E-ISSN 2602-4837

The Turkish Journal of Ear Nose and Throat

Volume 31, Number 4 / December 2021

İSTANBUL UNIVERSITY PRESS

The Turkish Journal of Ear Nose and Throat
E-ISSN 2602-4837
Volume 31, Number 4 / December 2021

INDEXING AND ABSTRACTING

TÜBİTAK-ULAKBİM TR Index

DOAJ

OWNER

Prof. Dr. Tufan TÜKEK
Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

RESPONSIBLE MANAGER

Prof. Dr. Bülent BAYRAKTAR
Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

CORRESPONDENCE ADDRESS

Istanbul University, Istanbul Faculty of Medicine Deanery, Publication Commission
Turgut Özal Caddesi 34093 Çapa, Fatih, Istanbul, Turkey
Phone: +90 (212) 414 21 61
E-mail: tr-ent@istanbul.edu.tr
https://dergipark.org.tr/tr/pub/trent
https://iupress.istanbul.edu.tr/tr/journal/tr-ent/home

PUBLISHER

Istanbul University Press
Istanbul University Central Campus,
34452 Beyazit, Fatih / Istanbul, Turkey
Phone: +90 (212) 440 00 00

Yayın dili İngilizce'dir.
The publication language of the journal is English.

Mart, Haziran, Eylül ve Aralık aylarında, yılda dört sayı olarak yayımlanan uluslararası, hakemli, açık erişimli ve bilimsel bir dergidir.
This is a scholarly, international, peer-reviewed and open-access journal published quarterly in March, June, September and December.

Publication Type: Periodical

The Turkish Journal of Ear Nose and Throat
E-ISSN 2602-4837
Volume 31, Number 4 / December 2021

EDITORIAL MANAGEMENT BOARD

The Turkish Journal of Ear Nose and Throat
E-ISSN 2602-4837
Volume 31, Number 4 / December 2021

EDITORIAL ADVISORY BOARD

The Turkish Journal of Ear Nose and Throat
E-ISSN 2602-4837
Volume 31, Number 4 / December 2021

CONTENTS

RESEARCH ARTICLE
DOI: 10.26650/Tr-ENT.2021.1027401
The Turkish Journal of Ear Nose and Throat 2021;31(4):81-85

Investigation of Injuries Due to Different Types of Button Batteries Stuck in Ear Canals

Gökhan Akgül[1], Mustafa Bakırtaş[2]

[1]University of Health Sciences, Samsun Health Practices and Research Center, Department of Otorhinolaryngology, Samsun, Turkey
[2]University of Health Sciences, Samsun Health Practices and Research Center, Department of Pathology, Samsun, Turkey

ORCID ID: G.A. 0000-0003-0699-6585; M.B. 0000-0003-3185-6947

Citation: Akgul G, Bakirtas M. Investigation of injuries due to different types of button batteries stuck in ear canals. Tr-ENT 2021;31(4):81-85. https://doi.org/10.26650/Tr-ENT.2021.1027401

ABSTRACT

Objective: Button Batteries (BB) stuck in the Ear Canal (EC) have a special importance among foreign bodies in terms of causing complications depending on the length of time they remain in place, especially in children. In the present study, the purpose was to compare the damaging effects of frequently used BB chemicals on EC and the differences among them.
Material and Methods: After 4 EC models prepared from freshly frozen cadaveric bovine ears were thawed, Lithium, Alkaline, Silver-oxide, and Zinc-air BBs with similar size were placed respectively in the canals as the negative poles in contact with the skin. The voltage, tissue temperatures, and pHs of the BBs were measured and visual damage was photographed at the 3rd, 6th, 12th, and 24th hours. The BBs were removed at the end of the 24th hour, and EC models were examined histopathologically in a single-blind manner.
Results: Although the visual damage could be observed in the first 1.5 hours in ECs with Lithium, Alkaline, and Silver-oxide BBs, it was observed that this time extended to 2.5 hours in Zinc-air. The highest pH value was measured in lithium BB at the end of 24 hours, and the lowest pH value was measured in Zinc-air BB. The least voltage loss was measured in alkaline BB, and not all BB types caused significant changes in tissue temperatures for 24 hours. No significant tissue necrosis depth was detected in Zinc-air BB, but it was most common in Lithium, Silver-oxide, and Alkaline BBs, respectively.
Conclusion: All BB chemicals, especially Lithium BB, might cause alkaline necrosis at varying degrees by increasing the pH in EC models without any heat change. Zinc-air BBs, which are generally used in hearing aids, appear to have less damage potential compared to others.

Keywords: Button battery, foreign bodies, ear canal, alkaline necrosis

INTRODUCTION

The upper aerodigestive system and EC foreign bodies pose a common problem, especially in the patient group of pediatric age (1). Foreign bodies are detected in advanced age groups, especially in mental retardation and patients with Alzheimer's Disease. Unlike other foreign bodies, BBs can cause serious complications (2, 3).

The use of BBs in devices such as hearing aids, household appliances, electronic toys, watches, and digital gadgets has increased (4). The shape and bright form of BBs attract the attention, especially from children (5). BB foreign bodies can be asymptomatic or have dangerous effects, which can cause fatal outcomes (4, 6). The clinical course of BBs depends on many factors (5). These factors include time; localization; type, size, and voltage of the battery; humidity; and chemical contents (5, 7). Although BBs that are stuck in EC can often be detected and removed early, cases that are admitted with complications were also reported. In the ECs of young children, the mentally retarded, and elderly dementia patients, the diagnosis of BBs may be delayed if there is no eyewitness, and the risk of complications because of the long stay increases (8). Also, the bloody and moist environment created in ECs when non-specialists try to remove BBs may cause rapid discharge from the BBs and increase the damage. Potential complications caused by BBs trapped in the EC include stenosis of the canal, tympanic membrane perforation, hearing loss, and ossicular and vestibular damage (9).

Four different chemicals, lithium (CR), alkaline (LR), zinc-air (PR), and silver oxide (SR), are frequently used in the BB

Corresponding Author: Gökhan Akgül **E-mail:** g.akgul-57@hotmail.com

Submitted: 23.11.2021 • **Accepted:** 09.12.2021 • **Published Online:** 16.12.2021

industry. BBs might have similar sizes but different voltages and chemical contents. Although Lithium and Alkaline BBs are mostly used in small electronic devices (i.e. watches, toys, etc.), Zinc-air constitutes most of the chemicals often used in hearing aids (10).

The damage caused by BBs and other foreign bodies in EC was discussed in the literature with case reports (11). The damaging effects of commonly used BB chemicals and the differences between them were investigated in the present study with *in vitro* EC models.

MATERIALS AND METHODS

The ethical aspect of this study was approved by the Ondokuz Mayıs University (OMU) Animal Experiments Local Ethics Committee (HADTEK) (68489742-604.01.03-E.18528, date: 23.10.2020), and the study was conducted in the Samsun Health Practices and Research Center Pathology Laboratory.

After EC preliminary models obtained from freshly frozen cadaveric cattle heads at similar size were thawed at room temperature (22°C), 4 EC models were prepared in the form of a ring (approximately 2-cm-long segments) in a way that the canal and skin integrity were preserved.

Lithium BB (CR927), Alkaline (LR736), Silver-oxide (SR736), and Zinc-air (PR41) BBs, respectively, were placed in the channel of each EC model with the negative poles in contact with the skin. All EC models were wetted with saline spray (pH: 6.8) for 2 puffs/30 min for 24 hours. The size and different characteristics of BBs are summarized in Table 1.

BBs were removed from all EC models with forceps at the end of the 3rd, 6th, 12th, and 24th hours, and their voltages were measured with a digital voltmeter (UNI-T UT 33D Digital Auto Range Multimeter, Dongguan City, China), tissue pH values were determined with litmus papers (Merck KGaA, Darmstadt, Germany), and tissue temperatures were measured and recorded with a digital infrared thermometer (Bosch PTD 1, Malaysia). All measurements were repeated twice, and the BBs were returned to their places. The visual damage at the end of each time period was photographed. All EC models were examined single-blindly by a pathologist for the depth of necrosis at the end of 24 hours and BBs were removed.

RESULTS

Gas bubbles and brown discoloration were observed after 1.5 hours in the EC models with lithium, alkaline, and silver-oxide BBs, and after 2.5 hours in the Zinc-air BB EC model. The least visual damage was detected in the EC model in which a zinc-air BB was placed at the end of 24 hours (Figure 1, 2).

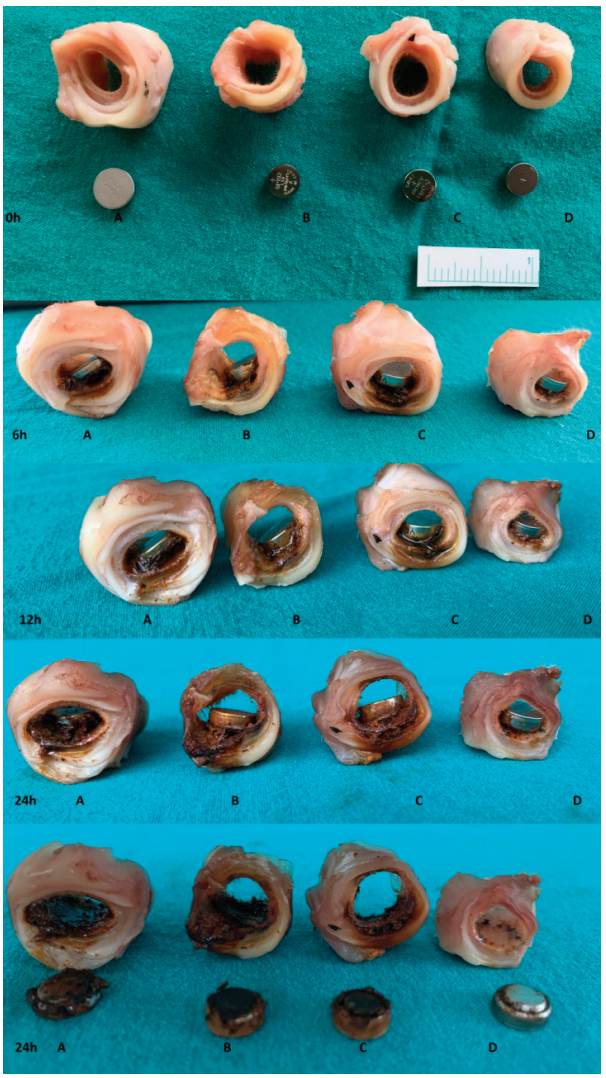

Figure 1: Visual changes of BBs at 0,6,12,24th hours. A: Lithium, B: Alkaline, C: Silver-oxide, D: Zinc-air.

Table 1: BB types and their properties.

BB types	IEC*	Dimensions Dia. x h. (mm)	Voltage (V)	Positive electrode	Negative electrode	Electrolyte
Lithium	CR927	9.5 x 2.7	3	Manganese dioxide	Lithium	Organic
Alkaline	LR736	7.9 x 3.6	1.5	Manganese dioxide	Zinc	Alkaline
Silver-oxide	SR736	7.9 x 3.6	1.55	Silver oxide	Zinc	Alkaline
Zinc-air	PR41	7.9 x 3.6	1.45	Oxygen	Zinc	Alkaline

*: International Electrotechnical Commission

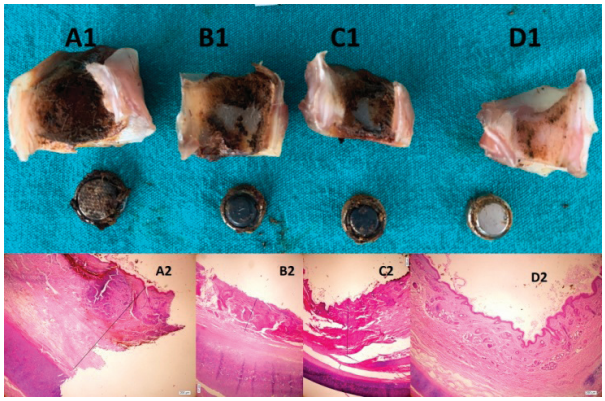

Figure 2: Images of BBs extracted from tissue at the end of 24 hours (A1: Lithium, B1: Alkaline, C1: Silver-oxide, D1: Zinc-air). After 24 hours, pathological images of A2: Lithium, B2: Alkaline, C2: Silver-oxide, D2: Zinc-air (×40 magnification; H&E paint; Olympus light microscope shot using DP2 program, Olympus Corp. Shinjuku, Tokyo, Japan). Necrosis depth: A2: 1983 µm, B2:854µm, C2: 1420µm, D2: normal epithelium.

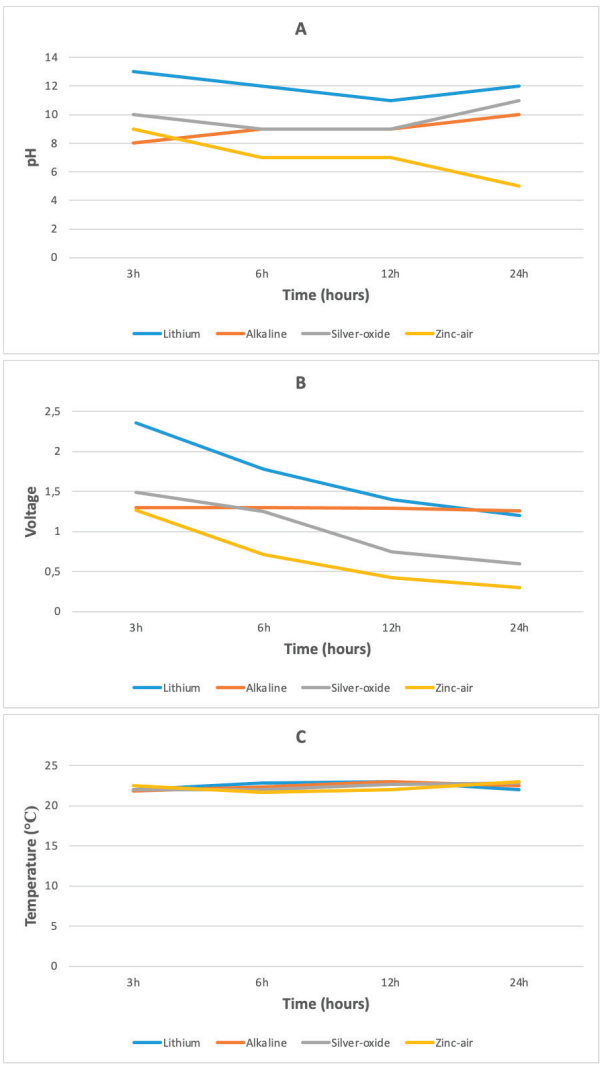

Figure 3: BB tissue Ph (A), voltage (B), and temperature (C) change values measured according to hours in EC models.

In the EC model with Lithium BB, the most significant pH elevation (pH:13) was detected at the 3rd hour, and the most significant voltage drop was observed between 3-6 hours. In the EC model with alkaline BB, the most significant pH elevation (pH:10) was detected at the 24th hour, and no significant voltage changes were detected in all time periods. In the EC model with silver-oxide BB, it was observed that the BB voltage decreased in direct proportion to time, and the pH changes did not accompany the voltage decrease in harmony. In the EC model with Zinc-air BB, the decreasing voltage was accompanied by a slight increase in pH value (pH:9) at the 3rd hour, and it was detected that the pH value was around neutral pH from the 6th hour. No significant changes were detected in tissue temperatures in all time periods. The changes in pH, voltage, and temperature of BBs at 3, 6, 12, and 24th hours are shown in Figure 3.

The depth of necrosis was measured as 1983 µm in lithium BB model, 854 µm in alkaline, and 1420 µm in silver-oxide at the end of 24 hours in EC models that were examined single-blind. No tissue necrosis was detected in the Zinc-air BB model (Figure 2).

DISCUSSION

The use of BBs has gradually increased in our daily life with advancing technology (4). In particular, children's access to them has become easier with the reduction of BB size, and it has become easier for them to get stuck in narrow areas, such as the EC and nasal cavity. BBs stuck in EC are also frequently experienced by the elderly population, who use hearing aids (12, 13). It is important for the clinician, who will remove the FB, to know what the foreign body in the EC is to prevent possible complications (11).

It was reported that approximately 20% of patients using hearing aids experience many problems (12, 14). It was also reported that approximately half of the BB-induced injuries in elderly adults occur because of the dislocation of device batteries and their jamming in the EC in patients using hearing aids; even patients mistook the batteries for the device itself and placed them in the EC (12, 15, 16). One article reported that in three cases, a hearing-aid BB stuck in an ear canal induced necrosis and edema in the EC, which were detected at the time of diagnosis. This progressed to a granulomatous reaction in the following weeks (12). It was also reported that tympanic membrane perforation, cartilage and bone necrosis, meatal stenosis, resistant otitis externa, and middle and inner ear damage might develop in patients with delayed diagnosis (17).

It was reported that 85.9% of 17,325 EC foreign body admissions (2,887/year) recorded in the UK between 2010 and 2016 consisted of pediatric patients (3). It was also reported that a total of 3.748 individuals under the age of 18 were admitted with BBs in EC between 1990 and 2009 in the USA (18). Lithium BBs that have a diameter of 20 mm are the most commonly detected BBs in case reports and case series in the literature. They result in serious complications, and may result

in mortality when swallowed (19). It was observed that lithium BBs begin to cause damage to the aerodigestive system mucosa within as few as 2 hours (20,21).

Jatana et al. (7) reported that lithium, alkaline, and silver-oxide BBs caused significant damages in the mucosa in cadaveric porcine esophagus models, but zinc-air BB did not cause any visible changes. Sancaktar et al. (1) observed that visual damage because of BBs started at the 15th minute in cadaveric sheep nasal septum models, the maximum change was detected in Lithium BBs, and the least was in zinc-air BBs at the end of the 6th hour. They also found that the depth of necrosis in the mucoperichondrium was caused by lithium, alkaline, silver-oxide, and zinc-air BB, respectively (1). The effects of BBs on mucosal structures, such as the esophagus and nasal septum, were investigated in these studies. In our study, however, BB injuries were investigated in EC models that had a different anatomical and histological structure, and similar results were obtained. In porcine esophagus modeling, 3 V lithium BBs and 1.5 V smaller BBs were compared, and the tissue damage scores of small BBs were found to be slower but at the same level (22). In our EC modeling, no histological damage was detected to EC skin after 24 hours only in 1.45 V zinc-air BB.

The tissue damage due to button batteries occurs through three mechanisms, the first being the penetration of the alkaline electrolyte solution in the battery into deep tissues as a result of alkaline necrosis in the tissue, the second being the damage caused by cumulative electrical current, and the third being because of the pressure necrosis of the button battery (17, 20). It is already known that BBs cause more rapid and serious damage in humid environments such as the mucosa (23). The resistance of an electrolysis cell depends on the electrode area (a), the electrode distance (d), and the conductivity of the medium (σ) (r (c) = d / aσ) (23). The distance between the electrodes reduces the resistance and the current increases. Although the proximity of the negative and positive ends is technically advantageous because of the small dimension, it can also cause rapid electrochemical reactions in narrow annular organs. The BB negative pole is the part held responsible for the damage (16). It causes the formation of hydroxide ions around the negative pole that is in contact with the tissue and then elevated basic pH, which results in local burns (24, 25). For this reason, it is necessary to examine the tissue that is close to the negative pole of the BB more carefully. The fluid that leaks from the damaged tissue increases the electrolyte concentration in the medium and causes the electrolysis reaction to increase (24).

BBs are defined as small single-cell batteries. Their diameters are usually larger (5.8 -30 mm) than their heights (1.2-5.4 mm), and voltages range between 1.45 and 3 V, depending on their models (19). It was speculated in previous studies that if the residual voltage of BBs is higher than 1.2 V, they may cause damage (1). Alkaline, silver oxide, and zinc-air batteries are smaller in size and have less voltage than lithium batteries. Although damages were reported in the literature mostly due to lithium BBs with a diameter of 20 mm or larger, it should be known that smaller BBs may also cause mucosal damage (22). In a meta-analysis of 6.262 swallowed BBs, it was found that more than 90% of the cases were BBs less than 20 mm in diameter (22).

It was reported in the literature that serious complications regarding BBs occur mostly after swallowing or inhalation (8). Cases that result in septum perforation, nasal synechia, esophageal structure and perforation, vocal cord paralysis, aortic perforation, or worse, death can be listed among these (26). Since BBs are more life-threatening than other foreign bodies, they must be evaluated urgently.

Although EC is not as wet as the mucosal structures, the damage might be accelerated because of BB discharges based on bleeding that occurs during unsuccessful removal attempts in some healthcare centers, depending on the duration of stay of BBs. Also, ear drops that are given mistakenly might accelerate the damage done by BBs that are forgotten in EC or whose removal is delayed. Although the complications due to BBs stuck in the EC seem to be rarer compared to those compressed in the airway, such as the esophagus or nose, the rapid spread of the use of BBs, the high child population in rural areas, as in Turkey, and the presence of refugee children, whose number has increased rapidly in recent years, all increase the importance of addressing these risks.

Special attention should be paid to all BB foreign bodies, including when they are stuck in EC, and cases must be referred to specialist centers urgently.

CONCLUSION

Because of the different chemical structures and voltages of BBs, their effects on tissues may also be different. According to the results of our study, although many believe that zinc-air BBs do not cause as much damage as lithium, alkaline, and silver oxide, it is not reasonable to argue that one BB type is less harmful than others, based on this *in vitro* study. These results must be confirmed in experiments more comprehensively in advanced in vivo studies. The fact that all BBs should be removed from their locations as soon as possible remains true.

Ethics Committee Approval: The ethical aspect of this study was approved by the Ondokuz Mayıs University (OMU) Animal Experiments Local Ethics Committee (HADTEK) (68489742-604.01.03-E.18528, date: 23.10.2020).

Informed Consent: Written informed consent was obtained.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- G.A.; Data Acquisition- G.A., M.B.; Data Analysis/Interpretation- G.A., M.B.; Drafting Manuscript- G.A.; Critical Revision of Manuscript- M.B.; Final Approval and Accountability- G.A.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Sancaktar ME, Bayraktar C, Bakırtaş M. Injury Mechanism of Button Batteries in the Nasal Cavity and Possible Mitigation Strategies During Impaction. Laryngoscope 2020;130(10):2487-93.
2. Buttazzoni E, Gregori D, Paoli B, Soriani N, Baldas S, Rodriguez H, et al. Susy Safe Working Group. Symptoms associated with button batteries injuries in children: An epidemiological review. Int J Pediatr Otorhinolaryngol 2015;79(12):2200-7
3. Morris S, Osborne MS, McDermott AL. Will children ever learn? Removal of nasal and aural foreign bodies: a study of hospital episode statistics. Ann R Coll Surg Engl 2018;100(8):1-3.
4. Thabet MH, Basha WM, Askar S. Button battery foreign bodies in children: hazards, management, and recommendations. Biomed Res Int 2013;2013:846091.
5. Lin VY, Daniel SJ, Papsin BC. Button batteries in the ear, nose and upper aerodigestive tract. Int J Pediatr Otorhinolaryngol 2004;68(4):473-9.
6. Litovitz TL. Battery ingestions: product accessibility and clinical course. Pediatrics 1985;75(3):469-76.
7. Jatana KR, Rhoades K, Milkovich S, Jacobs IN. Basic mechanism of button battery ingestion injuries and novel mitigation strategies after diagnosis and removal. Laryngoscope 2017;127(6):1276-82.
8. Huang T, Li WQ, Xia ZF, Li J, Rao KC, Xu EM. Characteristics and outcome of impacted button batteries among young children less than 7 years of age in China: a retrospective analysis of 116 cases. World J Pediatr 2018;14(6):570-5.
9. Premachandra DJ, McRae D. Severe tissue destruction in the ear caused by alkaline button batteries. Postgrad Med J 1990;66(771):52-3.
10. Penteado SP, Bento RF. Performance analysis of ten brands of batteries for hearing aids. Int Arch Otorhinolaryngol 2013;17(3):291-304.
11. Svider PF, Vong A, Sheyn A, Bojrab DI 2nd, Hong RS, Eloy JA, et al. What are we putting in our ears? A consumer product analysis of aural foreign bodies. Laryngoscope 2015;125(3):709-14.
12. Strachan DR, Kenny H, Hope GA. The hearing-aid battery: a hazard to elderly patients. Age Ageing 1994;23(5):425-6.
13. Holdstein Y, Mazzawi S, Watad W, Shupak A. Wrong impression: middle ear foreign body following hearing aid fitting. Otolaryngol Head Neck Surg 2013;149(4):647-8.
14. Wasson JH, Gall V, McDonald R, Liang MH. The prescription of assistive devices for the elderly: practical considerations. J Gen Intern Med 1990;5(1):46-54.
15. Jatana KR, Litovitz T, Reilly JS, Koltai PJ, Rider G, Jacobs IN. Pediatric button battery injuries: 2013 task force update. Int J Pediatr Otorhinolaryngol 2013;77(9):1392-9.
16. Svider PF, Johnson AP, Folbe AJ, Carron MA, Eloy JA, Zuliani G. Assault by battery: battery-related injury in the head and neck. Laryngoscope 2014;124(10):2257-61.
17. Bhisitkul DM, Dunham M. An unsuspected alkaline battery foreign body presenting as malignant otitis externa. Pediatr Emerg Care 1992;8(3):141-2.
18. Sharpe SJ, Rochette LM, Smith GA. Pediatric battery-related emergency department visits in the United States, 1990-2009. Pediatrics 2012;129(6):1111-7.
19. Labadie M, O'Mahony E, Capaldo L, Courtois A, Lamireau T, Nisse P, et al. Severity of button batteries ingestions: data from French Poison Control Centres between 1999 and 2015. Eur J Emerg Med 2018;25(4):e1-8.
20. Litovitz T, Whitaker N, Clark L. Preventing battery ingestions: an analysis of 8648 cases. Pediatrics 2010;125(6):1178.
21. Anfang RR, Jatana KR, Linn RL, Rhoades K, Fry J, Jacobs IN. pH-neutralizing esophageal irrigations as a novel mitigation strategy for button battery injury. Laryngoscope 2019;129(1):49-57.
22. Jatana KR, Barron CL, Jacobs IN. Initial clinical application of tissue pH neutralization after esophageal button battery removal in children. Laryngoscope 2019;129(8):1772-6
23. Voelker J, Voelker C, Engert J, Schendzielorz P, Hagen R, Rak K. Severe tracheobronchial harm due to lithium button battery aspiration: An in vitro study of the pathomechanism and injury pattern. Int J Pediatr Otorhinolaryngol 2020;139:110431.
24. Eliason MJ, Melzer JM, Winters JR, Gallagher TQ. Identifying predictive factors for long-term complications following button battery impactions: A case series and literature review. Int J Pediatr Otorhinolaryngol 2016;87:198-202.
25. Shaffer AD, Jacobs IN, Derkay CS, Goldstein NA, Giordano T, Ho S, et al. Management and Outcomes of Button Batteries in the Aerodigestive Tract: A Multi-institutional Study. Laryngoscope 2021;131(1):E298-306.
26. Liao W, Wen G, Zhang X. Button battery intake as foreign body in Chinese children: review of case reports and the literature. Pediatr Emerg Care 2015;31(6):412-5.

RESEARCH ARTICLE
DOI: 10.26650/Tr-ENT.2021.1033996
The Turkish Journal of Ear Nose and Throat 2021;31(4):86-93

An Analysis of the Mutual Publications of Anatomists and Otorhinolaryngologists: A Bibliometric Study based on the Web of Science Database

Ahmet Mahmut Tekin[1], **İlhan Bahşi**[2]

[1]Klinikum Bad Salzungen, Department of Otorhinolaryngology, Bad Salzungen, Germany
[2]Gaziantep University, Faculty of Medicine, Department of Anatomy, Gaziantep, Turkey

ORCID ID: A.M.T. 0000-0003-1604-3382; İ.B. 0000-0001-8078-7074

Citation: Tekin AM, Bahsi I. An analysis of the mutual publications of anatomists and otorhinolaryngologists: a bibliometric study based on the web of science database. Tr-ENT 2021;31(4):86-93. https://doi.org/10.26650/Tr-ENT.2021.1033996

ABSTRACT

Objective: The aim of this study is to bibliometrically examine the mutual studies in the fields of anatomy and otorhinolaryngology (ORL) recorded in the Web of Science (WoS) database between 1980-2020.
Material and Methods: The mutual publications of anatomists and otolaryngologists on 31.01.2021 are listed in the Science Citation Index-Expanded category of the Advanced Search section of the WoS database. Thus, in the search field tags, Department of Anatomy for anatomists and Department of Ear, Nose, and Throat (ENT) or Department of Otorhinolaryngology or Clinic of ENT or Clinic of Otorhinolaryngology for otolaryngologists were used for the address section. Publications from 2021, meeting abstracts, proceedings papers, early accesses, and book chapters were excluded. After the exclusion criteria were applied, the bibliometric characteristics of the remaining publications were examined.
Results: After the exclusion criteria were applied, 1395 articles were found. The total number of citations made to these articles was 42537, and at least one citation was made to 1279 of the 1395 articles (91.68%). The h-index of these articles was 82, and the average number of citations was 30.49. In these articles, the most frequently used first five keywords were immunohistochemistry (44 times), rat (39 times), cochlea (38 times), anatomy (36 times), and facial nerve (27 times).
Conclusion: The results of our bibliometric study which evaluated the last 40 years of data in terms of networks, collaborations, and institutions could be an inspiration and source for future researchers. We may state that with the increasing technology, the applicability of interventional methods in the field of ORL might be increased by conducting more anatomical studies and yield safer results.

Keywords: Anatomy, otorhinolaryngology, article, bibliometric analysis

INTRODUCTION

Anatomy is one of the oldest fields of medicine that examines the organs that make up the body and the functionality between these organs (1, 2). In this long process, the mysteries of the human body have become more understandable thanks to anatomical dissections (1). Especially with the development of high-resolution imaging methods in the last half-century, radiological and clinical studies have been added to anatomic cadaver studies (3). Continuously increasing technological developments have also increased the capacity of medical imaging techniques and have enabled a more detailed and accurate understanding of anatomical structures (4). In this way, the functions and anatomy of these structures and the relationship between them can be investigated in more detail, and solutions are sought for complex clinical situations (5). Thanks to many anatomical studies in the field of otorhinolaryngology (ORL), a more detailed understanding of the structures has been provided, the relationship of these structures with clinical situations can be evaluated, and even the surgical methods to be applied can be planned (6-9).

Many researchers need to collaborate in medical publications, unlike in other fields (10). This is because co-authorship is essential in the emergence of publications in the medical field (11). Bibliometric analysis is gaining in importance and evaluates existing research data accurately and efficiently on an evidence-based basis (12, 13). Bibliometric analysis is a

Corresponding Author: Ahmet Mahmut Tekin **E-mail:** drtekinahmet@gmail.com

Submitted: 15.12.2021 • **Accepted:** 08.12.2021 • **Published Online:** 04.01.2022

compelling method for predicting the change and evolution of a research field (11, 13). It can also provide evidence for a better understanding of the developmental trend in a particular area (14, 15). Bibliometry evaluates the productivity of countries and institutes, as well as objective analysis such as a change in research topics (15, 16).

The Web of Science (WoS) database is one of the most popular databases used in bibliometric research today (13, 17). One of the most critical criteria of international productivity is the number of articles in the WoS database and the number of citations made to these articles. Since this criterion is seen as an indicator of quality, it can be widely used in the evaluation of countries, institutions, and academicians (17).

As a result of the detailed literature review, it was seen that although there have been separate bibliometric studies conducted in the field of anatomy (5, 11), and ORL (18), no bibliometric study evaluating the joint publications of both fields was found.

The aim of this study is to bibliometrically examine the joint studies in the fields of anatomy and ORL recorded in the WoS database between 1980-2020.

MATERIAL AND METHODS

The mutual publications of anatomists and otolaryngologists on 31.01.2021 are listed in the Advanced Search section of the WoS database. Thus, in the search field tags, Department of Anatomy for anatomists and Department of Ear, Nose, and Throat (ENT) or Department of Otorhinolaryngology or Clinic of ENT or Clinic of Otorhinolaryngology for otolaryngologists were used for the address section *[AD= (Dept ENT* OR Dept Otorhinolaryngol* OR ENT Clin* OR Otorhinolaryngol Clin*) AND AD= (Dept Anat*)].*

Firstly, in the index section of the WoS, the Science Citation Index-Expanded (SCI-E) category was selected. Later, publications from 2021, meeting abstracts, proceedings papers, early accesses, and book chapters were excluded. After the exclusion criteria were applied, bibliometric characteristics of the determined publications, such as the distribution of the country and institutes, distribution of keywords, the journals they were published in, number of articles, and number of citations, were examined. VOSviewer (Visualizing scientific landscapes) software was used for the detailed analysis of bibliometric data (12).

RESULTS

As of 31.01.2021, the number of articles published mutually by anatomists and otorhinolaryngologists between 1980-2020 in SCI-E indexed journals in the WoS database was determined as 1596. After the exclusion criteria was applied, 1395 articles were found. The distribution of these articles by year is given in Figure 1. It was determined that the number of citations made to these articles was 42537, and the distribution of citations by years is given in Figure 2. It was determined that at least one citation was made to 1279 of 1395 (91.68%) articles. The h-index of these articles was 82, and the average number of citations was 30.49.

The top 25 countries with the most articles are shown in Table 1. The first five of these countries were Japan (n: 303, 21.72%), the USA (n: 301, 21.58%), Germany (n: 223, 15.99%), South Korea (n: 178, 12.76%), and Turkey (n: 127, 9.10%), (since studies with authors from more than one country were not excluded in this distribution, the total value was more than 100%).

The number of publications from the top 20 most productive institutes is shown in Table 2. The top 5 ranks were Yonsei University (n: 81, 5.81%), Umea University (n: 72, 5.16%), the

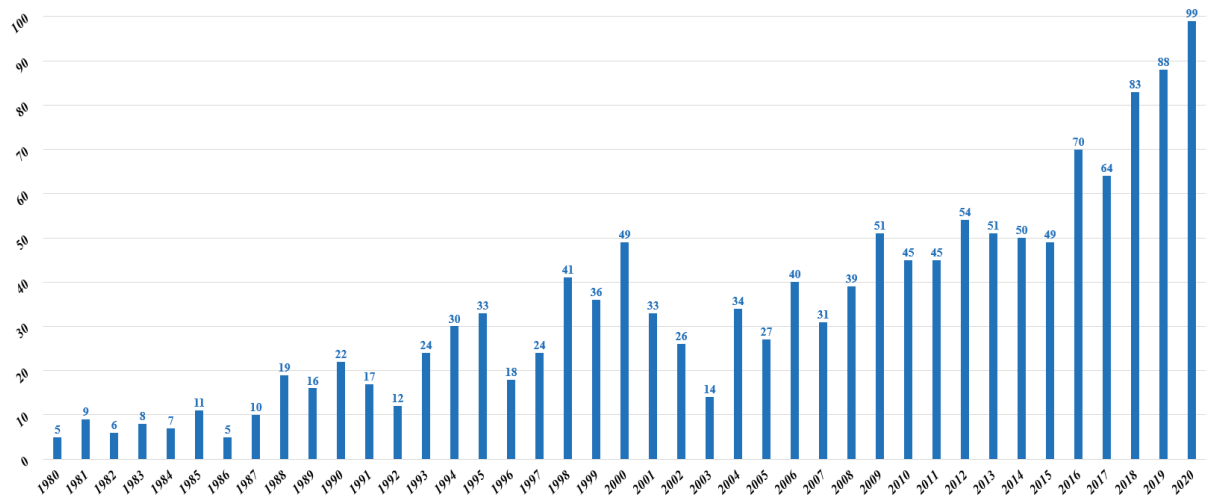

Figure 1: Annual trend of publications on analysis of mutual publications of anatomists and otorhinolaryngologists (1980-2020).

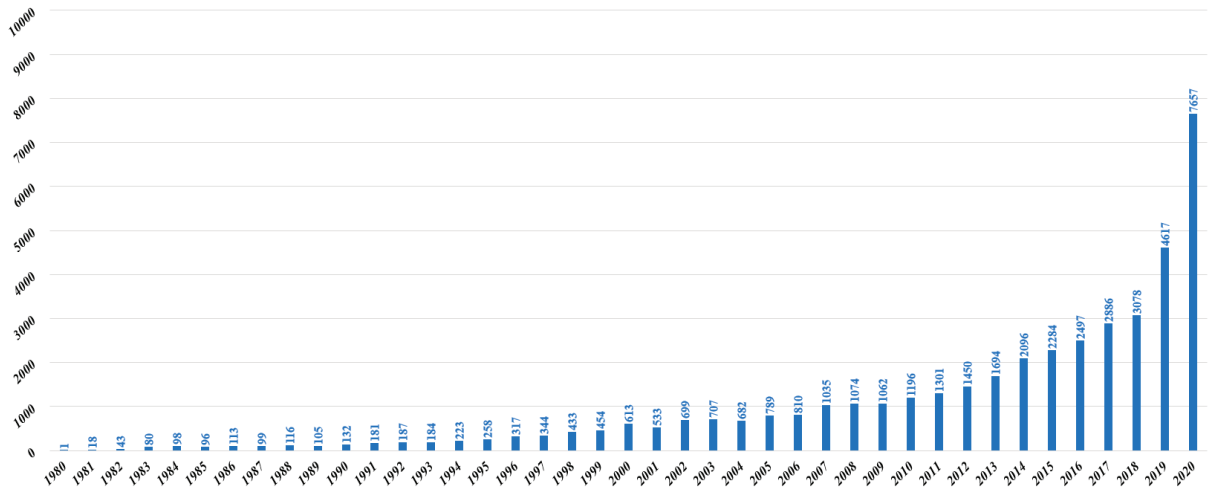

Figure 2: Annual trend of total citations on analysis of mutual publications of anatomists and otorhinolaryngologists (1980-2019).

Table 1: The number of mutual publications of anatomists and otorhinolaryngologists of the top 25 countries.

Country	Number of publications	Percent
Japan	303	21.720
USA	301	21.577
Germany	223	15.986
South Korea	178	12.760
Turkey	127	9.104
Sweden	114	8.172
Peoples R China	94	6.738
Netherlands	80	5.735
France	77	5.520
Australia	75	5.376
Belgium	73	5.233
England	70	5.018
Italy	68	4.875
Spain	68	4.875
Canada	60	4.301
Finland	57	4.086
India	55	3.943
Austria	53	3.799
Greece	50	3.584
Norway	41	2.939
Switzerland	41	2.939
Brazil	39	2.796
Romania	37	2.652
Iran	34	2.437
Portugal	33	2.366

Table 2: The number of mutual publications of anatomists and otorhinolaryngologists of the top 20 institutes.

Institute	Number of publications	Percent
Yonsei University	81	5.806
Umea University	72	5.161
University of California System	67	4.803
University of Cologne	61	4.373
Kyushu University	48	3.441
Chinese University of Hong Kong	45	3.226
Karolinska Institutet	41	2.939
Kyung Hee University	41	2.939
Seoul National University	40	2.867
University of Helsinki	39	2.796
University of Oslo	36	2.581
Johns Hopkins University	35	2.509
National Institutes of Health	35	2.509
University of Western Australia	35	2.509
University System of Maryland	35	2.509
Friedrich Schiller University of Jena	34	2.437
Harvard University	33	2.366
State University System of Florida	33	2.366
University of Barcelona	33	2.366
University of Maryland Baltimore	32	2.294

Table 3: The number of mutual publications of anatomists and otorhinolaryngologists of the top 25 journals.

Journal	Number of publications	Percent
Acta Oto Laryngologica	78	5.591
European Archives of Oto Rhino Laryngology	56	4.014
Laryngoscope	36	2.581
Hearing Research	35	2.509
Journal of Laryngology And Otology	28	2.007
Annals of Otology Rhinology And Laryngology	23	1.649
Surgical And Radiologic Anatomy	23	1.649
Brain Research	21	1.505
Annals of Anatomy Anatomischer Anzeiger	18	1.290
International Journal of Pediatric Otorhinolaryngology	16	1.147
Neuroscience Letters	15	1.075
Auris Nasus Larynx	14	1.004
Clinical Anatomy	14	1.004
Otolaryngology Head And Neck Surgery	14	1.004
Otology Neurotology	14	1.004
Plos One	14	1.004
Journal of Neuroscience	13	0.932
Romanian Journal of Morphology And Embryology	13	0.932
Cell And Tissue Research	12	0.860
Lancet	12	0.860
Neuroscience	12	0.860
Journal of Craniofacial Surgery	11	0.789
Experimental Neurology	10	0.717
Scientific Reports	10	0.717
American Journal of Rhinology Allergy	9	0.645

University of California System (n: 67, 4.80%), the University of Cologne (n: 61, 4.37%) and Kyushu University (n: 48, 3.44%).

The top 25 journals with the most articles are shown in Table 3. The first five of these journals were Acta Oto Laryngologica (n: 78, 5,59 %), European Archives of Oto Rhino Laryngology (n: 56, 4,01%), Laryngoscope (n: 36, 2,58%), Hearing Research (n: 35, 2.50%), and Journal of Laryngology and Otology (n: 28, 2.00%).

By using VoSviewer software, the distribution of the top 20 most used keywords in the examined articles were visualized and can be seen in Figure 3. The first five keywords are immunohistochemistry (44 times), rat (39 times), cochlea (38 times), anatomy (36 times), and facial nerve (27 times). By using VoSviewer software, it was determined that there was a significant change in the use of keywords between 2006-2012 (Figure 4).

By using VoSviewer software, the distribution of the top 50 most used words in the abstract of these articles were visualized and are shown in Figure 5. It was determined that there was a significant change in the use of these words between 2007-2012 (Figure 6).

DISCUSSION

Scientific publications are generally accepted as the objective parameters of the scientific success of any institution or researcher, as well as being accepted as a way to share new medical information and current clinical practices with a wide audience (19). The productivity of countries, institutions, and international cooperation in a particular field of research can be evaluated using the bibliometric method of analysis (20).

In the present study, Japan and the USA were found to be the two leading countries with regard to the number of co-produced articles in the field of anatomy and ORL. In a study which compared the articles published in 11 journals with the

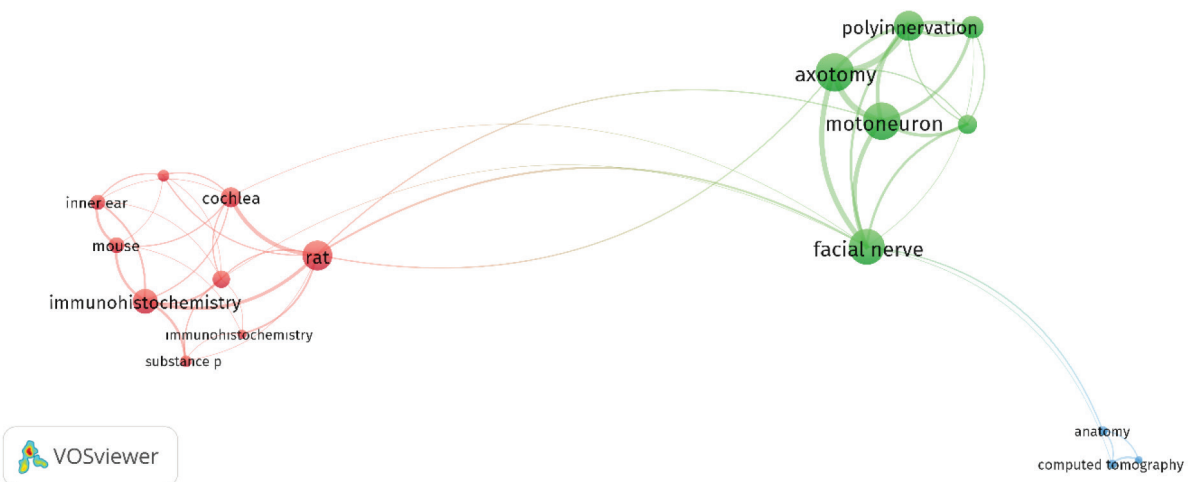

Figure 3: Network visualization map for cluster analysis based on keyword analysis on analysis of mutual publications of anatomists and otorhinolaryngologists from 1980–2020 (the size of the circle indicates a large number of publications; thick lines indicate strong relationship and colors indicate cluster idem).

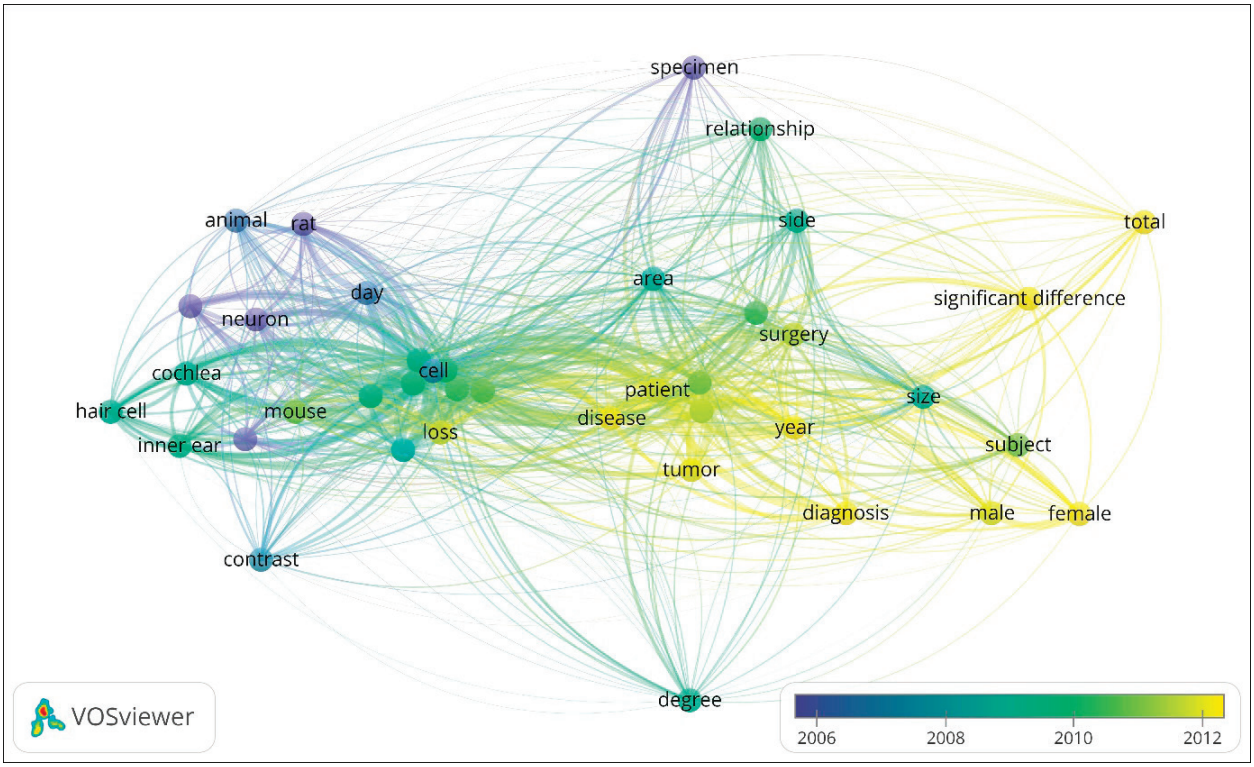

Figure 4: Network visualization map for trends based on keyword analysis on analysis of mutual publications of anatomists and otorhinolaryngologists from 1980–2020 (indicator shows current publications from blue to yellow).

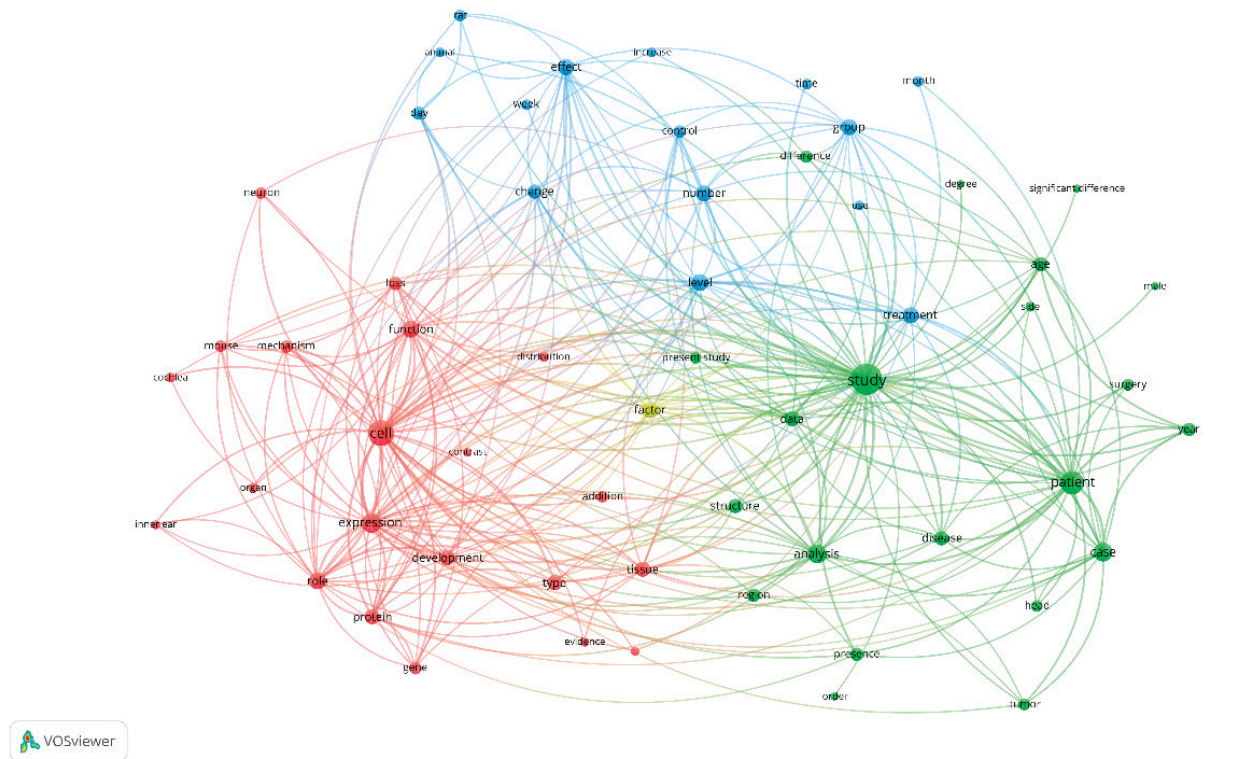

Figure 5: Network visualization map for cluster analysis based on abstract analysis on analysis of mutual publications of anatomists and otorhinolaryngologists from 1980–2020 (the size of the circle indicates a large number of publications; thick lines indicate strong relationship and colors indicate cluster idem).

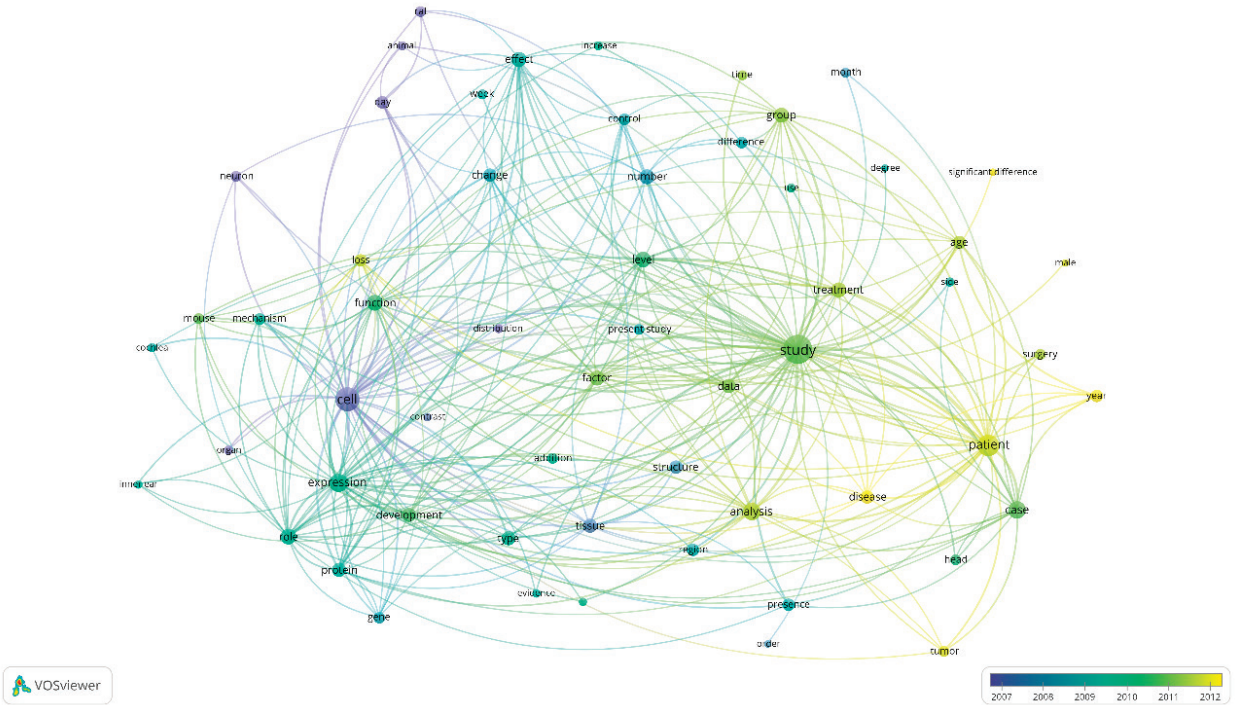

Figure 6: Network visualization map for trends based on abstract analysis on analysis of mutual publications of anatomists and otorhinolaryngologists from 1980–2020 (indicator shows current publications from blue to yellow).

highest impact factor between 2009 and 2013, Japan stood out as the country with the highest growth curve (18). The increase seen in the USA for the production of articles may be associated with greater research funds being awarded. More specifically, the National Health Institutes in USA are reported to have received awards of 30 billion dollars for medical research in 2014 (21). In developing countries, including Africa, some researchers make studies on their own or independently instead of collaborating with developed countries (22). This may be one of the reasons why developing countries produce fewer articles as compared to the other parts of the world. Also, in our study, there are no African countries among the first leading 25 countries. We consider that this problem may be solved through bringing international collaboration resources and the researchers in developing countries together. When the mutual articles in the field of anatomy and ORL were analyzed with regard to distribution according to universities, about one-third of the first leading 20 universities were seen to be located in the USA. This performance may be associated with national and international collaborations that could affect the visibility of the research and frequency of citations (23) alongside the availability of economic power, support funds, and research opportunities (24, 25). In addition, in a bibliometric analysis evaluating university-industry relationships in the USA, it was emphasized that universities had high-quality research environments that have strong research bonds (26). In conclusion, it is seen that many qualified articles can be produced when a trained workforce and sufficient financial and technological support come together. Identifying the universities where co-published articles in anatomy and ORL are produced will guide young researchers interested in the subject in terms of future research environments.

The journals that are active in a certain research field may be identified by detecting the distribution of the articles related to that subject and the researchers may select journals accordingly (20). Callaham et al. (27) reported that an article published in a journal with a low impact factor attracts less attention than it deserves, and an article published in a journal with a high impact factor attracts more attention than it deserves. From this point of view, bibliometric analysis can help find active journals in the field of research, guiding researchers to get their articles more accepted.

The keywords in an article indicate the relevant points in the related article (28). These points not only represent those key elements but also the potential trends of future research (29). As authors use prominent points as keywords in their articles, it is important to easily scan the frequency and distribution of keywords in the article using bibliometric analysis to highlight the important points of the topic. In co-published articles in the field of ORL and anatomy, the three most common keywords are “cochlea”, “facial nerve” and “inner ear” in the field of otology. In an anatomy study conducted in the field of a cochlear implant, the significant increase in cochlear implant procedures in recent years has led to the need for a detailed and accurate understanding of the anatomy of the inner ear not only from the point of view of experimental scientists but also from the point of view of otorhinolaryngologists

(30). Furthermore, together with the integration of robotic techniques in cochlear implant surgery in recent years (31), many anatomical cadaver studies have been conducted which evaluated facial nerves and the other anatomic structures in the inner ear and indicated the feasibility of robotic technology (32-35). In terms of determining the boundaries of future research areas, this study shows that any technological development integrated into interventional treatment, such as in robotic cochlear implant surgery, can be supported by anatomical studies.

As part of medical education, it was emphasized that teamwork skills should be developed, and researchers should work with different disciplines where the responsibilities of health care workers are shared, and abilities overlap (36). It has been stated that anatomy studies are part of medical education along with other disciplines in cadaver studies related to the human body (37). The present study, which evaluated co-published articles in the field of anatomy and ORL over the past 40 years, shows that research between different disciplines on the subject is gradually increasing and suggests that there will be more in the future. We consider that this study might guide young researchers who plan to study in the field of anatomy and ORL in terms of ideas and foresight.

Our analyses are based on the articles reported in SCI-E in the WoS database over the last 40 years. While data analysis is relatively objective and comprehensive, it has some limitations specific to bibliometric methodology. Databases other than the WoS, for example, Scopus, Pubmed, and Google Scholar were not included since many databases could not be technically joined. Moreover, the language of WoS is English, although it is a global tool. As a result, several articles might be overlooked as articles published in other languages are not included. Finally, the database is still open, and the research can continuously be updated. Over time, these data should be updated by comparing with the results in different databases.

CONCLUSION

Bibliometric analysis is an extremely useful tool for determining global publication trends in peer-reviewed journals and its importance is gradually increasing. Herein, we evaluated 1395 articles co-published in anatomy and ORL between 1980 and 2020 in terms of countries, institutes, journals, and keywords used. The results of our bibliometric study evaluating the last 40 years in terms of networks, collaborations, and institutions could be an inspiration and source for future researchers. We can state that with advances in technology, the applicability of interventional methods in the field of ORL might be increased by conducting more anatomical studies and yield safer results.

Ethics Committee Approval: Ethics committee approval was not received due to the nature of this study.

Informed Consent: Informed consent was not obtained due to the nature of the study.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- A.M.T., İ.B.; Data Acquisition- İ.B.; Data Analysis/Interpretation- A.M.T., İ.B.; Drafting Manuscript- A.M.T., İ.B.; Critical Revision of Manuscript- A.M.T., İ.B.; Final Approval and Accountability- A.M.T., İ.B.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Bahşi İ, Çetkin M, Orhan M. Anatomy of kidney: A comparative historical study. Eur J Ther 2016;22:66-71.
2. Bahşi İ, Topal Z, Çetkin M, Orhan M, Kervancıoğlu P, Odabaşıoğlu ME, et al. Evaluation of attitudes and opinions of medical faculty students against the use of cadaver in anatomy education and investigation of the factors affecting their emotional responses related thereto. Surg Radiol Anat 2021;43(4):481-7.
3. McMenamin PG, McLachlan J, Wilson A, McBride JM, Pickering J, Evans D. et al. Do we really need cadavers anymore to learn anatomy in undergraduate medicine? Med Teach 2018;40(10):1020-9.
4. Grignon B. Anatomy and medical imaging: a symbiotic relationship. Surg Radiol Anat 2012;34(8):673-4.
5. Wing L, Massoud TF. Trends in performance indicators of neuroimaging anatomy research publications: a bibliometric study of major neuroradiology journal output over four decades based on web of science database. Clin Anat 2015;28(1):16-26.
6. Gualtieri T, Verzeletti V, Ferrari M, Perotti P, Morello R, Taboni S, et al. A new landmark for lingual artery identification during transoral surgery: Anatomic-radiologic study. Head Neck 2021;43(5):1487-98.
7. Noiphithak R, Yanez-Siller JC, Revuelta Barbero JM, Otto BA, Carrau RL, Prevedello DM. Comparative Analysis Between Lateral Orbital Rim Preservation and Osteotomy for Transorbital Endoscopic Approaches to the Cavernous Sinus: An Anatomic Study. Oper Neurosurg (Hagerstown) 2019;16(1):86-93.
8. Vural A, Carobbio ALC, Ferrari M, Rampinelli V, Schreiber A, Mattavelli D, et al. Transorbital endoscopic approaches to the skull base: a systematic literature review and anatomical description. Neurosurg Rev 2021;44:2857-78.
9. Bahşi İ, Orhan M, Kervancıoğlu P, Yalçın ED. The anatomical and radiological evaluation of the Vidian canal on cone-beam computed tomography images. Eur Arch Otorhinolaryngol 2019;276(5):1373-83.
10. Yang H, Pan BC, Chen J. Citation analysis of five journals in andrology. Arch Androl 2006;52(6):433-40.
11. Adanır SS, Bahşi İ, Kervancıoğlu P, Orhan M, Cihan ÖF. Bibliometric analysis of articles published in Anatomy, the official publication of the Turkish Society of Anatomy and Clinical Anatomy between 2007–2018. Anatomy 2020;14(1):39-43.
12. Aria M, Cuccurullo C. bibliometrix: An R-tool for comprehensive sciencemappinganalysis.JournalofInformetrics2017;11(4):959-75.
13. Topal Z, Bahsi I, Tufan AE. Evaluation of The Psychiatric Research Output From Turkey Via Web Of Science Database: A Bibliometric Analysis. Psychiatry Clin Psychopharmacol 2020;30(4):423-33.
14. Miao L, Ji J, Wan L, Zhang J, Yin L, Pu Y. An overview of research trends and genetic polymorphisms for noise-induced hearing loss from 2009 to 2018. Environ Sci Pollut Res Int 2019;26(34):34754-74.

15. Tekin AM, Bahşi İ. Global Research on Maxillofacial Fracture over the last 40 years: A Bibliometric Study. J Craniofac Surg 2021;32(6):e568-72. doi: 10.1097/SCS.0000000000007627.
16. Shi M, Huang W, Shu L, Hou G, Guan Y, Song G. Research on polycystic ovary syndrome: a bibliometric analysis from 2009 to 2019. Gynecol Endocrinol 2021;37(2):121-5.
17. Kulkarni AV, Aziz B, Shams I, Busse JW. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. Jama 2009;302(10):1092-6.
18. Saunders TFC, Rymer BC, McNamara KJ. A global bibliometric analysis of otolaryngology: Head and neck surgery literature. Clin Otolaryngol 2017;42(6):1338-42.
19. Xue T, Wei L, Zha DJ, Qiao L, Qiu JH, Lu LJ, et al. Publications about hearing in otorhinolaryngology journals from chinese authors: a 11-year survey of the literature. Indian J Otolaryngol Head Neck Surg 2012;64(2):106-9.
20. Gao H, Huang FY, Wang ZP. Research Trends of Macrophage Polarization: A Bibliometric Analysis. Chin Med J (Engl) 2018;131(24):2968-75.
21. Grepin KA, Pinkstaff CB, Shroff ZC, Ghaffar A. Donor funding health policy and systems research in low- and middle-income countries: how much, from where and to whom. Health Res Policy Syst 2017;15:68.
22. Vanni T, Mesa-Frias M, Sanchez-Garcia R, Roesler R, Schwartsmann G, Goldani MZ, et al. International scientific collaboration in HIV and HPV: a network analysis. PLoS One 2014;9(3):e93376.
23. Li T, Ho YS, Li CY. Bibliometric analysis on global Parkinson's disease research trends during 1991-2006. Neurosci Lett 2008;441(3):248-52.
24. Ekundayo TC, Okoh AI. A global bibliometric analysis of Plesiomonas-related research (1990 - 2017). PLoS One 2018;13(11):e0207655.
25. Zyoud SH. Global toxocariasis research trends from 1932 to 2015: a bibliometric analysis. Health Res Policy Syst 2017;15(1):14.
26. Zhou P, Tijssen R, Leydesdorff L. University-Industry Collaboration in China and the USA: A Bibliometric Comparison. PLoS One 2016;11(11):e0165277. doi: 10.1371/journal.pone.0165277.
27. Callaham M, Wears RL, Weber E. Journal prestige, publication bias, and other characteristics associated with citation of published studies in peer-reviewed journals. Jama 2002;287(21):2847-50.
28. Zongyi Y, Dongying C, Baifeng L. Global Regulatory T-Cell Research from 2000 to 2015: A Bibliometric Analysis. PLoS One 2016;11(9):e0162099. doi: 10.1371/journal.pone.0162099.
29. Shen S, Cheng C, Yang J, Yang S. Visualized analysis of developing trends and hot topics in natural disaster research. PLoS One. 2018;13(1):e0191250. doi: 10.1371/journal.pone.0191250.
30. Mehanna AM, Abdelnaby MM, Eid M. The Anatomy and Anatomical Variations of the Round Window Prechamber and Their Implications on Cochlear Implantation: An Anatomical, Imaging, and Surgical Study. Int Arch Otorhinolaryngol 2020;24(3):e288-98. doi: 10.1055/s-0039-1698783.
31. Tekin AM, Matulic M, Wuyts W, Assadi MZ, Mertens G, Rompaey VV, et al. A New Pathogenic Variant in POU3F4 Causing Deafness Due to an Incomplete Partition of the Cochlea Paved the Way for Innovative Surgery. Genes (Basel) 2021;12(5):613.
32. Rathgeb C, Wagner F, Wimmer W, Gerber N, Williamson T, Anschütz L, et al. The accuracy of image-based safety analysis for robotic cochlear implantation. Int J Comput Assist Radiol Surg 2019;14(1):83-92.
33. Schneider D, Stenin I, Anso J, Hermann J, Mueller F, Pereira Bom Braga G, et al. Robotic cochlear implantation: feasibility of a multiport approach in an ex vivo model. Eur Arch Otorhinolaryngol 2019;276(5):1283-9.
34. Torres R, Jia H, Drouillard M, Bensimon JL, Sterkers O, Ferrary E, et al. An Optimized Robot-Based Technique for Cochlear Implantation to Reduce Array Insertion Trauma. Otolaryngol Head Neck Surg 2018;159(5):900-7.
35. Torres R, Kazmitcheff G, De Seta D, Ferrary E, Sterkers O, Nguyen Y. Improvement of the insertion axis for cochlear implantation with a robot-based system. Eur Arch Otorhinolaryngol 2017;274(2):715-21.
36. Hall P, Weaver L. Interdisciplinary education and teamwork: a long and winding road. Med Educ 2001;35(9):867-75.
37. Greene JR. Design and development of a new facility for teaching and research in clinical anatomy. Anat Sci Educ 2009;2(1):34-40.

RESEARCH ARTICLE
DOI: 10.26650/Tr-ENT.2021.997578
The Turkish Journal of Ear Nose and Throat 2021;31(4):94-99

Are Platelet Distribution and Volume Values Parameters for Meniere's Disease?

Fatih Turan[1], Sena Genç Elden[2], Mahmut Sinan Yılmaz[3], Mahmut Emre Gündogan[3], Mehmet Güven[3]

[1]Sakarya University Training and Research Hospital, Department of Otorhinolayngology, Sakarya, Turkey
[2]Pamukova State Hospital, Department of Otorhinolayngology, Sakarya, Turkey
[3]Sakarya University Faculty of Medicine, Department of Otorhinolaryngology, Sakarya, Turkey

ORCID ID: F.T. 0000-0002-5389-8243; S.G.E. 0000-0002-3479-1600; M.S.Y. 0000-0002-5323-0059; M.E.G. 0000-0001-9225-8268; M.G. 0000-0002-3665-2428

Citation: Turan F, Genc Elden S, Yilmaz MS, Gundogan ME, Guven M. Are platelet distribution and volume values parameters for meniere's disease?. Tr-ENT 2021;31(4):94-99. https://doi.org/10.26650/Tr-ENT.2021.997578

ABSTRACT

Objective: To evaluate the relationship between mean platelet volume (MPV), platelet distribution width (PDW), as well as the other parameters of complete blood counts (CBC) and diagnosis and prognosis in Meniere's disease (MD).
Material and Methods: Complete blood count data of 54 MD patients who were followed in our clinic between 2010 and 2018 and age/sex-matched controls were analyzed retrospectively. MPV, PDW, and the other parameters of CBC were compared. Subjects with normal serum glucose, cholesterol, vitamin, and liver and kidney function test levels were included in the study. Subjects with chronic diseases that may affect CBC values were excluded. The Meniere's group was divided into subgroups according to the degree of hearing loss and CBC values were compared within subgroups.
Results: MPV and PDW values were significantly high in the Meniere's group. There was no significant difference in the other parameters of CBC between the MD and control groups. Statistically significant correlation was obtained in MPV and PDW values in the Meniere's group. As the audiometry values increased, MPV and PDW were found to increase.
Conclusion: MPV and PDW, which are markers of vascular pathology, might be potential new serum markers in Meniere's disease.

Keywords: Complete Blood Counts; Meniere's Disease, Mean platelet volume, Platelet distribution width, Sensorineural hearing loss

INTRODUCTION

Meniere's Disease (MD) is defined as an idiopathic syndrome characterized by recurrent episodes of vertigo, hearing loss, fullness in the ear, tinnitus, and endolymphatic hydrops in the inner ear (1). The hearing loss in MD is of the sensorineural type and is initially in fluctuant style, which holds low frequencies (200-600Hz) (2). As the course of MD progresses, the hearing level decreases at other frequencies and flat hearing loss occurs (3).

Although many factors are suspected in the etiology of MD, the exact cause is still unclear (4). Endolymphatic hydrops has been the most important finding in studies on the pathophysiology of MD (5). Endolymphatic hydrops is associated with endolymph release, absorption dysfunction, and endolymphatic duct obstruction (6). Factors such as genetic predisposition, autoimmune disease, inflammation, endocrine system abnormalities, viral infections, vascular system abnormalities, allergy, syphilis, leukemia, and trauma are at fault in the hydrops mechanism.

Vascular mechanisms of MD have been attributed to decreased intracerebral arterial pressure, venous obstruction, chronic CSF pressure increase, and chronic hypoxia, which reduce the perfusion rate (7). It has been reported that disruption of the venous absorption mechanism of endolymph as a result of these mechanisms may be associated with vascular pathology (5, 8, 9). The vascular pathology that disrupts this hemostasis

Corresponding Author: Sena Genç Elden **E-mail:** ssenagenc@gmail.com
Submitted: 20.09.2021 • **Accepted:** 09.12.2021 • **Published Online:** 04.01.2022

balance in MD is the presence of venous insufficiency in the paravestibular canalicular (PVC) vein network, which is very important for the inner ear fluid mechanisms (10).

Platelets involved in hemostasis play a role in the formation of thrombosis. Platelets secrete mediators that are important for coagulation, thrombosis, atherosclerosis, and inflammation (11). MPV shows the function and activity of platelets. Volumetrically large platelets are more metabolically and enzymatically active and have greater thrombotic potential (11). Mean platelet volume (MPV) is a marker used in systemic inflammatory conditions and cardiovascular pathologies (12). Platelet distribution width (PDW) represents heterogeneity in platelet morphology. MPV and PDW values are more specific parameters than platelet count in evaluating platelet function (12). MPV and PDW are complete blood count elements that can be performed quickly and cheaply in routine blood tests.

The amount of MPV and PDW is closely related to cardiovascular risk factor such as atherosclerosis, acute syndromes, venous and arterial thrombosis, carotid and peripheral artery disease, or thromboembolism (13-15). In the study by Ulu et al., MPV value was found to be significantly higher in patients with sudden hearing loss and it was associated with vascular pathologies (16). Likewise, in the study by Sagit et al., MPV and PDW values were found to be significantly higher in patients with sudden hearing loss (17).

In the present study, we aimed to evaluate MPV and PDW, as well as the other parameters of complete blood counts (CBC), supporting the hypothesis of vascular pathology in MH. To the best of our knowledge, this is the first study to evaluate CBC parameters in MD.

MATERIALS AND METHODS

Ethics committee approval was obtained from the Local Ethics Committee (Ethics Committee No:71522473/050.01.04/162). The study was carried out by retrospectively examining the records of patients diagnosed with MD who applied to the ENT clinic of Sakarya University Training and Research Hospital.

Fifty-four patients who presented with peripheral vertigo attack and were diagnosed with MD after detailed anamnesis, physical examination and tests were included in the study. Routine blood test results and audiometry values of these patients during the attack period and at the 3rd month after the attack were evaluated. Patients were evaluated with respect to CBC, glucose, cholesterol, liver function tests, renal function tests, and vitamin B9 and B12. Audiometric and vestibular tests (VHIT, VNG) were performed to differentiate peripheral and central vertigo. It was requested that patients who had not been diagnosed with neurological diseases be evaluated for them. At the end of this process, patients diagnosed with MD were included in the study. The control group was selected from the patients who applied to the otorhinolaryngology outpatient clinic for routine checkups. Patients in the control group who were found to have pathology (such as vertigo, nasal septum deviation, nasal polyposis, sensory hearing loss, obstructive sleep apnea syndrome, malignancy) in the detailed otolaryngology examination were excluded from the study. People with any chronic disease were not included in either group so that the CBC value was not affected.

Neutrophil, lymphocyte, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) MPV, and PDW values were compared. Glucose, cholesterol, liver function tests, renal function tests, and vitamin values were evaluated in both groups, in order to avoid any chronic disease that might affect CBC values.

The affected ear was identified in the Meniere's group. Meniere's patients were divided into subgroups according to the degree of hearing loss on the affected ear side during the non-attack periods and during the attack periods. Hearing losses were found to be 0-25 dB normal hearing, 26-40dB mild sensorineural hearing loss (SNHL), 41-70dB medium SNHL, 71-90dB advanced SNHL, and 91dB + profound SNHL, according to the pure sound averages of 500, 1000, 2000, and 4000Hz.

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) 22.0 program. Hematological data were analyzed by the Shapiro-Wilk test for normal distribution in each group and subgroups. Descriptive results of the data with normal distribution according to normality distribution were stated as mean±SD, and non-normal distribution was defined as median [IR]. The normal distribution data of the groups were compared with the independent-samples t-test and the non-normal distribution data were compared with the Mann-Whitney U test. The normal distribution of CBC data of subgroups according to hearing loss in the Meniere's group were compared with the one way ANOVA test, and the non-normal distribution data were compared with the Kruskal Wallis test. MPV and PDW results which were statistically significant for these groups were evaluated by linear regression test. Results were evaluated at 95% confidence interval and $p<0.05$ significance level.

RESULTS

The mean age was 48.15±11.91 years and consisted of 26 (48.1%) women and 28 (51.9%) men in the Meniere's group. The mean age was 45.05±7.72 years and consisted of 25 (46.3%) women and 29 (53.7%) men in the control group. There was no significant difference between Meniere's and control groups in terms of age, sex, glucose, cholesterol, liver function tests, renal function tests, and vitamin values ($p\geq0.05$) (Table 1).

While there was no significant difference in neutrophil, lymphocyte, platelet, NLR, and PLR values between the Meniere's group and the control group in CBC ($p\geq0.05$), a statistically significant difference was found in MPV and PDW values ($p<0.05$) (Table 2) (Figure 1, Figure 2).

In the Meniere's group, 22 (40.7%) right and 32 (59.3%) left ears were affected. Meniere's patients during the attack period of the affected ears had 12 (22.2%) normal, 13 (24.1%) mild

Table 1: Glucose, cholesterol, renal and liver function tests and B12, folic acid mean values between control and Meniere's groups.

Variable	Meniere's group	Control group	p value
Glucose (mg/d)	100 [18.7]	99.5 [17]	0.411
Total cholesterol (mg/d)	198.7±26.1	199.3±44.8	0.217
HDL-cholesterol (mg/d)	49.9±11.4	45.7±9.9	0.879
LDL-cholesterol (mg/d)	124.5±26.8	129.4±35.7	0.758
AST (U/L)	22.5 [7]	18.0 [7]	0.462
ALT (U/L)	22.5 [13]	21.0 [15]	0.809
Serum urea (mg/dL)	29.2±7.2	28.6±8.4	0.374
Creatinine (mg/dL)	0.7 [0.16]	0.7 [0.15]	0.279
Vitamin B12 (pg/mL)	357 [124.7]	344 [181.7]	0.815
Folate (ng/mL)	7.0±2.3	6.46±2.2	0.816

Continuous variables were presented as mean ± standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein

Table 2: Mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW between Meniere's and control groups.

Variable	Meniere's group	Control group	p value
Neutrophil count (10^9/L)	3.9 [1.7]	3.9 [2.3]	0.982
Lymphocyte count (10^9/L)	2.1 [1.2]	2.5 [0.9]	0.490
Platelet count (10^3/mm^3)	253.6±53.5	261.0±61.4	0.537
MPV (fl)	**7.98 [1.81]**	**7.53 [1.18]**	**0.023***
PDW (fl)	**18.2 ±1.1**	**17.5 ±0.6**	**0.001***
NLR	1.68 [1.12]	1.60 [1.11]	0.372
PLR	106.50 [48.50]	106.32 [53.79]	0.949

Continuous variables were presented as mean ± standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
*A statistically significant difference was obtained between MPV and PDW values.
MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio

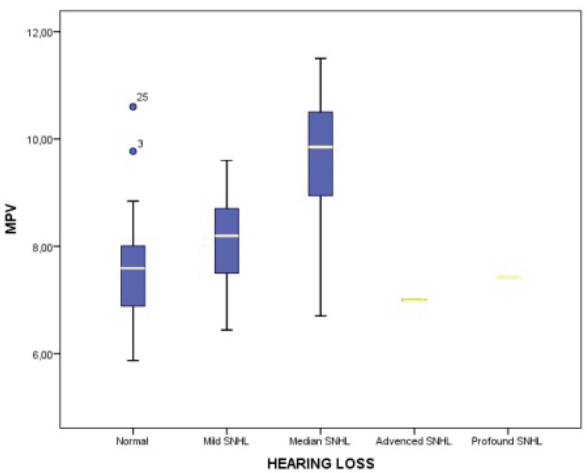

Figure 1: Distribution of MPV value between groups.

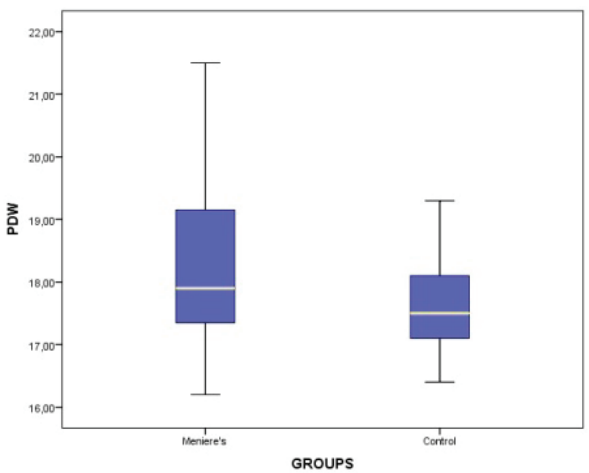

Figure 2: Distribution of PDW value between groups.

SNHL, 25 (46.3%) medium SNHL, 2 (3.7%) advanced SNHL, and 2 (3.7%) profound SNHL according to the pure sound averages of 500, 1000, 2000, and 4000Hz. There were no significant difference in CBC values according to the degree of hearing loss (p≥0.05) (Table 3).

During the nonattack period, 20 (37.1%) of Meniere's patients had normal hearing, 19 (35.1%) mild SNHL, 12 (22.2%) medium SNHL, and 2 (3.7%) advanced SNHL, and 1 (1.9%) patient had profound SNHL according to the pure sound averages of 500, 1000, 2000, and 4000Hz. A significant correlation was found between MPV and PDW levels and the degree of hearing loss during the non-attack period (p<0.05). When verification was performed by regression analysis, the difference in MPV and PDW values was significant (p<0.05) (Figure 3) (Figure 4). There was no significant difference in the other CBC values between groups (p≥0.05) (Table 4).

Table 3: Meniere's group, mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW according to hearing loss during attack period.

Variable	Normal (n=12)	Mild SNHL (n=13)	Medium SNHL (n=25)	Advanced SNHL (n=2)	Profound SNHL (n=2)	p value
Neutrophil count (10^9/L)	4.0±1.0	3.9±1.2	4.8±2.6	3.9±0.6	4.8±3.4	0.749
Lymphocyte count (10^9/L)	2.4 [1.5]	2.4 [1.0]	2.1 [1.3]	1.8 [0.5]	2.7 [0]	0.776
Platelet count (10^3/mm^3)	263±62	269±63	245±48	244±41	219±10	0.656
MPV (fl)	7.6±1.3	8.3±0.8	8.7±1.5	6.9±0.2	7.1±0.4	0.112
PDW (fl)	17.5 [1.3]	17.5 [2.1]	18.9 [1.7]	18.8 [-]	16.9 [-]	0.078
NLR	1.7 [2.1]	1.4 [2.4]	1.7 [0.9]	2.1 [-]	1.6 [-]	0.778
PLR	121±58	109±28	114±34	134±49	84±25	0.395

Continuous variables were presented as mean±standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio

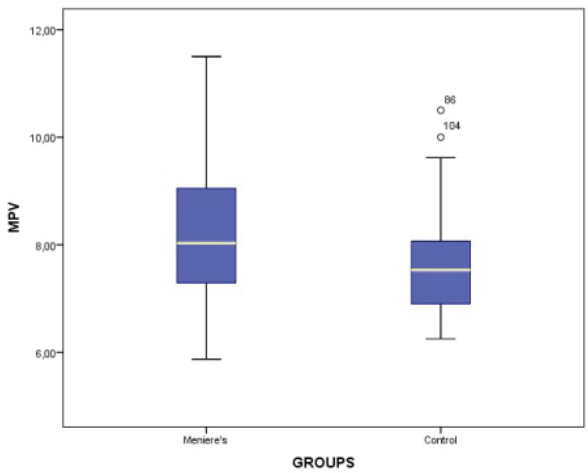

Figure 3: MPV distribution according to the degree of hearing loss in non-attack period.

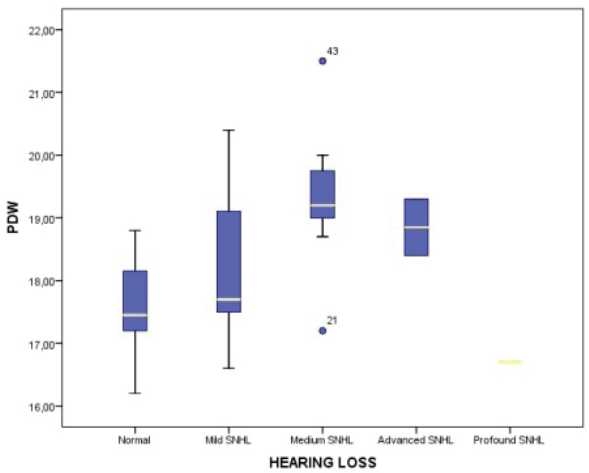

Figure 4: PDW distribution according to the degree of hearing loss in non-attack period.

Table 4: Meniere's group, mean values of neutrophils, lymphocytes, platelets, NLR, PLR, MPV, PDW according to hearing loss during nonattack period.

Variable	Normal (n=20)	Mild SNHL (n=19)	Medium SNHL (n=12)	Advanced SNHL (n=2)	Profound SNHL (n=1)	p value
Neutrophil count (10^9/L)	4.1 [1.8]	3.6 [1.9]	4.2 [2.6]	3.9 [-]	2.3 [-]	0.660
Lymphocyte count (10^9/L)	2.6 [1.4]	2.0 [0.9]	2.3 [1.6]	1.8 [-]	2.0 [-]	0.876
Platelet count (10^3/mm^3)	262±51	253±54	250±61	244±41	212	0.913
MPV (fl)	**7.7±1.2**	**8.1±0.8**	**9.5±1.6**	**6.9±0.2**	**7.4**	**0.004*** **0.002****
PDW (fl)	**17.5±0.7**	**18.0±1.0**	**19.3±1.0**	**18.8±0.6**	**19.7**	**0.001*** **0.014****
NLR	1.6 [2.6]	1.7 [0.7]	1.7 [0.9]	2.1 [1.0]	1.1	0.676
PLR	98 [48]	117 [45]	105 [67]	134 [-]	169	0.668

Continuous variables were presented as mean±standard deviation if normal distribution, and median [interquartile range] if not normal distribution.
MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio
*There is a statistically significant difference between MPV and PDW values.
**In the regression analysis, there was a significant difference in MPV and PDW values.

DISCUSSION

Hematologic data were used to evaluate the vascular pathologies that are important in the pathogenesis of MD in the present study. To the best of our knowledge, this is the first study to evaluate complete blood count parameters in MD. MPV and PDW values were significantly high in the Meniere group. In addition, there was a significant correlation between hearing loss and MPV and PDW values in the Meniere group.

The male to female ratio in MD was found to be 1.3/1 in several studies, but in the present study, the ratio was 1/1. (4, 14). Although the course of MD can be highly variable, it usually occurs in the fourth to seventh decade, with episodic vertigo

or sensorineural hearing loss affecting low frequencies. In the present study, the mean age was found to be 48.15±11.917 in accordance with the literature.

Increased PVC venous pressure leads to inadequate drainage of vestibular organs and is one of the important mechanisms in the pathophysiology of MD (10). Friberg et al., in their study, emphasized the classical triad of MD, vertigo, tinnitus, and hearing loss as the only symptom of radiologically detected thrombosis of the sigmoid sinus and jugular bulbus (18). In another study, it was shown that cerebral atherosclerosis, transient ischemic attack, MD, and equilibrium disorders can be seen together with the common etiology of vascular pathology and the underlying mechanism of this status was thought to be due to possible episodic labyrinth ischemia (19).

MPV is a measure of platelet size. Platelets play an important role in initiating atherosclerosis and thrombogenesis (3). Large platelets contain more dense alpha granules, express more adhesion receptors, and have higher thrombotic activity (20). Therefore, MPV is a marker of platelet activation. MPV value is a more specific parameter than platelet count in the evaluation of platelet function (3). MPV is a marker used in systemic inflammatory conditions and cardiovascular pathologies (12). There is a close association between MPV and cardiovascular risk factors such as impaired fasting glucose levels, diabetes mellitus, hypertension, hypercholesterolemia, obesity, and metabolic syndrome (12, 20).

PDW represents heterogeneity in platelet morphology and is clinically associated with platelet activation, such as MPV (21). Increased MPV and PDW reflect increased platelet activation or an increased number of large, hyper aggregated platelets and are considered an independent risk factor for coronary and peripheral arterial disease (13, 14, 22). MPV and PDW values in the present study support vascular pathology. Endler et al. reported that increased MPV and PDW values were independent risk factors for acute myocardial infarction, and other studies have also shown that they are associated with increased mortality and recurrent vascular events after myocardial infarction (23-25).

In a study which examined the CBC results of patients presenting with peripheral vertigo, only NLR values were found to be significant among the other CBC values (26). We were unable to duplicate this result as we did not find a significant difference in NLR values. The reason for this might be due to the low number of patients with MD in our study. In another study comparing CBC values of peripheral vertigo patients with vestibular neuritis, significant results were obtained in NLR, PLR and MPV values (27). The significant results in NLR and PLR values were attributed to inflammatory pathology and the absence of significant results in the present study might indicate that MD is not primarily an inflammatory pathology.

A significant result in MPV value in the present study suggests the important role of the vascular process in MD. Several other researchers examined CBC results in patients with sudden SNHL and tinnitus. In these studies, a significant increase was found in NLR rates, but no significant change was found in MPV values and they associated their results with inflammatory pathology (28,29). In the study in which patients with sudden hearing loss were grouped according to their audiometry grade, it was found that the MPV value was significantly higher in patients with total deafness and in whom all frequencies were affected compared to the control group (30). In the present study, MPV and PDW values showed a correlation with hearing loss in Meniere's patients, suggesting that there may be a correlation between the severity of MD and MPV and PDW values.

CONCLUSION

MPV and PDW values indicate vascular pathologies that are important in the pathogenesis of MD. Our study suggests that MPV and PDW may be potential new markers in evaluating MD, and there may be a significant relationship between MPV and PDW values and disease course and severity. Since the number of patients with advanced and profound SNHL is limited in our study, further studies with MD with advanced hearing loss are required to support our data.

Ethics Committee Approval: Ethics committee approval was obtained from the Local Ethics Committee (Ethics Committee No:71522473/050.01.04/162).

Informed Consent: Written informed consent was obtained.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- F.T., S.G.E., M.E.G.; Data Acquisition- F.T., S.G.E., M.E.G.; Data Analysis/Interpretation- F.T., S.G.E., M.S.Y.; Drafting Manuscript- F.T., S.G.E., M.G.; Critical Revision of Manuscript- F.T., S.G.E., M.G., M.S.Y.; Final Approval and Accountability- F.T., S.G.E., M.S.Y., M.E.G., M.G.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Ciccone MM, Scicchitano P, Gesualdo M, Cortese F, Zito A, Manca F, et al. Idiopathic sudden sensorineural hearing loss and Meniere syndrome: The role of cerebral venous drainage. Clin Otolaryngol 2018;43(1):230-9.
2. Havia M, Kentala E. Progression of symptoms of dizziness in Meniere's disease. Arch Otolaryngol Head Neck Surg 2004;130(4):431-435.
3. Mateijsen DJ, Van Hengel PW, Van Huffelen WM, Wit HP, Albers FW. Puretone and speech audiometry in patients with Meniere's disease. Clin Otolaryngol Allied Sci 2001;26(5):379-387.
4. Liu Y, Xu H. The intimate relationship between vestibular migraine and Meniere disease: a review of pathogenesis and presentation. Behav Neurol 2016;2016:3182735.
5. Paparella MM, Djalilian HR. Etiology, pathophysiology of symptoms, and pathogenesis of Meniere's disease. Otolaryngol Clin North Am 2002;35(3):529-45.
6. Paparella MM. Pathogenesis and pathophysiology of Meniere's disease. Acta Otolaryngol 1991;485:26-35.

7. Foster CA, Breeze RE. The Meniere attack: an ischemia/reperfusion disorder of inner ear sensory tissues. Med Hypotheses 2013;81(6):1108-15.
8. Bruno A, Napolitano M, Califano L, Attanasio G, Giugliano V, Cavazzuti PP6, et al. The Prevalence of Chronic Cerebrospinal Venous Insufficiency in Meniere Disease: 24-Month Follow-up after Angioplasty. J Vasc Interv Radiol 2017;28(3):388-91.
9. Mancini F, Catalani M, Carru M, Monti B. History of Meniere's disease and its clinical presentation. Otolaryngol Clin North Am 2002;35(3):565-80.
10. Gussen R. Vascular mechanisms in Meniere's disease. Theoretical considerations. Arch Otolaryngol 1982;108(9):544-9.
11. Karli R, Alacam H, Unal R, Kucuk H, Aksoy A, Ayhan E. Mean platelet volume: is it a predictive parameter in the diagnosis of sudden sensorineural hearing loss? Indian J Otolaryngol Head Neck Surg 2013;65(4):350-3.
12. Demirkol S, Balta S, Unlu M, Yuksel UC, Celik T, Arslan Z, et al. Evaluation of the mean platelet volume in patients with cardiac syndrome X. Clinics (Sao Paulo) 2012;67(9):1019-22.
13. Mayer FJ, Hoke M, Schillinger M, Minar E, Arbesú I, Koppensteiner R, et al. Mean platelet volume predicts outcome in patients with asymptomatic carotid artery disease. Eur J Clin Invest 2014;44(1):22-8.
14. Berger JS, Eraso LH, Xie D, Sha D, Mohler ER 3rd. Mean platelet volume and prevalence of peripheral artery disease, the National Health and Nutrition Examination Survey, 1999-2004. Atherosclerosis 2010;213(2):586-91.
15. Braekkan SK, Mathiesen EB, Njølstad I, Wilsgaard T, Størmer J, Hansen JB Mean platelet volume is a risk factor for venous thromboembolism: the Tromsø Study, Tromsø, Norway. J Thromb Haemost 2010;8(1):157-62.
16. Ulu S, Ulu MS, Ahsen A, Yucedag F, Aycicek A, Celik S. Increased levels of mean platelet volume: a possible relationship with idiopathic sudden hearing loss. Eur Arch Otorhinolaryngol 2013;270(11):2875-8.
17. Sagit M, Kavugudurmaz M, Guler S, Somdas MA. Impact of mean platelet volume on the occurrence and severity of sudden sensorineural hearing loss. J Laryngol Otol 2013;127(10):972-6.
18. Friberg U, Rask-Andersen H. Vascular occlusion in the endolymphatic sac in Meniere's disease. Ann Otol Rhinol Laryngol 2002;111(3 Pt 1):237-45.
19. Hood NA. Diseases of the central nervous system. Cerebral atherosclerosis, transient ischaemic attacks, Menière's disease, and disorders of balance. Br Med J 197515;4(5993):398-400.
20. Sansanayudh N, Numthavaj P, Muntham D, Yamwong S, McEvoy M, Attia J, et al. Prognostic effect of mean platelet volume in patients with coronary artery disease. A systematic review and meta-analysis. Thromb Haemost 2015;114(6):1299-309.
21. Yang SW, Cho SH, Kwon HS, Sohn IS, Hwang HS. Significance of the platelet distribution width as a severity marker for the development of preeclampsia. Eur J Obstet Gynecol Reprod Biol 2014;175:107-11.
22. Zheng YG, Yang T, Xiong CM, He JG, Liu ZH, Gu Q, et al. Platelet distribution width and mean platelet volume in idiopathic pulmonary arterial hypertension. Heart Lung Circ 2015;24(6):566-72.
23. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haematol 2002;117(2):399-404.
24. Huczek Z, Kochman J, Filipiak KJ, Horszczaruk GJ, Grabowski M, Piatkowski R, et al. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005;46(2):284-90.
25. Rechciński T, Jasińska A, Foryś J, Krzemińska-Pakuła M, Wierzbowska-Drabik K, Plewka M, et al. Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous coronary intervention. Cardiol J 2013;20(5):491-8.
26. Ozbay I, Kahraman C, Balikci HH, Kucur C, Kahraman NK, Ozkaya DP, et al. Neutrophil-to-lymphocyte ratio in patients with peripheral vertigo: a prospective controlled clinical study. Am J Otolaryngol 2014;35(6):699-702.
27. Şahin MI, Kokoğlu K, Gulmez E. Mean platelet volume, neutrophil- and platelet to lymphocyte ratios are elevated in vestibular neuritis. J Clin Neurosci 2019;67:134-38.
28. Gunes A, Karali E, Ural A, Ruzgar F, Bayatkara T. The relationship of high-frequency distortion product otoacoustic emission (DPOAE) values with hematological parameters in tinnitus patients. Eur Arch Otorhinolaryngol 2019;276(11):3013-9.
29. Lee JS, Hong SK, Kim DH, Lee JH, Lee HJ, Park B, et al. The neutrophil-to-lymphocyte ratio in children with sudden sensorineural hearing loss: a retrospective study. Acta Otolaryngol 2017;137(1):35-8.
30. Sun Y, Guo Y, Wang H, Chen Z, Wu Y, Shi, H, et al. Differences in platelet-related parameters among patients with audiographically distinct sudden sensorineural hearing loss: A retrospective study. Medicine (Baltimore) 2017;96(36):e7877.

RESEARCH ARTICLE
DOI: 10.26650/Tr-ENT.2021.1001317
The Turkish Journal of Ear Nose and Throat 2021;31(4):100-104

Nose Obstruction Symptom Evaluation Scale Outcomes in Covid 19 Patients in the Turkish Population and Prognostic Factors Affecting the Scale

Ayse Çeçen[1], Cem Bayraktar[2], Abdulkadir Özgür[2], Gökhan Akgül[2], Özgür Günal[3], Mehmet Eser Sancaktar[2], Merve Mutlu[2]

[1]Samsun University, Faculty of Medicine, Department of Otolaryngology, Samsun, Turkey
[2]Samsun Education and Research Hospital, Department of Otolaryngology, Samsun, Turkey
[3]Samsun Education and Research Hospital, Department of Clinic of Infectious Diseases and Clinical Microbiology, Samsun, Turkey

ORCID ID: A.Ç. 0000-0001-6255-6125; C.B. 0000-0002-7446-9077; A.Ö. 0000-0002-6155-5988; G.A. 0000-0003-0699-6585; Ö.G. 0000-0002-7744-4123; M.E.S. 0000-0002-1498-5539; M.M. 0000-0002-2532-1009

Citation: Cecen A, Bayraktar C, Ozgur A, Akgul G, Gunal O, Sancaktar MS, Mutlu M. Nose obstruction symptom evaluation scale outcomes in Covid 19 patients in the Turkish population and prognostic factors affecting the scale. Tr-ENT 2021;31(4):100-104. https://doi.org/10.26650/Tr-ENT.2021.1001317

ABSTRACT

Objective: Coronavirus Disease 2019 (Covid 19) is a viral pandemic that emerged in East Asia and spread rapidly to the rest of the world and continues in our country. This study aims to evaluate the subjective severity of nasal obstruction with the Turkish Nasal Obstruction Symptom Evaluation (T-NOSE) in patients with laboratory-confirmed Covid 19 infection and to compare with the control group.
Material and Methods: One hundred fifty-seven patients with confirmed Covid 19 infection (group 1, n=157) and 91 individuals without Covid 19 infection as the control group (group 2, n=91) were included in the study. Nasal obstruction complaints of adult patients with Covid 19 infection were evaluated with the T-NOSE scale test and compared with the control group. Covid 19 patients were grouped according to the degree of thoracic CT involvement and the day that the NOSE test was performed.
Results: There was no statistically significant difference between the NOSE scale parameters of the Covid group and the control group (p=0.19). Also, Covid 19 patients were grouped according to the thoracic CT involvement degree and divided into three groups according to the day of the NOSE test. The relationship between these values, and NOSE was evaluated, and no statistically significant difference was found (p=0.65, p=0.385).
Conclusion: T-NOSE is a valid instrument with good internal consistency, reliability, and responsive instrument that is brief and easy to complete and has potential use for outcome studies in adults Covid 19 patients with nasal obstruction.

Keywords: NOSE, Turkish NOSE, Covid 19, Nasal obstruction, adult

INTRODUCTION

It is known that acute respiratory distress syndrome, which started in Wuhan city of Hubei region of China in December 2019, affected the whole world. Coronavirus disease 2019 (Covid 19) is an infectious respiratory disease caused by coronavirus 2, a coronavirus family member, which has a high potential of human-to-human transmission (1).

An infected person may experience symptoms after an incubation period that can range from about 2 to 14 days (there have been rare cases of an incubation period of 29 days), while the person can still be contagious. Precautions such as careful personal hygiene, frequent hand washing, wearing masks and social distancing should be taken to limit the transmission (2).

Coronavirus mainly affects the lower respiratory tract and when the symptoms are examined, fever, fatigue, cough and dyspnea are at the forefront. However, anosmia-hyposmia, lack of taste, diarrhea, sore throat, headache, nasal congestion, rhinorrhea and skin lesions may also develop. In severe cases, pneumonia, acute respiratory distress syndrome, sepsis and septic shock, extending to patient's death, can occur (3, 4).

Corresponding Author: Ayşe Çeçen **E-mail:** aysebel55@hotmail.com
Submitted: 20.09.2021 • **Accepted:** 24.01.2022

In patients without pneumonia, the Covid 19 clinic is similar to some diseases frequently encountered by ENT physicians in the outpatient clinic. Cough, sore throat, shortness of breath, sputum production, fever, rhinorrhea, nasal congestion, oropharynx hyperemia and edema, lymphadenopathy and anosmia are among the ENT complaints and findings of Covid 19 (5, 6).

Nasal congestion is a common symptom with multifactorial origin, stated as a feeling of blockage or insufficient airflow through the nose by the patients. An otolaryngologist encounters this symptom during the examination of Covid 19 patients, as in other viral infections (7, 8).

The NOSE scale is a simple, commonly used, and well-validated quality of life tool specific to nasal airway obstruction. This scale determines the patient's subjective feelings (7).

The Nasal Obstruction Symptom Assessment (NOSE) scale was designed by Stewart et al. (9) in 2004 and has been validated in French (10), Portuguese (11), Italian (12) and Greek (13). Karahatay et al. It adapted the scale to Turkish in 2018 (7).

This study evaluates the subjective severity of nasal obstruction with the NOSE scale (T-NOSE) in patients with laboratory-confirmed Covid 19 infection and to compare it with the control group.

MATERIALS AND METHODS

Study design

The study was conducted between May 2020 and September 2020, in Samsun Training and Research Hospital, by the Department of Otorhinolaryngology and Department of Infectious Diseases and Clinical Microbiology after approved by the SamsunTraining and Research Hospital Human Ethics Committee (Decision number: 2020/6/10). The study was conducted under the rules of the Helsinki Declaration. Patients hospitalized during this study and agreed to participate in the study were included in the study. The study was conducted on patients hospitalized in the Department of Infectious Diseases and Clinical Microbiology. One hundred fifty-seven patients with laboratory-confirmed Covid 19 infection (group 1, n=157) and 91 individuals without Covid 19 infection as the control group (group 2, n=91) were included in the study. A written consent form was obtained from all patients.

Patients

Two hundred forty-eight cases, including 157 patients having Covid 19 (Covid Group) and 91 healthy controls (Control Group), were included in this prospective study.

Covid 19 infection diagnosis is based on serological tests with Covid 19 specific IgM or IgG and/or reverse transcriptase-polymerase chain reaction (RT-PCR).

Researchers applied current tests to patients with appropriate protective equipment to avoid viral transmission. Age, gender, accompanying systemic disease, smoking status, and nasal surgery history of all patients were questioned.

Those with nasal polyps, allergic rhinitis, chronic sinusitis, vasomotor rhinitis, sinonasal malignancy, significant septal deviation, conchal hypertrophy, trauma, or epistaxis history in the last 48 h, who used drugs that may affect nasal obstruction such as systemic and local decongestants, local nasal steroids, anticholinergic agents in the last three months and patients who have had previous nasal surgery were excluded from the study.

All patients underwent anterior rhinoscopic examinations, and those with nasal pathologies such as sinusitis, septum deviation, and nasal polyposis that can cause nasal obstruction were also excluded from the study. A control group was formed from healthy individuals of appropriate age and gender for the patient group. All patients included in the study had NOSE tests.

The NOSE questionnaire, consisting of 5 questions about nasal obstruction experienced by the patients (nasal congestion or stuffiness, nasal blockage or obstruction, trouble breathing through the nose, trouble sleeping, unable to get enough air through) was validated by Stewart et al. (9). Each question is scored using a 5-point Likert scale, and the tool is then scaled to 0 to 100 total points, multiplying the raw score by 5. Higher NOSE survey scores correspond to severe nasal congestion. The reliability and consistency of this scale make it useful to understand how nasal obstruction affects the patient's quality of life. All participants completed the questionnaire themselves without assistance. The NOSE scores of the Covid group were compared with the scores of the control group.

Routine thoracic computed tomography (CT) of Covid 19 patients were grouped according to the normal, focal, and diffuse involvement, and the relationship between these groups and NOSE tests was evaluated. Patients without pulmonary involvement were accepted as normal, those limited to one lung lobe as focal and those with widespread involvement in both lungs as diffuse.

The patients were divided into three groups (group: 1, 1^{st}-3^{rd} days, group 2: 4^{th}-7^{th} days, group 3: 8^{th}-14^{th} days) according to the day of the NOSE test, and the relationship between these groups and NOSE scale was evaluated.

Statistical methods

Statistical Package for Social Science (SPSS) version 21.0 (SPSS Inc., Chicago, IL, and USA) was used for statistical analysis. In data assessment, Kolmogrof -Siminorv was used to test whether data normally distributed or not. The Kruskal-Wallis test was used as a non-parametric test to compare the groups. Chi-square test was used to assess the intergroup difference between groups in gender. Significance level was taken as 0.05.

RESULTS

Two hundred forty-eight cases, including 157 Covid 19 patients (group 1: 71 females and 86 males) (Covid Group) and 91 healthy controls (group 2: 44 females and 47 males) (Control Group), were included in this prospective study. The mean age of Covid (group 1) and control groups (group 2) were

45.80±16.84 and 46.62±15.35 years, respectively. The groups were similar in terms of age and gender (p=0.45, p=0.63$^{\Psi}$) (Table 1).

Table 1: The Results of NOSE Test in Patients with Covid 19 and Healthy Controls and Demographic Features

	Covid group (n= 157)	Control group (n= 91)	p$^{\Upsilon}$ value
Gender			
Male	86	47	0.63$^{\Psi}$
Female	71	44	
Age	45.80±16.84	46.62±15.35	0.45
NOSE questionnaire	0.82±1.26	0.59±1.06	0.19

Υ: Mann-Whitney U test, Ψ: Chi-square test

The mean scores for the NOSE test were determined as 0.82±1.26 for group 1 and 0.59±1.06 for group 2. There was no statistically significant difference between the groups in terms of NOSE tests (p=0.19) (Table 1).

Covid 19 patients were grouped according to the degree of thoracic CT involvement. The relationship between these groups and NOSE tests was evaluated, and the result was not statistically significant (p=0.65) (Table 2).

Table 2: Correlation table between NOSE test and the degree of thoracic CT involvement

CT involvement type (n)	NOSE score	p value*
Normal (95)	0.81±1.33	
Focal (12)	0.66±1.23	0.65
Diffuse (50)	0.88±1.15	

*Kruskal Wallis test

The patients were also divided into three groups according to the day the NOSE test was performed. The relationship between these values and NOSES was evaluated, and no statistically significant difference was found (p=0.385) (Table 3).

Table 3: Comparisons between NOSE test and days

Days (n)	NOSE score	p value*
1st – 3rd days (n=50)	0.880±1.533	0.385
4th – 7th days (n=99)	1.656±2.839	
8th – 14th days (n=8)	1.500±1.603	

*Kruskal Wallis test

DISCUSSION

SARS-CoV-2, the agent of Covid 19, is a sub-type of the coronavirus family defined in the 1960s. Coronaviruses are a family of viruses that can cause respiratory and gastrointestinal infections in animals and humans, settle in the lower respiratory tract, cause pneumonia, and then death due to respiratory failure. These viruses are animal diseases (zoonoses), but they can infect humans and cause epidemics via mutations (14).

The clinical picture of SARS-CoV-2 infection can be asymptomatic, mild, severe, or fatal. According to China's data, 80% of Covid 19 cases are relatively mild, while 15% of patients have severe clinical course. However, more than 80% of the cases are asymptomatic and cannot be identified since they are not tested (6).

The complaints of Covid 19 patients are nonspecific like other respiratory infections. Fever (43%-98%), cough (68%-82%), fatigue (38-44%), sore throat (13.9-17.4%), dry cough (59.4%) and sputum (28-33%) can be seen. Publications have reported that nearly half of the patients have a loss of smell and taste. Nasal obstruction (4.8%) and rhinorrhea (4%) have been reported to be very rare, unlike other upper respiratory tract infections (8).

According to Krajewska et al. review, fever, fatigue, and dry cough are considered the most common symptoms of Covid 19. Anorexia, shortness of breath, sputum production, and myalgia have been reported in more than 25% of cases. Sore throat, rhinorrhea, headache, nausea, and diarrhea are less common symptoms that are present in mild or moderate disease forms (15).

In a meta-analysis of Lovato et al., when evaluated in terms of otolaryngology symptoms, they reported that sore throat (12.4%), nasal congestion (3.7%), and rhinorrhea were the most common symptoms among patients with Covid 19 (16).

Covid 19 can be confused with the flu or common cold regarding initial symptoms, causing patients to apply to the otorhinolaryngology clinic in the foreground. In patients without pneumonia, the clinical presentation of Covid 19 is similar to some diseases that ENT physicians frequently encounter in the outpatient clinic. While the rhinorrhea is more common in colds than other diseases, dry cough is prominent in influenza and Sars-CoV-2 infection. Sudden onset symptoms are more compatible with Covid 19 (5).

In the literature, the rates of nasal symptoms accompanying Covid 19 vary (nasal congestion: 3.7%-67.8%, rhinorrhea: 4%-60.1%). Therefore, we planned to perform the NOSE questionnaire in Covid 19 patients (5, 6, 8, 15-17).

Similar to the literature, the most common symptoms in our patients were fever (22.9%, n=36), fatigue (19.1%,n=30), cough (16.5%, n=26), and dyspnea (12.7%, n=20). Loss of taste and smell (10.1%), n=16, nasal congestion (7.6%, n=12), rhinorrhea (6.3%, n=10), and sore throat (4.4%, n=7) are among the rare upper respiratory tract symptoms we observed in our patients.

Nasal airway obstruction (NAO) is one of the most common clinical indications for otolaryngology referral. The estimated economic burden of this symptom is more than $ 5 billion per year (18). Numerous studies have tried improving this condition's diagnosis. However, NAO remains a diagnostic

challenge due to inconsistencies between subjective symptoms and objective findings such as physical examination, rhinomanometry, peak nasal inspiratory flow, acoustic rhinometry, or radiographic findings (18, 19).

The consensus has shifted toward weighing subjective assessments more due to inconsistencies between objective measurements and subjective evaluations (20). There has been a trend toward using patient-reported outcome measures to assess nasal obstruction, particularly in the form of the NOSE scale. The NOSE scale is a questionnaire used to evaluate patients' quality of life with nasal congestion (9, 20, 21).

In the literature, the NOSE scale has been used in many studies to evaluate the quality of life in patients with nasal obstruction. The NOSE scale has been the most structurally relevant disease-specific quality of life tool that was developed to assess nasal congestion, and it has evidence supporting its validity, reliability and sensitivity (13, 21, 22).

Based on this information in the literature, we evaluated the subjective severity of nasal obstruction with the NOSE scale (T-NOSE) to evaluate nasal symptoms in Covid 19 patients, compared with the control group. In accordance with the literature, we observed that the complaints of nasal obstruction in Covid 19 disease are among the rare upper respiratory tract symptoms in our patients.

Due to high virus concentrations in the nasal cavity, nasopharynx, and oropharynx and close contact of otolaryngologists with the upper respiratory mucosa of the patients, the highest nosocomial transmission rates were reported among otolaryngologists (8, 23).

This study is also critical since it is the first study to investigate NOSE scale changes in patients with Covid 19 in the adult population and compare them with healthy individuals.

One of the crucial limitations of our study is the relatively small number of patients. We think that studies with a larger sample size may contribute to further knowledge.

We applied the NOSE questionnaire to Covid 19 patients who were hospitalized in the Covid inpatient clinic. It is thought that nasal symptoms of outpatients are more common than inpatients. Comparing the test with outpatients and inpatients would have changed the results of our study (17).

Covid 19 is a disease with increasing importance in many countries, including Turkey.

We think that the Covid 19 does not significantly change the NOSE tests, which aims to evaluate the upper respiratory tract activity since it dominantly affects the lower respiratory tract.

Since specific otolaryngological symptoms such as nasal obstruction and rhinorrhea are rare in Covid 19 disease, unlike other upper respiratory tract infections, otolaryngologists should consider every patient as positive.

Ethics Committee Approval: The study was conducted between May 2020 and September 2020, in SamsunTraining and Research Hospital, by the Department of Otorhinolaryngology and Department of Infectious Diseases and Clinical Microbiology after approved by the SamsunTraining and Research Hospital Human Ethics Committee (Decision number: 2020/6/10). The study was conducted under the rules of the Helsinki Declaration.

Informed Consent: Written informed consent was obtained.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- A.Ç., C.B., A.Ö., G.A., Ö.G., M.E.S., M.M.; Data Acquisition- G.A., M.B.; Data Analysis/Interpretation- A.Ç., C.B., A.Ö., G.A., Ö.G., M.E.S., M.M.; Drafting Manuscript- A.Ç., C.B., A.Ö., G.A., Ö.G., M.E.S., M.M.; Critical Revision of Manuscript- A.Ç., C.B., A.Ö., G.A., Ö.G., M.E.S., M.M.; Final Approval and Accountability- A.Ç., C.B., A.Ö., G.A., Ö.G., M.E.S., M.M.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Ozen G, Koc H, Aksoy C. Health anxiety status of elite athletes in COVID-19 social isolation period. Bratisl Med J 2020;121(12): 888-93.
2. Fiorillo L, Cervino G, Matarese M, D'Amico Cesare, Surace Giovanni, Paduano Valeria, et al. COVID-19 Surface Persistence: A Recent Data Summary and Its Importance for Medical and Dental Settings. Int J Environ Res Public Health 2020;17(9):3132.
3. Zhang Y, Xu J, Li H, Cao B. A novel coronavirus (COVID-19) outbreak: A call for action. Chest 2020;157(4):e99-e101.
4. Yang Y, Shang W, Rao X. Facing the COVID-19 outbreak: What should we know and what could we do? J Med Virol 2020;92(6):536-7.
5. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382(18):1708-20.
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497-506.
7. Karahatay S, Taşlı H, Karakoç Ö, Aydın Ü, Türker T. Reliability and validity of the Turkish Nose Obstruction Symptom Evaluation (NOSE) scale. Turk J Med Sci 2018;48:212-6.
8. Vukkadala N, Qian ZJ, Holsinger FC, Patel ZM, Rosenthal E. COVID-19 and the Otolaryngologist: Preliminary Evidence-Based Review. Laryngoscope 2020;130(11):2537-43.
9. Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngol Head Neck Surg 2004;130(2):157-63.
10. Marro M, Mondina M, Stoll D, de Gabory L. French validation of the NOSE and Rhino QOL questionnaires in the management of nasal obstruction. Otolaryngol Head Neck Surg 2011;144(6):988-93.
11. Bezerra TF, Padua FG, Pilan RR, Stewart MG, Voegels RL. Cross-cultural adaptation and validation of a quality of life questionnaire: the Nasal Obstruction Symptom Evaluation questionnaire. Rhinology 2011;49(2):227-31.

12. Mozzanica F, Urbani E, Atac M, Scotta G, Luciano K, Bulgheroni C, et al. Reliability and validity of the Italian Nose Obstruction Symptom Evaluation (I-NOSE) scale. Eur Arch Otorhinolaryngol 2013;270(12):3087-94.
13. Lachanas VA, Tsiouvaka S, Tsea M, Hajiioannou JK, Skoulakis CE. Validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale for Greek patients. Otolaryngol Head Neck Surg 2014;151(5):819-23.
14. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokinestorm and immunopathology. Semin Immunopathol 2017;39(5):529-39.
15. Krajewska J, Krajewski W, Zub K, Zatoński T. COVID-19 in otolaryngologist practice: a review of current knowledge. Eur Arch Otorhinolaryngol 2020;277(7):1885-97.
16. Lovato A, de Filippis C. Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms. Ear Nose Throat J 2020;99(9):569-76.
17. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med 2020;288(3):335-44.
18. Casey KP, Borojeni AAT, Koenig LJ, Rhee JS, Garcia GJM. Correlation between subjective nasal patency and ınıranasal airflow distribution. Otolaryngol Head Neck Surg 2017;156 (4):741-50.
19. Lam DJ, James KT, Weaver EM. Comparison of anatomic, physiological, and subjective measures of the nasalairway. Am J Rhinol 2006;20(5):463-70.
20. Cannon DE, Rhee JS. Evidence-Based Practice: Functional Rhinoplasty. Otolaryngol Clin North Am 2012;45(5):1033-43.
21. Gu JT, Kaplan S, Greenfield S, Calloway H, Wong BJF. Validation of a Septoplasty Deformity Grading System for the Evaluation of Nasal Obstruction. Laryngoscope 2019;129(3):586-93.
22. Barone M, Cogliandro A, Di Stefano N, Tambone V, Persichetti P. A Systematic review of patient-reported outcome measures after rhinoplasty. Eur Arch Otorhinolaryngol 2016;274(4):1807-11.
23. Lu R, Zhao X, Li J, Niu P, Yang P, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395(10224):565-74.

CASE REPORT
DOI: 10.26650/Tr-ENT.2021.1026815
The Turkish Journal of Ear Nose and Throat 2021;31(4):105-107

Pediatric Nodular Fasciitis in the Head and Neck Region

Mustafa Caner Kesimli[1], İbrahim Yağcı[1], Eren Yılmaz[2], Aysel Bayram[3], Murat Ünal[4]

[1]Istinye University, Faculty of Medicine, Department of Otolaryngology, Head and Neck Surgery, Istanbul, Turkey
[2]Gelişim University, Faculty of Medicine, Department of Otolaryngology, Head and Neck Surgery, Istanbul, Turkey
[4]Istanbul University, Faculty of Medicine, Department of Pathology, Istanbul, Turkey
[5]Mersin University, Facultyof Medicine, Department of Otolaryngology, Head and Neck Surgery, Mersin, Turkey

ORCID ID: M.C.K. 0000-0003-1675-0394; İ.Y. 0000-0003-2039-8362; E.Y. 0000-0002-5349-9699; A.B. 0000-0002-5014-0074; M.Ü. 0000-0002-5524-9175

Citation: Kesimli MC, Yagci I, Yilmaz E, Bayram A, Unal M. Pediatric nodular fasciitis in the head and neck region. Tr-ENT 2021;31(4):105-107. https://doi.org/10.26650/Tr-ENT.2021.1026815

ABSTRACT

Nodular fasciit is a rare benign tumor and may occur anywhere in the body. Pediatric patients constitute approximately 10% of the entire patient group.
The disease may show clinical and pathological features resembling malignancy. Therefore, it can be mistaken as sarcoma.
This report shows two cases of pediatric nodular fasciitis localized in the parotid region and maxillary sinus.

Keywords: Nodular fasciitis, Spindle cell tumors, Maxillofacial region, Head and neck

INTRODUCTION

Nodular fasciitis (NF) is an extremely rare benign tumor that is localized in the subcutaneous tissue and presents as a mass (1). It was first defined by Konwaller in 1955 as "subcutaneous pseudosarcomatous fibromatosis" (1). NF usually presents as painless, rapidly growing solitary tumors and is most common in the third and fourth decades (1). While tumor localization in NF is most common in the upper extremity (48%), it is less frequent in the trunk (20%), lower extremities (15%) and head and neck (15-20%) (1, 2).

The disease may show clinical and pathological features resembling malignancy, such as increased mitotic activity and rapid growth. For this reason, it can be confused with sarcoma (2). Therefore, a definitive diagnosis of the lesion should be made to avoid unnecessarily aggressive or inappropriate treatment. To increase awareness of NF as a differential diagnosis in rapid-growing solitary tumours in the head and neck region, we present two cases of NF the first, occurring in the parotid region, and the second in the maxillary sinus.

CASE REPORTS

Case-1

A 5-year-old male patient applied to our clinic complaining of facial swelling in the right parotid region which had progressed rapidly during a period of 3 months to the size of 3x2 cm (Figure 1). The

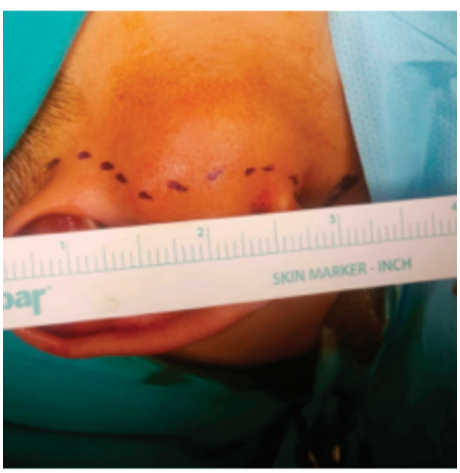

Figure 1: Right facial swelling in the pre-auricular region.

Corresponding Author: Mustafa Caner Kesimli **E-mail:** canerkesimli@gmail.com

Submitted: 11.01.2022 • **Accepted:** 18.01.2022 • **Published Online:** 28.01.2022

patient's medical history was unremarkable. The patient had no history of trauma or surgery.

The tumor was a mobile, firm mass palpable in the subcutaneous tissue of the left cheek. There was no facial nerve paralysis or paraesthesia and no local or regional enlarged lymph nodes.

Fine needle aspiration (FNA) cytological analysis revealed a neuronal tumor. Magnetic resonance imaging showed the presence of a round, intraparotid, solid nodule; no other masses or lymph nodes were detected.

A superficial parotidectomy was planned. Following a right modified Blair incision, the skin and superficial musculoaponeurotic system were elevated over the tumor. The mass was located at the middle border of the parotid gland sheath, so the surgical plan was changed to tumor excision. The mass was dissected from the parotid tissue and then removed. The skin was sutured. The post-operative hospital stay was uneventful.

The histopathologic report showed a moderately cellular tumor with a hypocellular spindle cell component with collagenous stroma (Figure 2). Immunohistochemical stains were negative for beta-catenin (fibromatosis marker), desmin (smooth muscle marker), S-100 protein (neural marker) with a slight increase in the proliferation marker KI-67. Such findings were thought to be indicative of nodular fasciitis. Over a 24-month follow-up period, ultrasonography (USG) findings were periodically evaluated and no recurrence was detected.

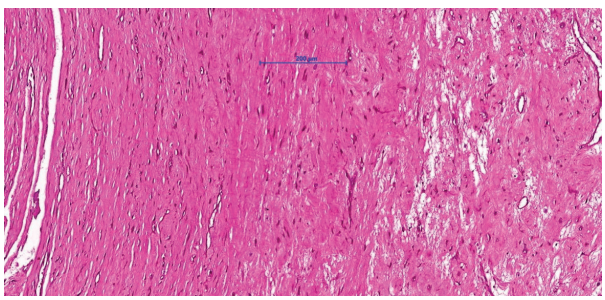

Figure 2: Hypocellular spindle cell tumour component with collagenous stroma (H-E, x100).

The patient's parents provided written consent after being informed about the procedures and aim of the study.

Case 2

A 6-year-old boy was admitted to our department after his parents noticed a facial fullness in the right maxillary region. They had also noticed a slight swelling at the right nasal sidewall, which had progressed rapidly during a period of 2 months. The medical and surgical history was normal and the patient had no history of trauma or surgery.

Examination revealed a 5x4 cm solid mass at the right maxillary area extending to the right nasal cavity. Nasal mucosa was normal; however, the inferior turbinate was pushed medially and compressed on the right side. A CT scan and MRI showed a right maxillary well-circumscribed mass, measuring 5x4.1 cm.

A mid-facial degloving procedure was performed. After right sub-labial incision, the mass was removed from the maxillar sinus cavity (Figure 3). Incisions were closed with appropriate sutures. The post-operative stay was normal.

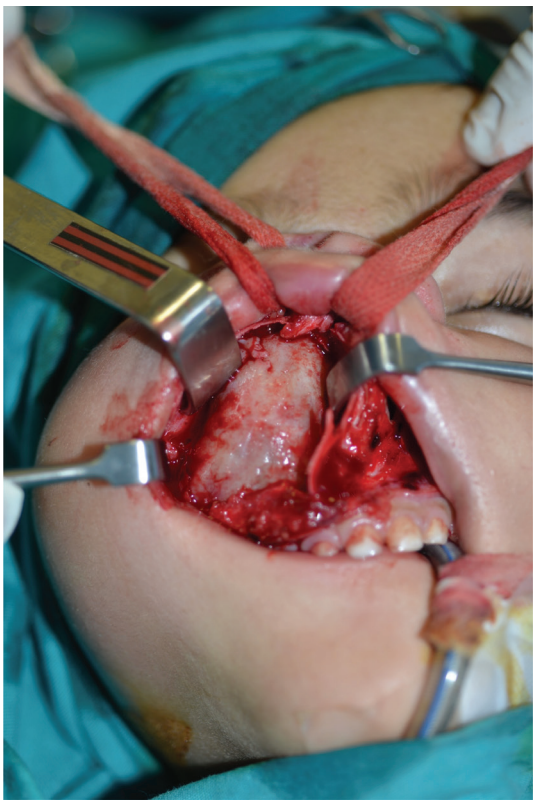

Figure 3: Right side well-circumscribied maxillary mass.

The histopathologic report showed a moderately cellular lesion comprising of proliferating spindle cells with collagenized stroma and focal myxomatous areas (Figure 4).

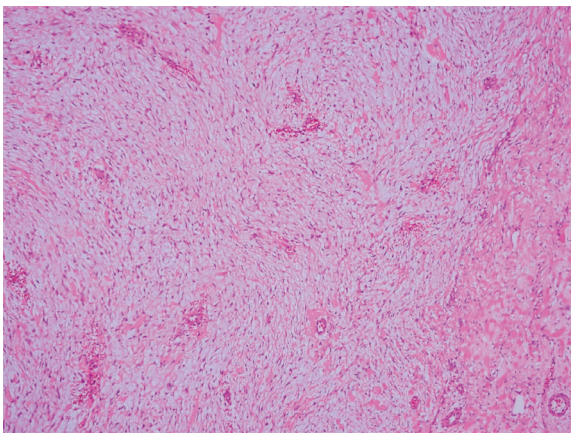

Figure 4: Proliferation of fibroblastic/myofibroblastic spindle cells within myxoid and collagenous stroma (Hematoxylin and eosin, x100).

Immunohistochemical stains were negative for sarcoma and diagnosis was accepted as NF.

Over an 18-month follow-up period, magnetic resonance imaging (MRI) findings were regularly evaluated and no recurrence was detected.

His parents provided written consent after being informed about the procedures and aim of the study.

DISCUSSION

The prevalence of NF in children is rare with 10% of cases being observed in pediatric patients (3). In pediatric patients, unlike in adult patients, tumor location is most commonly reported in the head and neck region: in the facial skin, scalp, tongue, mandible, cheek mucosa, throat and floor of the mouth (2, 3). Paranasal sinus involvement is extremely rare (2). In our series one patient had a tumor in the parotid region and the other was in the maxillary sinus.

The etiology of this hyperproliferative tumor is unknown. Formerly, trauma was believed to play an important role. However, in recent years Erickson-Johnson et al. found NF is associated with MYHP-USP6 gene fusion (4). In our cases, there was no history of trauma.

NF usually presents as a rapid growing mass and mimics malignancy when it occurs in the head and neck region. Nonspecific imaging findings often contribute to this misdiagnosis. Differential diagnosis is important to rule out other malignancies, especially sarcomas, schwannomas and salivary gland tumours (1-3). Fibrosarcoma can be differentiated from NF by its less myxoid matrix mitoses and higher hypercellularity (2). Schwannomas are well-defined, round and encapsulated. Histologic features typically include palisades and Antoni A/B areas. Immunohistochemical stains show S100 positivity and can confirm the epidermal origin of schwannoma (2). In Pleomorphic adenoma a spindle cell presence is similarly seen in a myxoid stroma with strong actin positivity, however, the presence of inflammatory cells and mitoses suggest NF (2).

The best treatment is complete surgical excision with negative surgical margins (5). Awareness of nodular fasciitis and its benign nature is very important to avoid misdiagnosis and over-treatment for the patient. Since very few of these masses occur in children and the head and neck region, clinicians should consider this when evaluating pediatric soft tissue masses.

Main Points

1) Nodular fasciitis is characterized by rare, benign, proliferative masses localized in the subcutaneous tissue.

2) It presents as painless, rapid-growing solitary tumours.

3) It is commonly misdiagnosed as sarcoma because of rapid growth and increased mitotic activity.

4) The best treatment is complete surgical excision.

Informed Consent: Written informed consent was obtained.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- M.C.K., İ.Y., E.Y., A.B., M.Ü.; Data Acquisition- M.C.K., İ.Y., E.Y., A.B., M.Ü.; Data Analysis/Interpretation- M.C.K., İ.Y., E.Y., A.B., M.Ü.; Drafting Manuscript- M.C.K., İ.Y., E.Y., A.B., M.Ü.; Critical Revision of Manuscript- M.C.K., İ.Y., E.Y., A.B., M.Ü.; Final Approval and Accountability- M.C.K., İ.Y., E.Y., A.B., M.Ü.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Be K. Subcutaneous pseudosarcomatous fibromatosis (fasciitis). Am J Clin Pathol 1955;25(3):241-52.
2. Allison DB, Wakely Jr PE, Siddiqui MT, Ali SZ. Nodular fasciitis: A frequent diagnostic pitfall on fine-needle aspiration. Cancer Cytopathol 2017;125(1):20-9.
3. DiNardo LJ, Wetmore RF, Potsic WP. Nodular fasciitis of the head and neck in children: a deceptive lesion. Arch Otolaryngol Neck Surg 1991;117(9):1001-2.
4. Erickson-Johnson MR, Chou MM, Evers BR, Roth CW, Seys AR, Jin L, et al. Nodular fasciitis: a novel model of transient neoplasia induced by MYH9-USP6 gene fusion. Lab Investig 2011;91(10):1427-33.
5. Oh BH, Kim J, Zheng Z, Roh MR, Chung KY. Treatment of nodular fasciitis occurring on the face. Ann Dermatol 2015;27(6):694-701.

AIM AND SCOPE

The Turkish Journal of Ear Nose and Throat (Tr-ENT) aims to contribute to the literature by publishing high quality original articles, case clinical reports, surgical techniques and invited reviews focusing on key subjects and contemporary developments in the field. The scope of the journal includes otology, neurootology, rhinology, head and neck, general ORL, facial plastic surgery and laryngology. The journal welcomes articles from other disciplines as well, provided that these are related to the major subject area. The target audience of the journal consists of academicians, researchers, professionals, students, related professional and academic bodies and institutions.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

The Turkish Journal of Ear Nose and Throat is currently indexed in TUBITAK ULAKBIM TR Index.

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process.

All expenses of the journal are covered by the İstanbul University.

INSTRUCTION TO AUTHORS

The Turkish Journal of Ear Nose and Throat (Tr-ENT) is an international, scientific, open acces and peer-reviewed publication of Istanbul University. It is published quarterly in March, June, September and December. The publication language of the journal is English. The journal started off in 1990 under the editorship of Professor Behbut Cevanşir. Since then it has been a significant source of knowledge in the field of otorhinolaryngology for researchers, residents and specialists. As of year 2018 Volume 28 Issue 1, the title of the journal was changed from “Kulak Burun Boğaz İhtisas Dergisi” (ISSN: 1300-7475, E-ISNN: 2147-67569) to “The Turkish Journal of Ear Nose and Throat” and the journal decided to publish articles only in English with a frequency of four issues per year. The Turkish Journal of Ear Nose and Throat aims to contribute to the literature by publishing high quality original articles, case reports, surgical techniques and invited reviews focusing on key subjects and contemporary developments in the field. The scope of the journal includes otology, neurootology, rhinology, head and neck, general ORL, facial plastic surgery and laryngology. The journal welcomes articles from other disciplines as well, provided that these are related to the major subject area. The target audience of the journal consists of academicians, researchers, professionals, students, related professional and academic bodies and institutions. Former title of the journal: Kulak Burun Boğaz İhtisas Dergisi (P-ISNN: 1300-7475 / E-ISNN: 2147-6756)

POLICIES

Publication Policy

The journal is committed to upholding the highest standards of publication ethics and pays regard to Principles of Transparency and Best Practice in Scholarly Publishing published by the Committee on Publication Ethics (COPE), the Directory of Open Access Journals (DOAJ), the Open Access Scholarly Publishers Association (OASPA), and the World Association of Medical Editors (WAME) on https://publicationethics.org/resources/guidelines-new/principles-transparency-and-best-practice-scholarly-publishing

The subjects covered in the manuscripts submitted to the Journal for publication must be in accordance with the aim and scope of the Journal. Only those manuscripts approved by every individual author and that were not published before in or sent to another journal, are accepted for evaluation.

Changing the name of an author (omission, addition or order) in papers submitted to the Journal requires written permission of all declared authors.

Plagiarism, duplication, fraud authorship/denied authorship, research/data fabrication, salami slicing/salami publication, breaching of copyrights, prevailing conflict of interest are unethical behaviors. All manuscripts not in accordance with the accepted ethical standards will be removed from the publication. This also contains any possible malpractice discovered after the publication.

Plagiarism

Submitted manuscripts that pass preliminary control are scanned for plagiarism using iThenticate software. If plagiarism/self-plagiarism will be found authors will be informed. Editors may resubmit manuscript for similarity check at any peer-review or production stage if required. High similarity scores may lead to rejection of a manuscript before and even after acceptance.

Depending on the type of article and the percentage of similarity score taken from each article, the overall similarity score is generally expected to be less than 15 or 20%.

Double Blind Peer-Review
After plagiarism check, the eligible ones are evaluated by the editors-in-chief for their originality, methodology, the importance of the subject covered and compliance with the journal scope. The editor provides a fair double-blind peer review of the submitted articles and hands over the papers matching the formal rules to at least two national/international referees for evaluation and gives green light for publication upon modification by the authors in accordance with the referees' claims.

Open Access Statement
The journal is an open access journal and all content is freely available without charge to the user or his/her institution. Except for commercial purposes, users are allowed to read, download, copy, print, search, or link to the full texts of the articles in this journal without asking prior permission from the publisher or the author. This is in accordance with the BOAI definition of open access.

Article Processing Charge

All expenses of the journal are covered by the Istanbul University. Processing and publication are free of charge with the journal. There is no article processing charges or submission fees for any submitted or accepted articles.

Copyright Notice
Authors publishing with the journal retain the copyright to their work licensed under the Creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0) (https://creativecommons.org/licenses/by-nc/4.0/) and grant the Publisher non-exclusive commercial right to publish the work. CC BY-NC 4.0 license permits unrestricted, non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ETHICS

Publication Ethics and Malpractice Statement
The Turkish Journal of Ear Nose and Throat (Tr-ENT) is committed to upholding the highest standards of publication ethics and pays regard to Principles of Transparency and Best Practice in Scholarly Publishing published by the Committee on Publication Ethics (COPE), the Directory of Open Access Journals (DOAJ), the Open Access Scholarly Publishers Association (OASPA), and the World Association of Medical Editors (WAME) on https://publicationethics.org/resources/guidelines-new/principles-transparency-and-best-practice-scholarly-publishing

All parties involved in the publishing process (Editors, Reviewers, Authors and Publishers) are expected to agree on the following ethical principles.

All submissions must be original, unpublished (including as full text in conference proceedings), and not under the review of any other publication synchronously. Authors must ensure that submitted work is original. They must certify that the manuscript has not previously been published elsewhere or is not currently being considered for publication elsewhere, in any language. Applicable copyright laws and conventions must be followed. Copyright material (e.g. tables, figures or extensive quotations) must be reproduced only with appropriate permission and acknowledgement. Any work or words of other authors, contributors, or sources must be appropriately credited and referenced.

Each manuscript is reviewed by at least two referees under double-blind peer review process. Plagiarism, duplication, fraud authorship/denied authorship, research/data fabrication, salami slicing/salami publication, breaching of copyrights, prevailing conflict of interest are unethical behaviors.

All manuscripts not in accordance with the accepted ethical standards will be removed from the publication. This also contains any possible malpractice discovered after the publication.

Research Ethics
The journal adheres to the highest standards in research ethics and follows the principles of international research ethics as defined below. The authors are responsible for the compliance of the manuscripts with the ethical rules.

- Principles of integrity, quality and transparency should be sustained in designing the research, reviewing the design and conducting the research.

- The research team and participants should be fully informed about the aim, methods, possible uses and requirements of the research and risks of participation in research.
- The confidentiality of the information provided by the research participants and the confidentiality of the respondents should be ensured. The research should be designed to protect the autonomy and dignity of the participants.
- Research participants should participate in the research voluntarily, not under any coercion.
- Any possible harm to participants must be avoided. The research should be planned in such a way that the participants are not at risk.
- The independence of research must be clear; and any conflict of interest or must be disclosed.
- In experimental studies with human subjects, written informed consent of the participants who decide to participate in the research must be obtained. In the case of children and those under wardship or with confirmed insanity, legal custodian's assent must be obtained.
- If the study is to be carried out in any institution or organization, approval must be obtained from this institution or organization.
- In studies with human subject, it must be noted in the method's section of the manuscript that the informed consent of the participants and ethics committee approval from the institution where the study has been conducted have been obtained.

Ethics Committee Approval and Informed Consent

The Turkish Journal of Ear Nose and Throat (Tr-ENT) takes as principle to comply with the ethical standards of World Medical Association (WMA) Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects revised in 2003 and WMA Statement on Animal Use in Biomedical Research revised in 2016.

An approval of research protocols by the Ethics Committee in accordance with international standards mentioned above is required for experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts concerning experimental research on humans, a statement should be included that shows that written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Materials and Methods section of the manuscript. It is the authors' responsibility to carefully protect the patients' anonymity. For photographs that may reveal the identity of the patients, signed releases of the patient or of their legal representative should be enclosed.

Author's Responsibilities

It is authors' responsibility to ensure that the article is in accordance with scientific and ethical standards and rules. And authors must ensure that submitted work is original. They must certify that the manuscript has not previously been published elsewhere or is not currently being considered for publication elsewhere, in any language. Applicable copyright laws and conventions must be followed. Copyright material (e.g. tables, figures or extensive quotations) must be reproduced only with appropriate permission and acknowledgement. Any work or words of other authors, contributors, or sources must be appropriately credited and referenced.

All the authors of a submitted manuscript must have direct scientific and academic contribution to the manuscript. The author(s) of the original research articles is defined as a person who is significantly involved in "conceptualization and design of the study", "collecting the data", "analyzing the data", "writing the manuscript", "reviewing the manuscript with a critical perspective" and "planning/conducting the study of the manuscript and/or revising it". Fund raising, data collection or supervision of the research group are not sufficient roles to be accepted as an author. The author(s) must meet all these criteria described above. The order of names in the author list of an article must be a co-decision and it must be indicated in the Copyright Agreement Form. The individuals who do not meet the authorship criteria but contributed to the study must take place in the acknowledgement section. Individuals providing technical support, assisting writing, providing a general support, providing material or financial support are examples to be indicated in acknowledgement section.

All authors must disclose all issues concerning financial relationship, conflict of interest, and competing interest that may potentially influence the results of the research or scientific judgment.

When an author discovers a significant error or inaccuracy in his/her own published paper, it is the author's obligation to promptly cooperate with the Editor to provide retractions or corrections of mistakes.

Responsibility for the Editor and Reviewers

Editor-in-Chief evaluates manuscripts for their scientific content without regard to ethnic origin, gender, sexual orientation, citizenship, religious belief or political philosophy of the authors. He/She provides a fair double-blind peer review of the submitted articles for publication and ensures that all the information related to submitted manuscripts is kept as confidential before publishing.

Editor-in-Chief is responsible for the contents and overall quality of the publication. He/She must publish errata pages or make corrections when needed.

Editor-in-Chief does not allow any conflicts of interest between the authors, editors and reviewers. Only he has the full authority to assign a reviewer and is responsible for final decision for publication of the manuscripts in the Journal.

Reviewers must have no conflict of interest with respect to the research, the authors and/or the research funders. Their judgments must be objective.

Reviewers must ensure that all the information related to submitted manuscripts is kept as confidential and must report to the editor if they are aware of copyright infringement and plagiarism on the author's side.

A reviewer who feels unqualified to review the topic of a manuscript or knows that its prompt review will be impossible should notify the editor and excuse himself from the review process.

The editor informs the reviewers that the manuscripts are confidential information and that this is a privileged interaction. The reviewers and editorial board cannot discuss the manuscripts with other persons. The anonymity of the referees must be ensured. In particular situations, the editor may share the review of one reviewer with other reviewers to clarify a particular point.

PEER REVIEW

Peer Review Policies
Only those manuscripts approved by its every individual author and that were not published before in or sent to another journal, are accepted for evaluation.

Submitted manuscripts that pass preliminary control are scanned for plagiarism using iThenticate software. After plagiarism check, the eligible ones are evaluated by editor-in-chief for their originality, methodology, the importance of the subject covered and compliance with the journal scope.

The editor hands over the papers matching the formal rules to at least two national/international referees for double-blind peer review evaluation and gives green light for publication upon modification by the authors in accordance with the referees' claims.

Responsibility for the Editor and Reviewers
Editor-in-Chief evaluates manuscripts for their scientific content without regard to ethnic origin, gender, citizenship, religious belief or political philosophy of the authors. Editor-in-Chief provides a fair double-blind peer review of the submitted articles for publication and ensures that all the information related to submitted manuscripts is kept as confidential before publishing.

Editor-in-Chief is responsible for the contents and overall quality of the publication. He/She must publish errata pages or make corrections when needed.

Editor-in-Chief does not allow any conflicts of interest between the authors, editors and reviewers. Only he has the full authority to assign a reviewer and is responsible for final decision for publication of the manuscripts in the Journal.

Reviewers must have no conflict of interest with respect to the research, the authors and/or the research funders. Their judgments must be objective.

Reviewers must ensure that all the information related to submitted manuscripts is kept as confidential and must report to the editor if they are aware of copyright infringement and plagiarism on the author's side.

A reviewer who feels unqualified to review the topic of a manuscript or knows that its prompt review will be impossible should notify the editor and excuse himself from the review process.

The editor informs the reviewers that the manuscripts are confidential information and that this is a privileged interaction. The reviewers and editorial board cannot discuss the manuscripts with other persons. The anonymity of the referees must be ensured. In particular situations, the editor may share the review of one reviewer with other reviewers to clarify a particular point.

Peer Review Process
Only those manuscripts approved by its every individual author and that were not published before in or sent to another journal, are accepted for evaluation.

Submitted manuscripts that pass preliminary control are scanned for plagiarism using iThenticate software. After plagiarism check, the eligible ones are evaluated by Editor-in-Chief for their originality, methodology, the importance of the subject covered and compliance with the journal scope.

Editor-in-Chief evaluates manuscripts for their scientific content without regard to ethnic origin, gender, citizenship, religious belief or political philosophy of the authors and ensures a fair double-blind peer review of the selected manuscripts. The selected manuscripts are sent to at least two national/international referees for evaluation and publication decision is given by Editor-in-Chief upon modification by the authors in accordance with the referees' claims. Editor-in-Chief does not allow any conflicts of interest between the authors, editors and reviewers and is responsible for final decision for publication of the manuscripts in the Journal. Reviewers' judgments must be objective. Reviewers' comments on the following aspects are expected while conducting the review.

- Does the manuscript contain new and significant information?
- Does the abstract clearly and accurately describe the content of the manuscript?
- Is the problem significant and concisely stated?
- Are the methods described comprehensively?
- Are the interpretations and consclusions justified by the results?
- Is adequate references made to other Works in the field?
- Is the language acceptable?

Reviewers must ensure that all the information related to submitted manuscripts is kept as confidential and must report to the editor if they are aware of copyright infringement and plagiarism on the author's side.

A reviewer who feels unqualified to review the topic of a manuscript or knows that its prompt review will be impossible should notify the editor and excuse himself from the review process.

The editor informs the reviewers that the manuscripts are confidential information and that this is a privileged interaction. The reviewers and editorial board cannot discuss the manuscripts with other persons. The anonymity of the referees is important.

Manuscript Organization and Submission

The manuscripts should be prepared in accordance with ICMJE-Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in December 2015 - http://www.icmje.org/icmje-recommendations.pdf). Author(s) are required to prepare manuscripts in accordance with the CONSORT guidelines for randomized research studies, STROBE guidelines for observational original research studies, STARD guidelines for studies on diagnostic accuracy, PRISMA guidelines for systematic reviews and meta-analysis, ARRIVE guidelines for experimental animal studies, and TREND guidelines for non-randomized public behavior.

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at https://dergipark.org.tr/tr/journal/3565/submission/step/manuscript/new Manuscripts submitted via any other medium will not be evaluated.

Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests.

Author(s) are required to submit the following documents together with the manuscript and must ensure that the abstract and keywords are in line with the standards explained in below.

- **Copyright Agreement Form**
- **Author Form and ICMJE Potential Conflict of Interest Disclosure Form**
- **Ethics Committee Approval**
- **Cover Letter to the Editor**
- **Title Page**: A separate title page should be submitted with all submissions and this page should include:

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,
- Name(s), affiliations, academic degree(s) and ORCID ID(s) of the author(s),
- Grant information and detailed information on the other sources of support,
- Name, address, telephone (including the mobile phone number) and fax numbers, and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfil the authorship criteria.

Abstract: Abstract should be submitted with all submissions except for Letters to the Editor. The abstract of Original Articles should be structured with subheadings (Objective, Materials and Methods, Results, and Conclusion). Abstracts of Case Reports and Reviews should be unstructured. Abstracts should be 200-250 words.

Keywords: Each submission must be accompanied by a minimum of 3 to a maximum of 6 keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (http://www.nlm.nih.gov/mesh/MBrowser.html) .

Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Material and Method, Results, Discussion, and Conclusion subheadings..

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

Units should be prepared in accordance with the International System of Units (SI).

Invited Review Articles: Reviews prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future studies. The main text should contain Introduction, Clinical and Research Consequences, and Conclusion sections. Please check Table 1 for the limitations for Review Articles.

Case Reports: There is limited space for case reports in the journal and reports on rare cases or conditions that constitute challenges in diagnosis and treatment, those offering new therapies or revealing knowledge not included in the literature, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Presentation, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Case Reports.

Letters to the Editor: This type of manuscript discusses important parts, overlooked aspects, or lacking parts of a previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a "Letter to the Editor." Readers can also present their comments on the published manuscripts in the form of a "Letter to the Editor." Abstract, Keywords, and Tables, Figures, Images, and other media should not be included. The text should be unstructured. The manuscript that is being commented on must be properly cited within this manuscript.

Tables

Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

Revisions

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be canceled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial 30-day period is over. Accepted manuscripts are copy-edited for grammar, punctuation, and format. Once the publication process of a manuscript is completed, it is published online on the journal's webpage as an ahead-of-print publication before it is included in its scheduled issue. A PDF proof of the accepted manuscript is sent to the corresponding author and their publication approval is requested within two days of their receipt of the proof. The latest status of the submitted manuscripts and other information about the journal can be accessed at http://tr-ent.com. The editorial and publication processes of the journal are conducted in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice). An ORCID ID is required for all authors during the submission of the manuscript. The ID is available at http://orcid.org with free of charge.

Reference Style and Examples

Authors are responsible for supply complete and correct references. References should be numbered according to the order used in the text. Numbers should be given in brackets and placed at the end of the sentence. Examples are given below on the use of references. Reference end note style Vancouver

Periodicals: Author(s) Last Name initial(s) name of author(s) (if there are six or fewer authors, all authors should be written; if the number of authors are seven or more, only the first six of the authors should be written and the rest as "et al"). The title of the article, the abbreviated name of the journal according to the Index Medicus, Year; Volume (Issue): The first and last page numbers.

Example: Robson A, Greene J, Ansari N, Kim B. Eccrine porocarcinoma (malignant eccrine poroma): a clinicopathologic study of 69 cases. The American Journal of Surgical Pathology 2001;25:710-20. Books: Surname of the author(s) initial name(s) of author(s). The name of the book. The edition number. Place of publication: Publisher, Publication year.

Book chapters: The author (s) surname of the chapter initial (s) letter of the name. Section title. In: Surname of editor (s) initial (s) letter of first name (s) ed / eds. The name of the book. Edition number. Place of publication: Publisher, year of publication: The first and last page numbers of the chapter. Web address: If a "web" address is used as the reference address, the web address date should be given in brackets with the address. The DOI (Digital Object Identifier) number must be provided, when a web access article used in the text as a reference.

Example: AB Author, CD Author. Title of document. Retrieved from http://Web address (Accession date: aa/bb/2016).

Congress papers:

Thesis: Maden KL. Experimental investigation of the ..... Master Thesis, Health Science Institute of Ankara University, Ankara, 2005.

SUBMISSION CHECKLIST

- Cover letter to the editor
  - The category of the manuscript
  - Confirming that "the paper is not under consideration for publication in another journal".
  - Including disclosure of any commercial or financial involvement.
  - Confirming that the statistical design of the research article is reviewed.
  - Confirming that last control for fluent English was done.
  - Confirming that journal policies detailed in Information for Authors have been reviewed.
  - Confirming that the references cited in the text and listed in the references section are in line with NLM.
- Copyright Agreement Form
- Author Form
- Permission of previous published material if used in the present manuscript
- Acknowledgement of the study "in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration.
- Statement that informed consent was obtained after the procedure(s) had been fully explained. Indicating whether the institutional and national guide for the care and use of laboratory animals was followed as in "Guide for the Care and Use of Laboratory Animals".
- Title page
  - The category of the manuscript
  - The title of the manuscript
  - Short title (running head)
  - All authors' names and affiliations (institution, faculty/department, city, country), e-mail addresses
  - Corresponding author's email address, full postal address, telephone and fax number
  - ORCIDs of all authors.
- Main Manuscript Document
  - The title of the manuscript
  - Abstract 200-250 words
  - Key words: 3 - 6 words
  - Main article sections
  - References
  - Acknowledgement (if exists)
  - All tables, illustrations (figures) (including title, description, footnotes)

Editor: İsmet Aslan
Address: Istanbul University, Istanbul Faculty of
Medicine Deanery, Turgut Özal Cad. 34093, Çapa,
Fatih, Istanbul, Turkey
Phone: +90 212 414 21 61
E-mail: tr-ent@istanbul.edu.tr

Publisher: Istanbul University Press
Address: İstanbul Üniversitesi Merkez Kampüsü,
34452 Beyazıt, Fatih / Istanbul, Turkey
Phone: +90 212 440 00 00