidosis cases. In one of those cases, a saddle nose deformity was present in similarity to our case. In 12 patients, there were sarcoidosis in the sinonasal area and the lungs [2]. Kirsten *et al*. [1] reported 12 (4 females, 8 males) sinonasal sarcoidosis cases proven through biopsy. All of the cases were applied sinus surgery and corticosteroid treatments similar to our case. The most common attachment location in these patients was the maxillary sinus. All cases had lymph nodes and pulmonary involvement [1].

In a case of sinonasal sarcoidosis in a 48-year-old male patient reported by Mazziotti *et al*. [4], perineural spreading was observed around the trigeminal and Vidian nerves. In the nasal mucosa biopsy, non-caseating granulomas were seen, and through the presence of hilar lymphadenopathy, the diagnosis of sarcoidosis was supported [3].

Systemic or topical use of steroids is commonly used modalities in treatment of sinonasal sarcoidosis [4]. However endoscopic sinus surgery may also be applied in selected cases such as intraorbital complication risk, massive disease and in case of medical treatment failure [4]. In our case, we applied surgery because of the massive granulations and intraorbital invasion risk. Additional topical steroids were applied to help control the local disease and systemic steroids for the pulmonary component [4]. Sinus surgery may decrease the need for systemic steroid use [4]. Gulati *et al*. [11] reported seven cases of sinonasal sarcoidosis, three of whom were treated with only systemic prednisolone. The remaining four cases were reported to undergo sinus surgery and topical steroids treatments [11]. In cases where the use of systemic corticosteroids is contraindicated, methotrexate is also stated to be usable [14].

CONCLUSION

Sinonasal involvement of sarcoidosis is a rare condition. Nasal crusting and obstruction being the most common complaints, this may be confused with other inflammatory nasal diseases, so differential diagnosis is important. It is usually accompanied by pulmonary involvement; however, it may be seen as isolated in that area. Treatment of sinonasal sarcoidosis depends upon the site and extent of the disease including oral and/or intranasal steroids, and in some cases, low-dose methotrexate. Sinus surgery may be necessary in the management of selected cases.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contributions

Concept – S.E.D., S.K.Ş.; Design - S.E.D., S.K.; Supervision - S.E.D., S.K.; Resource - S.E.D., S.K.; Materials - S.E.D., S.K.; Data Collection and/ or Processing - S.E.D., S.K.; Analysis and/or Interpretation - S.E.D., S.K.; Literature Search - S.E.D., S.K.; Writing - S.E.D., S.K.; Critical Reviews - S.E.D., S.K.

REFERENCES

1. Kirsten AM, Watz H, Kirsten D. Sarcoidosis with involvement of the paranasal sinuses - a retrospective analysis of 12 biopsy-proven cases. BMC Pulm Med 2013;13:59.
2. Braun JJ, Gentine A and Pauli G. Sinonasal sarcoidosis: review and report of fifteen cases. Laryngoscope 2004;114:1960-3.
3. Mazziotti S, Gaeta M, Blandino A, Vinci S, Pandolfo I. Perineural spread in a case of sinonasal sarcoidosis: case report. AJNR Am J Neuroradiol, 2001;22:1207-8.
4. Erbek S, Erbek SS, Tosun E, Çakmak O. A rare case sarcoidosis involving the middle turbinates: an incidental diagnosis. Diagn Pathol 2006;1:44.
5. Bianchini C, Tosin E, Ciorba A, Pelucchi S, Pastore A. Subcutaneoussarcoidosis: a rare involvement of the paralateral nasal region. Acta Otorhinolaryngol Ital 2011;31:118-20.
6. Mekhail P, Abo-Khatwa M, El-Hawary A, Khan A. Cutaneous nasal nodule: a warning sign for sinonasal sarcoidosis. Internet J Head Neck Surg 2008;3(1).

7. Mahfoudhi M, Khammassi K, Turki S, Salah MB. Systemic sarcoidosis revealed by a nasal lesion: a case report. Int J Clin Med 2015;6:257.
8. James WE, Koutroumpakis E, Saha B, Nathani A, Saavedra L, Yucel RM, et al. Clinical features of extrapulmonary sarcoidosis without lung involvement. Chest 2018;154:349-56.
9. Dessouky OY. Isolated sinonasal sarcoidosis with intracranial extension: case report. Acta Otorhinolaryngol Ital 2008;2:306-8.
10. McCaffrey TV, McDonald TJ. Sarcoidosis of the nose and paranasal sinuses. Laryngoscope 1983;93:1281-4.
11. Gulati S, Krossnes B, Olofsson J, Danielsen A. Sinonasal involvement in sarcoidosis: a report of seven cases and review of literature. Eur Arch Otorhinolaryngol 2012;269:891-6.
12. Badhey AK, Kadakia S, Carrau RL, Iacob C, Khorsandi A. Sarcoidosis of the head and neck. Head Neck Pathol 2015;9:260-8.
13. Helliwell TR. Non-infectious inflammatory lesions of the sinonasal tract. Head Neck Pathol 2016;10:32-9.
14. McCaffrey TV. Nasal manifestations of systemic dieseases. Otolaryngol Pol 2009;63:228-35.
15. Van den Boer C, Brutel G, de Vries N. Is routine histopathological examination of FESS material useful? Eur Arch Otorhinolaryngol 2010;267:381-4.

The European Research Journal 2020;6(3):265-267 Case Report

DOI: 10.18621/eurj.478539 *Dermatology*

Graham Little-Piccardi-Lassueur syndrome in a male patient: a case report

Sevgi Kulaklı[1], İlkay Ay[2]

[1]*Department of Dermatology, Giresun University School of Medicine, Giresun, Turkey*
[2]*Department of Pathology, Giresun University Prof. Dr. A. İlhan Özdemir Training and Research Hospital, Giresun, Turkey*

ABSTRACT

Graham Little-Piccardi-Lassueur syndrome is a type of lichen planopilaris characterized by the triad of patchy cicatricial alopecia of the scalp, non-cicatricial alopecia of the axilla and pubis, and follicular spinous papules on the body, scalp or both. This rare syndrome primarily affects middle-aged postmenopausal women with only three male cases being reported in literature. Herein we report a 53-year-old man who is fourth male patient diagnosed with Graham Little-Piccardi-Lassueur syndrome up to now.

Keywords: Graham Little-Piccardi-Lassueur syndrome, lichen planopilaris, male

Graham Little-Piccardi-Lassueur syndrome (GLPLS) is a type of lichen planopilaris characterized by the triad of patchy cicatricial alopecia of the scalp, non-cicatricial alopecia of the axillae and pubis, and follicular spinous papules on the body, scalp or both [1]. It is more common in postmenopausal women, with only few male cases being reported in literature [2]. Here we report a 53-year-old man diagnosed with GLPLS who is fourth male patient in the literature.

CASE PRESENTATION

A 53- year-old male patient presented with loss of hair on scalp, axilla, pubic region, arms and legs. The symptoms had started 40 years ago with hair loss on scalp, over the years the hair loss spread axilla, pubic region, arms and legs. He also complained of small pruritic lesions on the trunk, abdomen, forearms and thighs. He has no family history and received no treatment before.

Scarring alopecia on parietal area of scalp with multiple dilated follicular orifices plugged with keratotic debris and perifollicular violaceous hyperpigmentation was present on examination. There was axillar and pubic hypotrichosis without skin atrophy. Multiple follicular-oriented keratotic papules, perifollicular erythema and hair loss were present on the trunk, forearms and legs (Fig. 1).

Laboratory tests including hemogram, blood sugar, renal, liver and thyroid function tests, viral markers for hepatitis B and C, and serum antinuclear antibody levels were normal. Skin biopsy from the follicular papules on forearms showed follicular plugging, necrotic keratinocytes, basal vacuolar degeneration and dense band-like lymphocytic infiltration in superior segment of follicular epithelium (Fig. 2). Based on these findings, the patient was diagnosed with GLPLS and oral isotretinoin and topical corticosteroid treatments were started.

Received: *November 5, 2018;* ***Accepted:*** *November 26, 2019;* ***Published Online:*** *January 23, 2020*

How to cite this article: *Kulaklı S, Ay İ. Graham Little-Piccardi-Lassueur syndrome in a male patitent: a case report. Eur Res J 2020;6(3):265-267. DOI: 10.18621/eurj.478539*

Address for correspondence: *Sevgi Kulaklı, MD., Giresun University School of Medicine, Department of Dermatology, Giresun, Turkey. E-mail: sevgi.c@gmail.com*

e-ISSN: 2149-3189

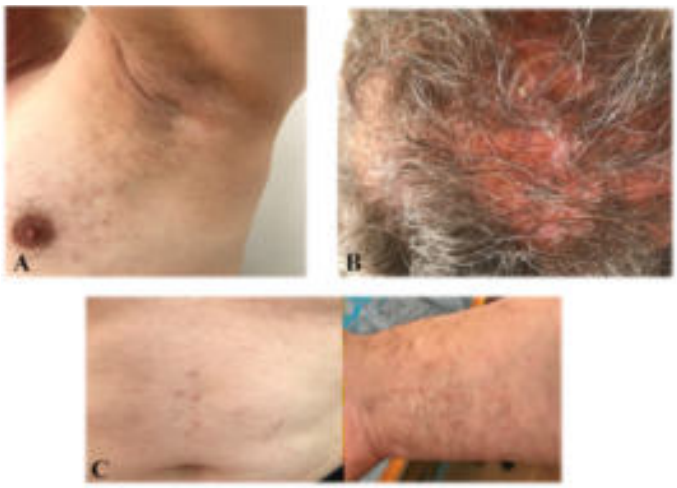


Fig. 1. (A) Axillar hypotrichosis without skin atrophy, (B) Alopecic areas with perifolicular erythema and desquamation, and (C) Folicular keratoic papules on abdomen and forearms.

DISCUSSION

GLPLS was initially described by Picardi in 1913 as a case of progressive scalp cicatricial alopecia, non-cicatricial alopecia in the axilla and pubic region, and follicular spinous papules on the trunk and extremities. Graham Little, in 1915 published a similar case of a woman observed by Lassueur, followed by many similar reports later [3]. A Pubmed search from 1951 to 2018 produced fewer than 50 cases of GLPLS in the literature and only three of them were male [4-6].

The etiology of GLPLS is unknown, but it is likely similar to the T-cell mediated immunological mechanism that triggers the clinical expression of lichen planus [7]. An autoimmune response against the inner centromere protein (INCENP) was reported in a patient with GLPLS. This protein is considered to be one of main antigen in this syndrome [8]. Few cases describing a familial pattern (HLA DR-1), association with hepatitis B vaccination and two female patients with androgen insensitivity syndrome have been reported [9-12].

Clinically, scarring alopecia often precedes the follicular eruption and the course of disease is slowly progressive [13]. Pruritus often can be severe although it is not always constant [4]. Most patients present with well-defined clinical findings that represent symptoms of the triad of GLPLS; however these findings need not present simultaneously [9]. Histopathology reveals a perifollicular lymphocytic infiltrate at the level of the infindibulum and the isthmus, along with vacuolar changes of the outer root sheath. More developed cases show perifollicular fibrosis and epithelial atrophy at the level of the infindibulum and the isthmus [14].

Treatment of GLPLS is really difficult. Topical, intralesional and systemic corticosteroids, retinoids, psoralen plus ultraviolet A (PUVA) photochemotherapy, antimalarials, topical tacrolimus, thalidomide and cyclosporin have been used with limited success [15].

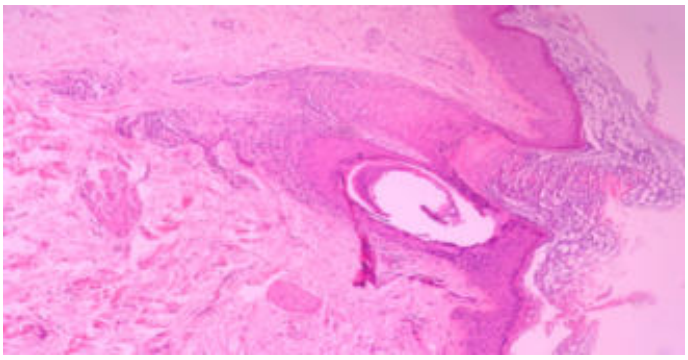


Fig. 2. Follicular plugging, necrotic keratinocytes, basal vacuolar degeneration and lymphocytic infiltration of follicular epithelium.

CONCLUSION

In conclusion, we reported this case because of extreme rarity of presentation in males. When similar clinical findings seen in a male patient like this case, GLPLS should be suspected.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Odom RB, James WD, Berger TG, editors. Andrews' Diseases

of the skin. Lichen planus and reletad conditions. 9th ed. Philadelphia: WB Saunders Company, 2000: pp. 274-5.
2. Assouly P, Reygagne P. Lichen planopilaris: update on diagnosis and treatment. Semin Cutan Med Surg 2009;28:3-10.
3. Graham-Little EG. Folliculitis decalvans et atrophicans. Br J Dermatol 1915;27:183-5.
4. Srivastata M, Mikkilineni R, Konstadt J. Lassueur-Graham Little-Piccardi syndrome. Dermatol Online J 2007;13:12.
5. Pai VV, Kikkeri NN, Sori T, Dinesh US. Graham Little-Picardi-Lassueur syndrome: an unusual variant of follicular lichen planus. Int J Trichology 2011;3:28-30.
6. Laszlo FG. Graham Little-Picardi-Lassueur syndrome: a case report and review of the syndrome in men. Int J Dermatol 2014;53:1019-22.
7. Teherney G, Nenoff P. Antigen mimicry followed by epitope spreading: a pathogenetic trigger for the clinical morphology of lichen planus and its transition to Graham Lassueur Piccardi Little syndrome and keratosis lichenoides chronic - Medical hypotesis or reality? Ann Bras Dermatol 2009;84:682-8.
8. Rodriguez-Bayona B, Ruchaud S, Rodriguez C, Linares M, Astola A, Ortiz M, et al. Autoantibodies against the chromosomal passenger protein INCENP found in a patient with Graham Little-Picardi-Lassueur syndrome. J Autoimmune Dis 2007;4:1.
9. Viglizzo G, Verrini A, Rongioletti F. Familial Lassueur-Graham Little-Piccardi syndrome. Dermatology 2004;208:142-4.
10. Bardazzi F, Landi C, Orlandi C, Neri I, Varotti C. Graham Little-Piccardi-Lassueur syndrome following HBV vaccination. Acta Derm Venereol 1999;79:93.
11. Vega Gutiérrez J, Miranda-Romero A, Pérez Milán F, Martínez García G. Graham Little-Piccardi-Lassueur syndrome associated with androgen insensitivity syndrome (testicular feminization). J Eur Acad Dermatol Venereol 2004;18:463-6.
12. Graham Little-Picardi-Lassueur syndrome in a patient with androgen insensitivity syndrome. Int J Dermatol 2016;55:211-2.
13. Ghislain PD, Van Eeckhout P, Ghislain E. Lassueur-Graham Little-Piccardi syndrome: a 20-year follox-up. Dermatology 2003;206:391-2.
14. Elder DE, Elenitsas R, Johnson BL, Murthy GF, editors. Lever's Histopathology of skin. Non infectious eythematous papular and squamous disease. 9th ed. Philadelphia: Lippincott William, 2005: pp. 179-214.
15. Hixon C, Blattner CM, Hurd D. Graham-Little-Piccardi-Lassueur syndrome: a case report. JAOCD 2015;33:36-7.

The European Research Journal 2020;6(3):268-269 Letter to the Editor

DOI: 10.18621/eurj.666806 *Immunology*

May cyproheptadine be a treatment choice for prophylaxis of PFAPA syndrome?

Arzu Ekici

Department of Pediatric Neurology, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

Dear Editor,

Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA syndrome) is a common periodic fever syndrome in Turkey. PFAPA is an auto inflammatory syndrome characterized by periodic episodes of recurrent febrile episodes associated with aphthous stomatitis, pharyngitis and cervical adenitis. Febrile episodes last 3 to 6 days and recur about every 3-8 weeks. The syndrome causes fatigue, chills, and occasionally abdominal pain and headache, as well as fever, pharyngitis, aphthous ulcers, and lymphadenopathy. Children are healthy between episodes, and have normal growth and development

There is no specific treatment to cure PFAPA and the treatment is optional. Single dose prednisolone therapy during attack, and tonsillectomy are the treatment options [1]. Cyproheptadine (CH) was started for migraine patients with PFAPA. I observed that the attack intervals was prolonged. I also noticed that attacks of PFAPA was exacerbated if the CH was cessated. CH is known that serotonin increases the release of pro-inflammatory cytokines and CH is a potent antiserotonergic drug.

The pathogenesis of PFAPA is known to be related to proinflammatory cytokines. Interferon-ϒ (IFN-ϒ), tumor necrosis factor-α (TNF-α), IL-1b, IL-6, and IL-12 concentrations elevate during attacks in PFAPA [2, 3]. Serotonin is a neurotransmitter released by activated platelets. Functional studies showed that serotonin is a potent regulator of human dendritic cell unction, increase the release of pro-inflammatory cytokines such as IL-1beta, IL-6, IL-8/CXCL8, IL-12p40 and tumor necrosis factor-alpha (TNF-alpha) [4]. Cimetidine, a selective histamine-2 receptor antagonist was recommended to use for prophylaxis and reduce the attacks of PFAPA syndrome. It inhibits suppressor CD8+ T-lymphocyte activation and chemotaxis [5]. Histamine-2 receptor antagonist markedly decreased serotonin concentrations by the prolonged treatment. I observed that CH is particularly useful for prophylaxis of PFAPA.

My hypothesis is that "May serotonin be an important role of pathogenesis of PFAPA? May CH be a choice for prophylaxis of PFAPA? Serotonin may play an important role in PFAPA and serotonin antagonist drugs such as CH may be a treatment choice for prophylaxis of PFAPA. This new medical hypothesis must be confirmed with clinical observational studies. And also my hypothesis should be evaluated with studies related to serotonin levels in PFAPA.

Conflict of interest

The author disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The author disclosed that they did not receive any

Received: ***December 28, 2019;*** ***Accepted:*** ***January 31, 2020;*** ***Published Online:*** ***February 27, 2020***

How to cite this article: *Ekici A. May cyproheptadine be a treatment choice for prophylaxis of PFAPA syndrome?. Eur Res J 2020;6(3):268-269. DOI: 10.18621/eurj.666806*

Address for correspondence: *Arzu Ekici, MD., Associate Professor, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Pediatric Neurology, Bursa, Turkey. E-mail: drarzuekici@gmail.com, Tel: +90 224 295500/3106*

c-ISSN: 2149-3189

grant during conduction or writing of this study.

Acknowledgement

This article does not contain any studies with animals and human participants. This article contains a clinical observation based hypothesis.

REFERENCES

1. Feder HM, Salazar JC. A clinical review of 105 patients with PFAPA (a periodic fever syndrome). Acta Paediatr 2010;99:178-84.
2. Thomas KT, Feder HM Jr, Lawton AR, Edwards KM. Periodic fever syndrome in children. J Pediatr 2013;135:15.
3. Stojanov S, Hoffmann F, Kéry A, Renner ED, Hartl D, Lohse P, et al. Cytokine profile in PFAPA syndrome suggests continuous inflammation and reduced anti-inflammatory response. Eur Cytokine Netw 2006;17:90-7.
4. Müller T, Dürk T, Blumenthal B, Grimm M, Cicko S, Panther E, et al. 5-hydroxytryptamine modulates migration, cytokine and chemokine release and T-cell priming capacity of dendritic cells in vitro and in vivo. PLoS One 2009;4:e6453.
5. Taniguchi K, Ono N, Sakai T, Ichiyama Y, Uemichi K. Response to cimetidine in a 1-year-old child with PFAPA syndrome. Turk J Pediatr 2016;58:687-9.