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Aims and Scope

The journal publishes clinical and experimental studies, interesting case reports, invited reviews and letters to the editor. Middle Black Sea Journal of Health Science is an international journal which is based on independent and unbiased double-blinded peer-review principles. The publishing language of the journal is English.

The aim of the journal is to publish original articles with highest clinical and scientific quality at the international level. Middle Black Sea Journal of Health Science also publishes reviews covering fundamental innovations in health education, editorial articles, case reports and original images.

The contents of all issues in full text can be accessed free of charge through the web site <http://dergipark.gov.tr/mbsjohs>

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Peer-review: Externally peer-reviewed.

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Chapter in Edited Book

Hornbeck P. Assay for antibody production. Colign JE, Kruisbeek AM, Marguiles DH, editors. *Current Protocols in Immunology*. New York: Greene Publishing Associates; 1991. p. 105-32.

Book with a Single Author

Fleiss JL. *Statistical Methods for Rates and Proportions*. Second Edition. New York: John Wiley and Sons; 1981.

Editor(s) as Author

Balows A, Mousier WJ, Herramaffl KL, editors. *Manual of Clinical Microbiology*. Fifth Edition. Washington DC: IRL Press. 1990.

Conference Paper

Entrala E, Mascaro C. New structural findings in *Cryptosporidium parvum* oocysts. Eighth International Congress of Parasitology (ICOPA VIII); October, 10-14; Izmir-Turkey: 1994. p. 1250-75

Thesis

Erakıncı G. Searching for antibodies against parasites in donors. İzmir: Ege University Health Sciences Institute. 1997.

Article in Electronic Format

Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: <http://www.cdc.gov/ncidod/EID/cid.htm>.

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Structure

English title, author names and institutions.

Abstract (average 200-400 word)

Introduction

Methods

Results

Discussion and conclusion

References (most 40)

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Methods

Results

Discussion and conclusion

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c) Case Report: They are rarely seen articles which differs in diagnosis and treatment. They should be supported by enough photographs and diagrams.

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Abstract (average 100-300 word)

Introduction

Case report

Discussion and conclusion

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The compilation text also including appropriate sub-headings,

Conclusion

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Discussion and conclusion

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Surgical technique

Conclusion

References (most 15)

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Structure

Abstract (average 100-150 word)

Topics related to the subject.

Conclusion

References (3-5 inter)

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300 words of text and original images about the subject

References (3-5 inter)

i) What is Your Diagnosis? Are the articles prepared as in questions and answers about rarely seen diseases which differ in the diagnosis and treatment?

Structure

Topics related to the subject.

References (3-5 inter)

i) Questions and Answers: Are the texts written in form of questions and answers about scientific educative –instructive medical issues.

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The fifth year...

This year there are seven articles in our first issue, 6 original and one compilation.

Original articles are as follows;

Patients with constipation and related factors study the aim of are to assess the etiologic causes, clinical features and factors related to constipation among cases attending with constipation complaints. In other study, examinations and treatments of patients hospitalized in the clinic with the complaint of corrosive substance ingestion were examined.

The researcher in the study about the obstetrics to appoint the risk of stillbirth and the other adverse maternal and perinatal outcomes in women of AMA (Advanced maternal age) that traditionally described as pregnancy in women aged 35 years or older. Also, in another research about the obstetrics, the researcher was conducted to determine osteoporosis health beliefs and self-efficacy of Turkish women and to investigate the relationship between women's characteristics with osteoporosis health beliefs and self-efficacy.

In other study the researches in cardiology and eye had together was to evaluate the relationship between the retinal findings and coronary artery disease by performing fundoscopic examination in patients diagnosed with coronary artery disease.

Our last article is on the field of microbiology analysis of the widely used antibiotics all susceptibility testing results from *Escherichia coli* (*E. coli*) cultured from clinical specimens' private hospital was performed.

In this issue the subject about the challenge of pathological diagnosis for precancerous cervical Lesions has been submitted as the compilation.

Many thanks to the authors, referees and editorial board who contributed to this issue hope to meet again in different and new issues you have pleasure while reading...

PhD, Assoc. Prof. Ülkü KARAMAN

Editor

Patients with Constipation and Related Factors

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Abstract

Objectives: Constipation is a widespread public health problem throughout the world and is commonly seen in the childhood period. The aim of this study is to assess the etiologic causes, clinical features and factors related to constipation among cases attending with constipation complaints.

Methods: The files and automation records of 162 cases aged from one month to 18 years attending the pediatric health and diseases clinic with the complaint of constipation from January 2018 to January 2019 were retrospectively investigated.

Home accidents were self-reported and questioned for the previous year. We developed a composite index to assess the overall housing conditions. Housing conditions were accepted “inadequate” if the score was below the median. We developed a logistic regression model to predict the housing-related factors in accidents.

Results: The mean age of cases included in the study was 51,1±40,8 months (2-192 months), with 53,1% of patients (n=86) in the one month-3 years age interval. Of cases, 62.3% were female and 37.7% were male. Toilet training had been given to 56.8% of cases, with mean age of toilet training 2±0.5 years. Fiber intake was insufficient in 72,2%, while fluid intake was insufficient for 84,5%. Of patients, 56,2% (n=91) had begun supplementary nutrition early (before 6 months). Of cases, 22,8% had developmental retardation, while 13% (n=21) had urinary tract infection as an additional accompanying problem. The most common accompanying complaints were abdominal pain and bleeding while defecating. In 39% of patients, there was family history of constipation. The functional constipation rate was 90.1%, while 1.9% had hypothyroidism, 1,9% had anal stenosis, 1,9% had medication use, 1,2% had Hirschprung disease, 1,2% had hypopotassemia, 1,2% had hypercalcemia and one case had vitamin D intoxication identified.

Conclusion: Constipation is associated with factors like toilet training age, beginning supplementary food early and insufficient fiber and fluid amounts in diet. It may cause growth development delay, urinary system infections and behavior problems.

Key words: Child, constipation, etiology

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Introduction

Constipation is a common complaint in the childhood period. It forms 3% of attendances at general pediatric clinics and 25% of attendances at pediatric gastroenterology clinics (Taitz et al., 1986; Loening, 1993). Apart from the neonatal period, 90-95% of cases have no organic cause identified and these patients receive functional constipation diagnosis (Baker et al., 1999; Benninga, 2004). There are many factors underlying functional constipation like fiber-poor nutrition, problems during toilet training and

holding feces (Loening, 1993; Benninga, 2004; Rajindrajith and Devanarayana, 2011). In our study, we aimed to assess the sociodemographic data, etiologic causes and factors related to constipation among pediatric patients attending due to constipation.

Methods

The study included patients aged from one month to 18 years attending Ministry of Health Ordu University Education-Research Hospital Pediatric Health and Diseases Clinic from January 2018 to January 2019 with complaint of constipation. Data for 162 patients with full information accessed in file and automation records were retrospectively investigated. The patient age, gender, initial complaint, age of toilet training, onset time of complaints, duration of breastfeeding, time of starting supplementary food, fiber and fluid amounts in diet, duration of complaints, growth development, physical examination findings, family history and laboratory parameters were assessed. Constipation was diagnosed according to Rome III criteria (Hyman et al., 2006; Rasquin et al., 2006).

A statistical package program was used for statistical analysis. Descriptive analysis of assessment results was given as numbers and percentage for categorical variables and as mean ± standard deviation, minimum and maximum for numerical variables.

Results

The number of cases included in the study was 162, with 101 female (62,3%) and 61 males (37,7%). The mean age of cases was 51.1 ±40.8 months (2-192 months), with 53.1% (n=86) in the 1 month-3 years age interval (Table 1).

Table 1. Distribution of cases with constipation according to age group.

Age group	(%) n
1month-3years	(53,1%) 86
4-6years	(24,7%) 40
≥7years	(22,2%) 36

Toilet training had been given to 92 cases (56,8%), with mean age of toilet training 2±0.5 years. Of cases, 62 (38,3%) had duration of constipation less than 2 months, while 100 (61,7%) had constipation for longer than 2 months. When the fiber and fluid intake of cases included in the study

was investigated, 27,8% (n=45) had sufficient fiber intake and 72,2% (n=117) had insufficient fiber intake, while 15,5% (n=25) had sufficient fluid intake and 84,5% (n=137) had insufficient fluid intake. Of patients, 56,2% (n=91) had begun supplementary food early (before 6 months). When patients are assessed in terms of developmental retardation, 37 (22,8%) had developmental retardation, while 125 (77,2%) did not. Of patients, 13% (n=21) had urinary tract infection as an additional accompanying problem.

When the main complaints of patients with constipation are assessed, 49 of the 162 cases (30,1%) had abdominal pain, 16 (9,8%) had bleeding while defecating, 15 (9,2%) had fecal incontinence and 11 (6,7%) had abdominal distension.

When cases are assessed in terms of constipation among family members, 99 (61%) had no history of constipation in the family, while 63 (39%) had family history of constipation. The most common family member with constipation history was the mother for 19,1% (n=31).

It was identified that 146 cases (90,1%) had functional constipation, while 16 (9,9%) had an organic cause. Organic causes identified for cases included hypothyroidism for three cases, anal stenosis for three cases, medication use for three cases, Hirschprung disease for two cases, hypopotassemia for two cases, hypercalcemia for two cases and vitamin D intoxication for one case (Table 2).

Table 2. Aetiology of constipation

Etiology	(%) n
Functional	(90,1%) 146
Organic	(9,9%) 16
Hypothyroidism	(1,9%) 3
Anal stenosis	(1,9%) 3
Drugs	(1,9%) 3
Hirschprung disease	(1,2%) 2
Hypokalemia	(1,2%) 2
Hypercalcemia	(1,2%) 2
Vitamin D intoxication	(0,6%) 1

Of children with constipation, 17,3% (n=28) bit their nails, 8,6% (n=14) sucked their fingers, 2.5% (n=4) stuttered, 1,9% (n=3) bit their nails and sucked their fingers and 0,6% (n=1) sucked their fingers and stuttered. There was no behavior problem for 112 (69,1%) children. Of the patients, 47 (29%) had received pharmacologic treatment in any period for the complaint, while 115 (71%) had not. Among

pharmacologic treatments administered, lactulose was in first place at 25,9% (n=42).

When trigger causes of the complaints were investigated, it was concluded that 10 cases (6,2%) had begun school, 8 (4,9%) had siblings born, 6 (3,7%) had moved, 2 (1,2%) had begun school and had a sibling born, 2 (1,2%) had parents divorce, 1 (0,6%) had lost a relative and 1 (0,6%) was affected by the behavior of a cartoon character. For 132 cases (81,6%), no trigger cause could be identified.

Discussion

Constipation is a defecation disorder commonly observed in the childhood period. In the literature, there are studies showing no difference in constipation incidence between the genders, in addition to studies showing higher incidence in male or female genders (Ip et al., 2005; Sarı and Dogan, 2012, Soylyu, 2013). In our study, 62,3% of cases were girls. Constipation is commonly observed in children from two-four years when toilet training is given (Rasquin et al., 2006; Afzal et al., 2011). When the age distribution of our patients is examined, the constipation complaint was most common in children from one month to three years of age (53,1%), with the mean age of toilet training two years. Our findings comply with the literature.

Chronic constipation is defined as hard and painful defecation for at least two months along with defecation frequency of less than three times per week. As families do not know for definite when constipation begins, this duration is assessed as shorter than two months (acute) and longer than two months (chronic). Accordingly, 61,7% of our cases had duration longer than two months and chronic constipation. Constipation is a situation that causes growth development delays (Guideline, 2006). The study by Sarı and Dogan (2012) found this rate was 17,2%, while Sanlı et al. (2014) found this rate was 10%. In our study, development delay was present in 22,8% (n=37) of cases.

There are studies showing children who begin supplementary feeding early have a higher tendency toward constipation (Cumingham et al., 2001; Coughlin, 2003). Of our patients, 56,2% (n=91) had begun supplementary food early. High-fiber nutrition and enough fluid intake is recommended to prevent constipation (Weber et al., 2014). A study assessing nutritional content observed most cases with constipation had insufficient fiber content and fluid intake in diet

(Sanlı et al., 2014). In our study, similarly, 72,2% of cases had insufficient nutritional fiber and 84,5% had insufficient fluid intake.

Constipation is accompanied by symptoms like abdominal pain, bleeding while defecating and abdominal distension. In the literature there are studies with rates of 12,2% and 66% for abdominal pain (Dogan et al., 2005; Sahin et al., 2014). In our study, 30,1% of cases had abdominal pain complaints. A study by Dogan et al. (2005) found the incidence of bleeding with defecation was 15%, while the abdominal distension rate was 2,9%. We found the incidence of bleeding while defecating was 9,8%, with abdominal distension rate of 6,7%. The differences in these rates may be due to differences in the study populations and the definitions of patient complaints.

Constipation being present in family members for more than 40% of children with constipation and constipation incidence being 6 times greater in single-egg twins compared to double-egg twins leads to the consideration of genetic tendency (Altaf and Sood, 2008). Soylyu (2013), in a study of 355 patients, found family constipation history for 41%. In our study this rate was similar at 39%.

In 95% of patients with constipation, no organic cause can be identified in the etiology. This situation is called functional constipation (Baker et al., 1999). Dogan et al. (2005) in a study of 269 patients, found the functional constipation rate was 91,4%. Soylyu (2013) identified this rate as 91%. In our study, the functional constipation rate was identified as 90,1%, with hypothyroidism, anal stenosis and medication use first place among organic constipation causes with equal incidence of 1,9%.

It is reported that in children with constipation and no anatomic or neurologic problems, urinary tract infections (UTI) may be observed (Mohkam, 2013). Two different studies found the UTI incidence rates were 8% and 9% among children with constipation (Loening, 1993; Sahin et al., 2014). In our patients, we found a similar rate of 13%.

It is stated that children with constipation may experience a range of behavior problems due to not coping with this problem and internalizing the problem. Among these problems, the most common is biting fingernails (Dijk et al., 2007). A study by Savaser et al. (2011) found 17,1% of cases bit their nails. Among our cases, 30,9% (n=50) had behavior problems and nail-biting was first place at 17,3% (n=28) in accordance with the literature.

The first stage of treatment for constipation is balanced nutrition with sorbitol-rich fruit, sufficient fiber and fluids and urination training for those who are toilet-trained. If there is no response, medical treatment may be arranged (Dogan et al., 2005). For medical treatment, the most commonly chosen medication is lactulose 13. In our study, lactulose was the most commonly chosen medication for 25,9% of cases given medical treatment.

Conclusion

Constipation is a complaint with no gender difference that may be seen in all age groups and frequently has chronic progression. Among important organic causes of constipation that require research are hypothyroidism, anorectal anomalies, medications causing constipation, Hirschsprung disease, hypopotassemia, hypercalcemia and vitamin D intoxication. The majority of cases have functional constipation, with early supplementary food, and lack of care about sufficient fiber and fluid intake causing this situation. To prevent constipation and to ensure treatment success for patients, the importance of focusing on these controllable risk factors should be explained to parents. Additionally, due to the presence of comorbid situations like urinary tract infection and behavior problems which may accompany constipation, constipation treatment should be completed in multidisciplinary fashion.

Ethics Committee Approval: Ethics committee approval was received for this study from Clinical Research Ethics Committee of Ordu University. (Decision Number: 2019-22)

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Assessment of Unavoidable Corrosive Substance Ingestion in Children

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Abstract

Objective: Corrosive substances are agents which ease our lives, but they can also make children's lives completely difficult as a result of contact with gastrointestinal tract, respiratory tract and skin. Examinations and treatments of patients hospitalized in our clinic with the complaint of corrosive substance ingestion were examined.

Methods: The records of 45 patients who were hospitalized in our clinic between May 2017 and December 2018 were examined retrospectively. The patients' ages, genders, ingested corrosive substance, admission and discharge inflammatory markers were examined according to diagnosis and treatment type.

Results: Of the 45 cases, 24 (53,3%) were male, while 21 (46,7%) were female. The youngest case was 9 months old, the oldest case was 168 months and average age of the cases was 24,7 months. The substances the cases were exposed to were bleach in 20 patients (44,4%), dishwasher detergent in 11 patients (24,4%), rinse aid in 5 patients (11,1%), drain cleaner in 4 patients (8,9%), washing machine detergent in 3 patients (6,7%), decalcifier in 1 patient (2,2%) and surface cleaner (sodium hypochlorite) in 1 patient (2,2%). Endoscopy was performed on two patients with clinical symptoms who ingested drain cleaner. Statistically significant difference was found between the hospitalization and discharge white blood cell count $\times 10^3/uL$ (WBC), lymphocyte count $\times 10^3/uL$ (LYM), platelet count $\times 10^3/uL$ (PLT), red blood cell width (RDW,%), mean platelet volume (MPV), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) values of the patients ($p < 0.05$).

Conclusion: With precautions taken to prevent the ingestion of corrosive substances, a significant cause of morbidity and mortality can be prevented significantly. It is important to raise awareness in families on this issue.

Key words: Child, corrosive substances, esophageal stricture

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Introduction

Chemical substances which are used in every area of our lives both increase the quality of life and also cause a serious risk. Accidental or deliberate ingestion of these by children cause unavoidable caustic intoxications. Due to reasons such as putting corrosive substances in colorful containers that can attract children's interest, in food and drink boxes and in places where children can easily reach, ingestion of corrosive substances is one of the most important and most frequent home accidents in childhood (Ashcraft and Padula, 1974). In the United States, more than ten thousand new cases are recorded annually. Although there is no specified

figure in Turkey, it is around 3-5 thousand annually (Sumeli, 2018).

Especially small children constitute the risky group because of their extreme interest in the environment and putting everything they find into their mouths. Corrosive substances are substances which give both histological and functional damage when they contact the mucosa (Rama and Robert, 1998). Corrosive substances can have alkali or acid properties. Irrespective of their being acid or alkali, these substances may not cause any harm depending on the amount they are ingested, their type or being in liquid or solid form; however, they can also frequently cause severe burnt that can be seen on the mouth and esophagus and even serious complications that can result in death. Corrosive esophagitis frequently occurs with alkali type agents. While all acids except hydrochloric acid cause coagulation necrosis, alkali agents cause liquefaction necrosis. The damage caused by alkalis can reach the depths of tissue (Berthet et al., 1994; Hugh and Kelly 1999). Acids cause superficial burnt, since they neutralize with saliva, they show less effect on esophagus; however, their passage is fast since their viscosity is low. They quickly transfer to the stomach and they can cause burnt in all parts of the stomach, especially the antrum and pylorus, by combining with stomach acids (Nicosia et al., 1974; Jelenko et al., 1974).

In this study, we planned to assess the frequency of contacted corrosive substances, clinical findings, changes in inflammatory markers, diagnosis and treatment phases of patients who referred to the emergency service of our hospital and who were hospitalized by our service due to corrosive substance contact, which does not have a standard treatment protocol yet.

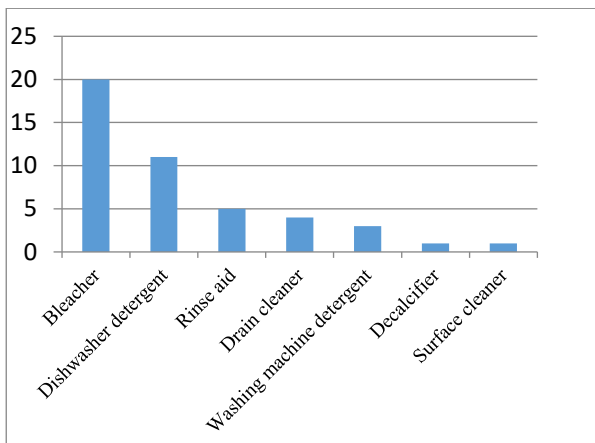
Methods

Ordu Provincial Health Directorate and Ordu University Medical Faculty Training and Research Hospital Clinical Practice Ethics Committee approvals were obtained (Date:07/02/2019, Number: 2019-23). All pediatric patients who were hospitalized in the pediatric surgery clinic of tertiary training and research hospital between May 2017 and December 2018 were included in the study. File records of a total of 45 patients were examined retrospectively in terms of gender, referral age, complete blood count device (ABX Pentra DX 120) was used for the measurement of blood parameters. White blood cell count $\times 10^3/uL$ (WBC), lymphocyte count $\times 10^3/uL$ (LYM), neutrophil count $\times 10^3/uL$ (NEU), platelet count $\times 10^3/uL$ (PLT), mean platelet

volume fL (MPV), red blood cell width (RDW,%), platelet distribution width fL (PDW), platelet /lymphocyte ratio (PLR), neutrophil / lymphocyte ratio (NLR), platelet/neutrophil ratio (PNR), platelet distribution width/red blood cell width ratio (PDW / RDW), C-reactive protein (CRP), biochemical blood tests, physical examination finding records, chest radiography, direct abdominal X-ray, treatment given during hospitalization period, total period of hospitalization, type of corrosive substances ingested, findings and surgery requirements. The cases whose files were found to be incomplete were excluded from the study. Oral intake of patients who had burnt was stopped for 48-72 hours and they were started maintenance fluid therapy, antibiotherapy and H2 receptor antagonist, and those with clinical symptoms were started intravenous steroid. The patients whose lesions regressed and who were able to ingest fluid food were discharged with esophagography planned for three weeks later. The cases were assessed in terms of age, gender, the quality of the ingested substance, examination results and treatment. A statistical package program was used for statistical analysis. Descriptive analysis of assessment results was given as numbers and percentage for categorical variables and as mean, standard deviation, minimum and maximum for numerical variables. Kolmogorov Smirnov test was used to test normality distribution. Paired t test was used in normally distributed parameters for intergroup comparisons, while Wilcoxon test was used for parameters which were not normally distributed. Statistical alpha significance level was accepted as $p < 0,05$.

Results

Of the 45 cases, 24 (53,3%) were male, while 21 (46,7%) were female. The youngest case was 9 months old, the oldest case was 168 months and average age of the cases was 24,7 months. The substances the cases were exposed to were bleacher in 20 patients (44,4%), dishwasher detergent in 11 patients (24,4%), rinse aid in 5 patients (11,1%), drain cleaner in 4 patients (8,9%), washing machine detergent in 3 patients (6,7%), decalcifier in 1 patient (2,2%) and surface cleaner (sodium hypochlorite) in 1 patient (2,2%) , respectively in terms of frequency (Graphic 1). The most frequent referral symptom was edema around the mouth. 2 (4,4%) of the patients were found to have chemical burnt on the femur. Two patients who ingested drain cleaner were



Graphic 1. Corrosive substances contacted

found to have lesion and hypersalivation inside the mouth. Diagnostic esophagoscopy was performed on these patients. Two of the patients were not found to have pathology. In the two patients who had burnt on femur, the burnt was found to recover in 5-7 days without any scars. None of the patients followed were found to have narrowing of the esophagus perforation in their checkups after discharge. No statistically significant difference was found between the hospitalization and discharge NEU, PDW, PNR, PDW/RDW and CRP values of the patients, ($p>0.05$). Statistically significant difference was found between the hospitalization and discharge WBC, LYM, PLT, RDW, MPV, NLR, PLR values of the patients ($p<0.05$) (Table 1).

Table 1. Comparison of hospitalization and discharge biomarker averages of patients

Parameters	Hospitalization (Mean±SD)	Discharge (Mean±SD)	P Value
WBC $\times 10^3/uL$	12,09±3,62	8,21±2,59	<0,01
Neutrophil count $\times 10^3/uL$	4,04±1,82	7,58±2,93	,296
Lymphocyte count $\times 10^3/uL$	6,58±3,27	3,28±1,37	<0,01
Platelet count $\times 10^3/uL$	372,23±118,74	336,46±103,36	<0,01
RDW, %	15,11±2,18	15,23±2,21	,002
MPV fL	8,8±1,06	8,93±1,02	,049
PDW fL	9,86±2,72	10,06±2,42	,217
PNR	114,95±75,46	91,87±46,05	,102
NLR	0,89±1,01	1,52±1,34	<0,01
PLR	92,78±193,73	114,32±64,64	<0,01
PDW/RDW	0,69±0,16	0,68±0,16	,376
CRP	0,15±0,13	0,16±0,18	,077

Discussion

In children, the degree of damage caused by burnt is associated with the type, concentration and amount of the substance ingested, the period of contact and secondary infections that may develop later (Oldham et al., 2005). In the first and second

weeks of corrosive substance ingestion, thrombosis in submucosal veins and therefore necrosis and increase in edema are seen. After the third week, with fibroblasts settling in the submucosa, stenosis can occur depending on the degree of fibrosis and damage. Stenosis, which is the feared complication in clinic, can occur in 25-50% of the cases. While the use of medical treatment is disputed today, the basis of treatment is the prevention of inflammatory reaction and stenosis (Ashcraft and Padula, 1974; Kasap and Ozutemiz, 2006).

Typical symptoms following corrosive substance ingestion are salivating from the side of the mouth, edema on the lips, burnt induced lesions around or inside the mouth, dyspnea, stridor, tachypnea, tachycardia, hoarseness and abdominal pain. Although these symptoms bring burnt into mind, they do not always mean that burnt is present. On the other hand, absence of these symptoms does not eliminate esophagus burnt (Cankorkmaz, 2009). In patients with corrosive substance ingestion, first cessation of oral feeding, intravenous fluid treatment and antibiotherapy are mostly accepted treatment approaches in the acute phase. The primary complication that can be seen in patients after the acute phase is esophageal stenosis (Oldham et al., 2005).

Steroid therapy in corrosive esophagitis is a disputed topic. Although it is reported in some studies that steroid therapy decreases the development of stenosis significantly, some other studies report that steroid is not useful in preventing stenosis and it can even cover mediastinitis clinic in patients with a high risk of perforation (Hawkins et al., 1980; Anderson et al., 1990; Fulton and Hoffman, 2007). In our study, we started intravenous steroid therapy in patients with symptoms. Corrosive substance use was most seen in pre-school children and boys. These results are in parallel with the literature (Kayaalp et al., 2006). Corrosive substance ingestion is seen to peak in two age groups. The first one is 0-5 age group in which children have too much curiosity and wish to learn, take everything into their mouths and imitate elders; while the second one is adolescence period for suicidal purposes (Wasserman and Ginsburg, 1985; Aksu and İnan, 2002). In parallel with the literature, the most frequently ingested substance is hypochloric acid (bleacher) in our study with a rate of 44,4% (Atabek et al., 2007). Complications related with corrosive substance ingestion were not seen in any of our patients who ingested bleacher and who were followed only with medical monitoring. In literature inflammatory markers are examined in many

diseases. RDW was found to be an independent predictor of esophageal burn (Aydin et al., 2017). In parallel with the literature we found some inflammatory markers (WBC, LYM, PLT, RDW, MPV, NLR, PLR) values of the patients were statistically different, ($p < 0.05$). But no statistically significant difference was found between the hospitalization and discharge NEU, PDW, PNR, PDW/RDW and CRP values of the patients, ($p > 0.05$). It can be related with our patients' number was smaller.

In studies conducted, routine esophagoscopy is still controversial in patients who have suspicious corrosive substance ingestion and who do not have any clinical symptoms. While some studies recommend routine esophagoscopy, some others recommend hospitalization and follow up (Gaudreault et al., 1983; Previtera et al., 1990; Romanczuk and Ryszard, 1992; Nuutinen et al., 1994; Roy et al., 1995). In order to keep inflammation in minimum level in patients who have symptoms and who cannot have endoscopy, oral intake should be closed for 72 hours (Genc and Mutaf, 2002; Ozguner et al., 2002). In our study, endoscopy was performed on 2 patients who ingested drain cleaner and had burnt induced lesions around or inside the mouth, hypersalivation and edema on the lips. Both patients were not found to have sign of burn.

Keeping corrosive substances in high shelves and locked cupboards where children cannot reach, educating families by means of media or institutions, making the packages of corrosive substances in colors and shapes that won't attract children's attention, making locks on the lids that children cannot open, putting warnings for families, keeping these substances away from the children and pouring them away immediately after they are put in glasses or different containers during cleaning will significantly reduce this important health problem.

Conclusion

Although no complications resulting from corrosive substance ingestion occurred in our study, complications have a serious impact on the life quality of children and their families. Hemogram parameters can be an independent predictor of esophageal burn for this, more comprehensive studies should be done. It is a fact that diagnosis and treatment are still disputed and corrosive substance ingestion, which is mostly a problem in developing countries, can be prevented to a great extent with some simple precautions.

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RESEARCH ARTICLE

Advanced Maternal Age and Adverse Perinatal Outcomes – One Decade Analysis

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Abstract

Objective: To appoint the risk of stillbirth and the other adverse maternal and perinatal outcomes in women of AMA (Advanced maternal age) that traditionally described as pregnancy in women aged 35 years or older.

Methods: Our study was a retrospective investigation of all women with singleton pregnancies who gave birth at > 20 weeks' gestation aged 35 - 39 years old (early advanced maternal aged group, group I, n=926), aged 40 - 49 years old (late advanced maternal aged group, group II, n=184) and aged 20 - 35 years old (control group, group III, n=1110) between January 2008 and January 2018. Parameters such as age, parity, fetal sex, fetal birth weight, birth pattern (cesarean and vaginal delivery) were examined. The variables investigated to determine perinatal outcomes were low birth weight, macrosomic fetus and stillbirth frequency.

Results: Advanced maternal aged birth ratio to all births was 4.5 %. 83.4% of the advanced age group were the early advanced maternal aged. The low birth weight rate was significantly higher in the AMA group (8.6 % - 5.9 %) (p=0.042). At the same time, the rate of macrosomia was significantly higher in the AMA group too. (9.5 % - 9.1 %) (p=0.042). The rate of caesarean delivery was significantly higher in AMA group (63.7 % - 56.4 %). The stillbirth rate was significantly higher in AMA group (1,6 % - 0,5 %) (p=0.005). In group II; male gender was lower (47.3 % - 55 %) (p=0.034), stillbirth rate was higher (3.8 % - 1.2 %) (p=0.019), birth weight was lower (3193 - 3287) (p=0.048).

Conclusion: The risk of stillbirth was significantly higher in the late advanced maternal aged group. Pregnancies over 35 years of age are high-risk pregnancies necessitating more careful antenatal follow-up in which follow-up of pregnancy must be done more carefully. National mother friendly health policies must focus more on AMA pregnancies. More research is needed to find suitable and well-timed interventions to decrease adverse maternal and also perinatal outcomes.

Key words: Advanced maternal age, stilbirth, high-risk pregnancies.

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Introduction

In past three decades, modern industrial life has had prominent effects on women's reproductive life. Today women commonly postpone their pregnancies and childbearing. Therefore, advanced maternal age (AMA) and related problems are rapidly increasing. AMA is traditionally defined as pregnancy in women aged 35 years or older even though some researchers have used the age limits of 40 and insomuch as 45 years (Bianco et al.,1996; Fretts et al.,1997; Dulitzki et al.,1998; van Katwijk et al.,1998; Gilbert et al.,1999).

This trend in today's society is mostly attributed to older primigravid women who postpone childbearing by various reasons include late marriage, longer life expectancy and higher education career pursuit. And also, multiparous women continue childbearing. On the other hand, effective contraceptive methods and modern infertility treatment options encourage women to delay their pregnancies and childbearing (Guedes et al.,2014).

AMA is reported to be associated with maternal complications and adverse pregnancy outcomes (Cleary-Goldman et al.,2005). Preexisting comorbidities (pregestational hypertension and diabetes) and increased risk of Caesarean birth are related with higher risk of maternal complications. Fetal growth restriction, preeclampsia, placental decolman, preterm delivery is more common among AMA women but the strongest association with AMA is stillbirth according to many researches (Cleary-Goldman et al.,2005; Salihu et al.,2008; Bayrampour et al.,2010; Haines et al.,2011; Giri et al.,2012; Kenny et al.,2013; Khalil et al.,2013). Authors investigating the relation between AMA and stillbirth have chiefly focused on placental aging, dysfunction and insufficiency (Smith et al.,2007; Flenady et al.,2011; RCOG Compaining and opinions 2011).

In our study we aimed to investigate the efficacy of AMA on the rate of stillbirth in Ordu, Turkey. And we determined the other adverse maternal and perinatal outcomes in women of AMA that traditionally defined as pregnancy in women aged 35 years or older.

Methods

This case control study was conducted after receiving approval from the ethics committee (Ordu University Clinical Research Ethics Committee, 26/04/2018, 2018-91). Our study was a retrospective investigation of all women with singleton pregnancies who gave birth at > 20 weeks' gestation aged 35 - 39 years old (early advanced maternal aged group, group I, n=926), aged 40 - 49 years old (late advanced maternal aged group, group II, n=184) and aged 20 - 35 years old (control group, group III, n=1110) at the clinic between January 2008 and January 2018. The control group was randomly formed aged 20 - 35 years old women from 24560 births in the last decade. Adolescent pregnant women (<19 years old) were excluded from the study for not to affect the pregnancy risks of control group. Maternal age was defined as the completed age of the pregnant at the time of delivery.

We separate these groups (named early and late advanced maternal age) because of significance was increasing statistically and also from social aspect maternal age bigger than 40's is increasing much more than maternal age of 35 years old. And we think that late advanced maternal aged pregnant women will increase at the next decades because marriage ages of women will increase due to social reasons especially in developed and developing countries.

Parameters such as age, parity, fetal sex, fetal birth weight, birth pattern (cesarean and vaginal delivery) were examined from hospital registry system and file scanning. The variables used to determine the perinatal outcomes were low birth weight (birth weight < 2500 gr), macrosomic fetus (birth weight > 4000 gr) and stillbirth (delivery of infant > 20 weeks' gestation or > 500 gram weight without cardiac activity) prevalences were investigated and compared between groups.

Statistical analyses were performed with the SPSS 20.0 program package. Mann Whitney-U test or independent samples-t test were used to equate continuous variables, chi square test was used to compare categorical variables.

Results

The records of 24560 patients who delivered between January 2008 and January 2018 were reviewed. Advanced maternal aged birth ratio to all births was 4.5 % (1110/24560). The mean age of advanced maternal aged pregnancies (> 35 years old) was 37.3 ± 2.2 (35 - 49). 83.4 % of the 1110 advanced age group (926/1110) were the early advanced maternal aged (group I), 16.6 % (184/1110) were the late advanced maternal aged group (group II). As control group, 1110 pregnant women aged 20 - 35-year-old who gave birth at our hospital between the same dates participated in the study (group III). Comparison of mean age among the groups were given in table 1.

There was a statistically significant difference between the groups according to parity. The average of parity was 3.19 (1-9) in the advanced maternal aged groups whereas 2.17 (1-7) in control group (p=0.000).

Birth weight was not significantly different between the groups. The average of birth weight was 3272 ± 593 in the advanced maternal aged group whereas 3316 ± 529 in control group (p=0.61).

Table 1. Mean age

	Number	%
Group I (age 35-39)	926/1110	83.4
Group II (age 40-49)	184/1110	16.6
Group III (age 20-35)	1110	

The low birth weight rate was significantly higher in the AMA group (8.6% - 5.9%) (p=0.042). At the same time, the rate of macrosomia was significantly higher in the AMA group too. (9.5% - 9.1%) (p=0.042).

The rate of caesarean delivery was significantly higher in the AMA group (63.7% - 56.4%). We attributed this to high parity in advanced age pregnancies, birth complications and an increased demand for tubal ligation.

There was no significant difference between the fetal sexes (53.7% - 53%) (p=0.383).

The stillbirth rate was significantly higher in advanced age pregnancies (1.6% - 0.5%) (p=0.005).

Comparison of variables among the groups were given in table 2.

Table 2. Comparison of Variables Between AMA and Control Group

	Group AMA (age 35-49)	Group Control (age 20-35)	
Parity	3.19 (1-9)	2.17 (1-7)	P=0.000
Low birth weight rate	8.6	5.9	P=0.042
Macrosomia rate	9.5	9.1	P=0.042
Stillbirth rate	1.6	0.5	P=0.005

There was statistically significant difference between Group I and Group II. In group II; male gender was lower (47.3% - 55%) (p=0.034), stillbirth rate was higher (3.8% - 1.2 %) (p=0.019), birth weight was lower (3193 - 3287) (p=0.048).

Comparison of variables among the AMA group I and II were given in table 3.

Table 3. Comparison of Variables Between AMA Group I and II

	Group I (age 35-39)	Group II (age 40-49)	
Birth weight	3193	3287	P=0.048
Fetal sexes (male)	55	47.3	P=0.034
Stillbirth rate	1.2	3.8	P=0.019

Discussion

In the past three decades, a growing number of women delay childbearing up to advanced ages of their lives. In 2013, 20 % of births in England and Wales were to women advanced maternal aged, compared to 6% in 1980 (RCOG Compaining and opinions 2011, ONS statistical bulletins 2014). According to a multi country data, the prevalence of AMA varied greatly from 2.8% in Nepal to 31.1 % in Japan. The overall prevalence of 29 countries (include 308 149 women) was found 12.3 %. And the highest prevalence of 9.5% was observed in women aged 35 - 39 years (Laopaiboon et al., 2014). In our study we have founded the prevalence 4.5 % below the world average. We also have seen that the early advanced maternal age group ratio to all advanced maternal aged group was 83.4 % whereas 77.2 % in the world average.

Women over age 35 are at increased maternal and perinatal complications when compared to younger women. Such that for no other reason being > 35 years old is associated with high risk pregnancy (Ihab et al., 2008).

Several studies have showed the association between increased feto-maternal adverse outcomes and AMA. Decreased fecundity, high risk of miscarriage, negative impact on in vitro fertilization are affecting the success in conception and pregnancy maintenance. In the antepartum and intrapartum period congenital anomalies, multiple gestation, preeclampsia, gestational diabetes, placental abruption, placenta previa, preterm delivery, low birth weight, macrosomia, malpresentation are important concerns that increasing the severe maternal adverse outcomes including maternal near miss, severe maternal outcome and maternal death and perinatal adverse outcomes. In the postpartum period hemorrhage and also depression is thought to be more prevalent among AMA women (Ihab et al.,2008; Laopaiboon et al., 2014).

Low birth weight may be due to age-related changes in the uterine vasculature, poorer placental perfusion. Multiparity, maternal obesity, smoking and maternal preexisting comorbidities (pregestational hypertension and gestational diabetes) are more common among the older pregnant and increases the adverse perinatal outcomes (Godfrey et al.,1999; Ihab et al.,2008). According to our study birth weight was significantly lower in the > 40 years old group (3193 vs 3287 and 3316). And the low birth weight rate was significantly higher in each AMA groups (8.6 % - 5.9 %).

Maternal obesity and gestational diabetes are also occurring macrosomia. In the recent study the rate of macrosomia was significantly higher in the AMA groups (9.5 % - 9.1 %).

Male: female fetus ratio is bigger than one in the young mothers. But female fetus dominance come up in the AMA women. That advanced aged women miscarry more male fetuses has been used to provide a comment for this observation. In the study male gender was lower in the > 40 years old group (47.3 % vs 55 % and 53 %).

Despite of the recommendations of World Health Organization the cesarean delivery rate has risen rapidly worldwide in recent years that is a important health concern. Because the proportion of advanced maternal aged women is growing, and intercalarily, the cesarean delivery rate is increasing. Several studies have found that advanced maternal age is a risk factor for cesarean delivery (Bayrampour et al.,2010). The rate of caesarean birth was significantly higher in the AMA group (63.7 % vs 56.4 %). We attributed this to high parity, birth complications and an increased demand for tubal ligation. Some authors identified maternal request as one of the factors subscribing to the increasing cesarean birth rate among primiparous women who had in vitro fertilization pregnancy (Roberts et al.,2002; Lin et al.,2004; O'Leary et al.,2007).

There are also some limitations in our article. We designed the study as a retrospective case control study. Prospective studies that including more women (like country studies) can give more information about this growing health concern.

Conclusion

The prevalence of ten years results of advanced aged pregnancies was 4.5 % in our study. Cesarean delivery, low birth weight and macrosomic fetus rate was found to be higher than control group. The risk of stillbirth was significantly higher in the over 40-year-old group compared to the control group. This data has showed that increase in adverse outcomes present from age 35 years but gains speed after 40 years.

Pregnancies over 35 years of age are high-risk pregnancies necessitating more careful antenatal follow-up in which follow-up of pregnancy must be done more carefully. AMA pregnant should referred to centers, including neonatal intensive care units.

Ethics Committee Approval: Ethics committee approval was received for this study from Clinical Research Ethics Committee of Ordu University Medical Faculty.

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Related Factors and Osteoporosis Health Beliefs and Self-Efficacy of Women

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Abstract

Objective: This study was conducted to determine osteoporosis health beliefs and self-efficacy of Turkish women and to investigate the relationship between women's characteristics with osteoporosis health beliefs and self-efficacy.

Methods: The study was planned as descriptive and cross-sectional study design. A convenience sample of 296 volunteer women who applied to the outpatient clinic of one public hospital was recruited. Data were collected via a questionnaire form, the Osteoporosis Health Belief Scale (OHBS) and the Osteoporosis Self-Efficacy Scale (OSES). The questionnaire form and scales were completed by the participants. Since the scales used self-reports, the inclusion criteria of this study required participants to be primary school graduates and being 18 age.

Results: The participants' OHBS subscales average scores were susceptibility, 18.53±4.74; seriousness, 14.68±4.46; benefits of exercise, 23.82±5.06; benefits of calcium intake, 22.12±4.63; barriers to exercise, 16.15±4.75; barriers to calcium intake, 14.68±4.46; health motivation, 22.80±4.7. The total OHBS average score was 138.27±17.93. It was determined that the women's total OSES average score was 790.64±260.96. The subscales of OSES; OSE-Exercise Scale average score was 361.38±162.72, and the OSE-Calcium Scale average score was 429.25±147.57.

Conclusion: The levels of health beliefs and self-efficacy regarding osteoporosis of women were low. Nevertheless, women's perceived benefits scores were found higher than perceived barriers. Nursing can take part in providing education to the public about life-long bone health, and they can also provide information about how to prevent osteoporosis and fracture risk.

Key words: Osteoporosis, health beliefs, self-efficacy, woman, nursing.

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Introduction

In past three decades, modern industrial life has Osteoporosis is a disease which decreases bone density and results in a loss of bone micro structure and a higher risk of fracture (Stubbs, 2010). Throughout the world, one in five men and one in three women are at risk for osteoporotic fracture, which is estimated to occur every three seconds (IOF, 2009). It is estimated 200 million women worldwide suffer from osteoporosis (Shirazi et al., 2007). In a study conducted with 26,424 individuals by the Turkish Osteoporosis Society, half of

participants over age 50 had osteopenia, 25% of them had osteoporosis, and the women's hip fracture rate was 4.1 times higher than men's (Tüzün et al., 2012). Risk factors for osteoporosis are classified as fixed risk factors and modifiable risk factors (IOF, 2009). Fixed risk factors include age, female gender, family osteoporosis history, personal fracture history, menopause, ethnicity, rheumatoid arthritis, long-term glucocorticoid therapy, and primary/secondary hypogonadism in men. Modifiable risk factors are smoking, alcohol use, poor nutrition, low body mass index, vitamin D deficiency, insufficient exercise, frequent falls, eating disorders, and low dietary calcium intake. Fixed risk factors cannot be changed. Everyone should become aware of these risk factors, so that steps can be taken to reduce bone mineral loss. Most of the modifiable risk factors directly impact bone biology, and some of these factors increase the risk of fracture independent of the effect on bones (Stubbs, 2010). The risks which cause a decrease in cancellous bone density are higher in women with estrogen deficiency after menopause (Çakmak et al., 2012).

The most effective way to manage osteoporosis is to promote behaviors associated with healthy living and the protection of bone health (Öztürk and Şendir, 2011). A person's beliefs about osteoporosis health play a very important role in whether one wants to avoid negative health behaviors and become motivated to focus on positive health behaviors and outcomes (Spector, 2000). Although being informed about osteoporosis is important in achieving and maintaining healthy life-style behaviours, knowledge is not enough (Öztürk and Şendir, 2011). The evaluation of osteoporosis health beliefs and a person's willingness and ability to work towards the prevention of this disease are important. The individual's ability to manage their own health issues plays an important role in adopting and continuing new behaviors. Osteoporosis self-efficacy has been shown to be effective in enhancing calcium intake, staying fit and connected to an exercise program, and in demonstrating protective behaviors (Spector, 2000; Sedlak et al., 2000; Piaseu et al., 2002).

The aim of this study was to determine their health beliefs and self-efficacy regarding osteoporosis and to investigate the relationship between women's characteristics with health beliefs and self-efficacy regarding osteoporosis.

The questions explored in this study were:

- What are women's osteoporosis health beliefs and self-efficacy?
- Is there a relationship between women's osteoporosis health beliefs and self-efficacy?
- What is the relationship, if any, among women's characteristics with osteoporosis health beliefs and self-efficacy?

Material and Methods

Study Design and sample

This study was planned as descriptive and cross-sectional design. A convenience sample of 296 volunteer women who applied to the outpatient clinic of one public hospital in a northern province of Turkey. Since the scales used self-reports, the inclusion criteria of this study required participants to be primary school graduates and being the least 18 age.

Data collection

Data were collected via a questionnaire form, the Osteoporosis Health Belief Scale and the Osteoporosis Self-Efficacy Scale (Kim et al., 1991a; Kim et al., 1991b; Kılıç and Erci, 2004). The questionnaire form and scales were completed by the participants in 15-20 minutes via method face to face.

Instruments

Questionnaire Form

Questionnaire form was developed based on the literature review. It consisted of questions including age, height, weight, education level, husband's education level, perception of outcome, living region, marital status, menopausal status, history of osteoporosis in herself, having information about osteoporosis, having bone density measurement, history of hip fracture in family, history of hip fracture in herself, and having bone density treatment.

Osteoporosis Health Belief Scale

Osteoporosis Health Belief Scale (OHBS) was developed to measure individual's health beliefs about developing osteoporosis (Kim et al., 1991a), and was adapted for Turkish use by Kılıç and Erci. OHBS includes total 42 items and seven subscales. The OHBS consist of seven subscale including susceptibility, seriousness, benefits of exercise,

benefits of calcium intake, barriers to exercise, barriers to calcium intake and health motivation of osteoporosis. The low scores from barriers to exercise and barriers to calcium intake subscales and high scores from other subscales means that positive health beliefs. The OHBS is rated using 5-point likert scale (1: strongly disagree, 5: strongly agree). Total score of each subscale is 6 to 30. Cronbach alpha coefficients of the original seven subscales of OHBS developed by Kim et al. in 1991 were between 0.71-0.82. Cronbach alpha coefficients of seven subscales of OHBS was determined between 0.72-0.91 in this study.

Osteoporosis Self-Efficacy Scale

Osteoporosis Self-Efficacy Scale (OSES) including two subscales was developed by Kim et al. (1991a) and adapted for Turkish use by Kılıç and Erci in 2004. OSES is a 12-item tool developed to define self-efficacy about doing weight-bearing exercises and taking calcium. Its subscales: The OSE-Exercise Scale (OSEES) and the OSE-Calcium Scale (OSECS). The range of each item is 0–100, and total score of OSES is 1200. Higher scores indicate better self-efficacy level. Cronbach’s alpha was found 0.94, 0.96 and 0.98, respectively for OSES, OSECS and OSEES were 0.94, 0.96 and 0.98, respectively (Kim et al., 1991a; 1991b). In this study, Cronbach alpha 0.90 for OSEES and 0.92 for OSECS.

Data analysis

The analysis of data was used frequency, percent, arithmetic mean, maximum, minimum as descriptive statistics methods. Also, correlation analysis test, One Way ANOVA test, t test, Kruskal Wallis testi and Mann-Whitney U test and Cronbach alpha coefficient was used in the present study. Statistical significance was set at $p < 0.05$.

Results

Sample characteristics

Two hundred ninety-six women between the ages of 18 and 75 years were enrolled in this study. Their average age was 34.88 ± 12.82 years. Two hundred thirty-three participants (78.7%) were married, 37.2% were primary school graduates, 58.8% were housewives, 56.5% had a mid-level perception of income, and 63.9% of them resided in the province. It was determined that 20.3% of women were menopausal, and 10.1% of them had a

family history of hip fracture. Only four women had experienced a hip fracture in the past, and 29.4% of them were informed about osteoporosis.

OHBS and OSES scores of participants

The participants’ OHBS subscales average scores were as follows: susceptibility, 18.53 ± 4.74 ; seriousness, 14.68 ± 4.46 ; benefits of exercise, 23.82 ± 5.06 ; benefits of calcium intake, 22.12 ± 4.63 ; barriers to exercise, 16.15 ± 4.75 ; barriers to calcium intake, 14.68 ± 4.46 ; health motivation, 22.80 ± 4.7 . The total OHBS scale average score was 138.27 ± 17.93 . It was determined that the women’s total OSES average score was 790.64 ± 260.96 . The OSEES subscale average score was 361.38 ± 162.72 , and OSECS subscale average score was 429.25 ± 147.57 . Women’s total OSES, OSEES and OSECS scores were low.

Correlations between scores of subscales of OHBS and OSES of participants

There was a statistically significant negative correlation between barriers to exercise subscale scores and barriers to calcium intake subscale scores and OSEES scores (respectively, $r = -.249$, $p = .000$, $r = -.157$, $p = .000$). There was a statistically significant negative correlation between barriers to calcium intake and OSECS scores ($r = -.186$, $p = .001$), and there was a statistically significant positive correlation between benefits of exercise and health motivation and OSECS scores (respectively, $r = .122$, $p = .036$, $r = .205$, $p = .000$). There were statistically significant negative correlations between barriers to exercise, barriers to calcium intake and total OSES scores (respectively, $r = -.211$, $p = .000$, $r = -.204$, $p = .000$). There was also a statistically significant positive correlation between health motivation and susceptibility and OSECS (respectively $r = .141$, $p = .015$), (see Table 1).

Table 1. Correlations between subscales of OHBS and OSES

Subscales of OHBS	OSES	OSES	Total OSES
	Exercise	Calcium	
	r	r	r
Perceived susceptibility	-0.051	0.027	-0.017
Perceived seriousness	-0.063	0.021	0.109
Benefits of exercise	0.064	0.122 [†]	0.109
Benefits of calcium intake	0.063	0.103	0.098
Barriers to exercise	-0.249 [‡]	-0.097	-0.211 [‡]
Barriers to calcium intake	-0.157 [‡]	-0.186 [‡]	0.495 [‡]
Health motivation	0.041	0.205 [‡]	0.141 [†]
Total OHBS	-0.092	0.057	-0.025

r; Pearson correlation test, [†] $p < 0.05$, [‡] $p < 0.01$

Osteoporosis health beliefs and self-efficacy of women

Comparisons of OSES scores according to women's sociodemographic and other characteristics

OSES subscales scores according to women's sociodemographic characteristics were compared (see Tables 2-3). The OSEES scores of women who had higher education ($p=.006$), were students

($p=.033$), had "good" income perception ($p=.001$), were premenopausal ($p=.044$), had information about osteoporosis ($p=.027$), and had a hip fracture in the past ($p=.035$) were higher than other women's scores.

Table 2. Comparisons of OSES scores according to women's sociodemographic characteristics (n=296)

Women's socio-demographic characteristics	OSES and subscales		
	OSES Exercise Mean \pm SD	OSES Calcium Mean \pm SD	Total OSES Mean \pm SD
Age groups (years)			
25 and lower	382.67 \pm 144.20	428.1 \pm 130.83	810.81 \pm 222.83
26-35	355.68 \pm 161.85	432.42 \pm 144.20	788.10 \pm 244.00
36-45	381.73 \pm 154.30	437.11 \pm 147.24	818.84 \pm 270.47
46 and higher	324.12 \pm 189.05	419.52 \pm 175.01	743.65 \pm 319.41
<i>P values</i> [†]	0.127	0.926	0.367
Education level			
Primary school	335.63 \pm 175.28	420.63 \pm 160.65	756.27 \pm 296.82
Secondary school	330.00 \pm 149.57	406.74 \pm 163.12	736.74 \pm 237.19
High school	374.00 \pm 151.87	423.90 \pm 136.75	797.90 \pm 231.60
University	429.30 \pm 147.18	486.27 \pm 105.74	915.58 \pm 211.67
<i>P values</i> [†]	0.006	0.047	0.003
Occupation			
Working	381.13 \pm 164.40	460.50 \pm 137.60	841.64 \pm 243.75
House wife	341.66 \pm 170.67	421.20 \pm 154.41	762.87 \pm 277.65
Student	404.88 \pm 107.35	404.41 \pm 129.82	809.30 \pm 204.95
<i>P values</i> [†]	0.033	0.071	0.074
Perception of income			
Low	285.75 \pm 180.21	390.75 \pm 179.53	676.50 \pm 316.74
Middle	358.32 \pm 151.81	422.57 \pm 140.93	780.89 \pm 232.43
Good	401.12 \pm 163.34	459.10 \pm 139.98	860.22 \pm 266.31
<i>P values</i> [†]	0.001	0.034	0.001
Living region			
Village	322.24 \pm 164.25	414.08 \pm 150.59	736.32 \pm 274.54
Town	387.93 \pm 161.44	435.51 \pm 150.60	823.44 \pm 266.22
City	363.38 \pm 161.67	431.26 \pm 146.39	794.65 \pm 254.97
<i>P values</i> [†]	0.110	0.721	0.214
Marital status			
Married	353.86 \pm 166.02	430.47 \pm 151.55	784.33 \pm 267.85
Single	389.20 \pm 147.81	424.76 \pm 132.86	813.96 \pm 234.24
<i>P values</i> [‡]	0.126	0.786	0.425
Husband's education level			
Illiterate	275.00 \pm 174.48	340.83 \pm 166.54	615.83 \pm 289.99
Primary school	357.65 \pm 173.97	447.34 \pm 140.39	805.00 \pm 277.03
Secondary school	360.73 \pm 161.76	402.43 \pm 168.87	763.17 \pm 272.84
High school	346.49 \pm 154.55	434.28 \pm 136.27	780.77 \pm 239.05
University	364.14 \pm 188.69	447.31 \pm 174.05	811.46 \pm 304.75
<i>P values</i> [§]	0.484	0.117	0.177

[†]One-Way ANOVA, [‡]t test, [§]Kruskal Wallis test, SD; Standard deviation

Table 3. Comparisons of OSES scores according to women’s some characteristics (n=296)

Variables	OSES and subscales		
	OSES Exercise Mean ± SD	OSES Calcium Mean ± SD	Total OSES Mean ± SD
BMI groups			
Lower than 18.5	375.26±153.88	397.89±163.86	773.15±290.47
18.5-24.9	381.79±154.50	427.51±146.17	809.31±247.55
25-29.9	343.08±176.25	437.03±142.84	780.12±276.50
Higher than 30	327.25±161.97	433.52±155.36	760.78±265.31
<i>P value</i> [†]	0.128	0.768	0.656
Menopausal status			
Yes	319.50±183.26	416.33±170.38	735.83±312.98
No	372.03±155.71	432.54±141.41	804.57±244.81
<i>P value</i> [‡]	0.044	0.499	0.118
Getting information about osteoporosis			
Yes	393.67±164.52	465.86±130.48	859.54±241.89
No	347.94±160.45	414.01±151.83	761.96±263.78
<i>P value</i> [‡]	0.027	0.006	0.003
History of osteoporosis			
Yes	380.95±188.70	423.33±182.65	804.28±310.97
No	371.96±151.54	428.23±140.79	800.20±247.13
I don't know	331.46±178.70	433.17±155.11	764.63±280.04
<i>P value</i> [†]	0.277	0.802	0.724
Bone density measurement			
Yes	368.26±174.71	448.91±146.07	817.17±280.11
No	360.12±160.76	425.64±147.85	785.76±257.58
<i>P value</i> [‡]	0.756	0.326	0.454
History of hip fracture in family			
Yes	319.50±183.26	416.33±170.38	735.83±312.19
No	372.03±155.71	432.54±141.41	804.57±244.81
<i>P value</i> [‡]	0.152	0.264	0.127
History of hip fracture			
Yes	195.00±119.02	325.00±150.00	520.00±238.18
No	363.66±162.20	430.68±292.00	794.34±259.67
<i>P value</i> [‡]	0.035	0.139	0.044
Bone density treatment			
Yes	338.88±183.36	411.66±165.68	750.55±319.23
No	362.84±161.56	430.39±146.58	793.23±257.22
<i>P value</i> [§]	0.634	0.736	0.733

Kruskal Wallis test, [†]t test, [‡]Mann-Whitney U test, SD; Standard deviation[†]

The differences were found to be statistically significant. The OSECS scores of women with a higher education level (p=.047), “good” perception of income (p=.034), and with information about osteoporosis (p=.006) were higher than other women’s scores. Again, the differences were statistically significant. The total OSES scores of women with a higher education level (p=.003), better perception of income (p=.001), information about osteoporosis (p=.003), and no hip fracture in the past (p=.044) were higher than other women’s scores. The differences were found statistically significant.

Comparisons and scores of OHBS subscales according to women’s sociodemographic and other characteristics

OHBS and its subscales scores of certain characteristics of women were compared (see Tables 4-5). Susceptibility subscale scores of women who were older (p=.002), menopausal (p=.006), had information about osteoporosis (p=.024), had a hip fracture in the past (p=.035),

had been screened for bone density measurement (p=.000), had a history of hip fracture in their family (p=.016) and had received treatment for bone

density ($p=.000$) were higher than other women's scores and the differences were statistically significant. The seriousness subscale scores of women according to occupation ($p=.000$), education level ($p=.000$), marital status ($p=.002$), and BMI groups ($p=.041$) were significantly different. The benefits of exercise subscale scores of women according to education level ($p=.024$) and marital status ($p=.007$) showed statistically significant

differences. The benefits of the calcium subscale scores of women with a university degree ($p=.001$), information about osteoporosis ($p=.019$), an osteoporosis history ($p=.002$), and who had been treated for bone density decline ($p=.042$) were greater than other women's scores and the differences were statistically significant.

Table 4. Comparisons and scores of OHBS subscales according to women's sociodemographic characteristics (n=296)

Women's characteristics	Susceptibility	Seriousness	Benefits of exercise	Benefitsof calcium	Barriertoe xercise	Barriertoc alcium	Health motivation
Age groups (years)	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
25 andlower	18.02±3.86	13.72±3.68	24.19±4.76	22.32±4.49	15.20±4.57	13.72±3.68	22.19±4.39
26-35	17.58±4.66	14.52±4.47	23.04±5.44	21.84±4.91	15.56±4.02	14.52±4.47	21.91±5.37
36-45	18.80±4.73	14.36±4.78	24.07±5.28	21.46±5.03	16.00±4.58	14.36±4.78	24.00±4.68
46 and higher	20.42±5.46	16.50±4.72	24.30±4.65	22.82±3.98	18.44±5.47	16.50±4.72	24.00±4.06
<i>P values</i> [†]	0.002	0.057	0.332	0.390	0.000	0.002	0.007
Education level							
Primary school	19.00±5.50	20.00±5.55	23.12±5.35	22.14±4.60	17.54±5.27	16.28±4.45	23.20±4.69
Secondary school	16.86±4.97	19.18±4.54	22.69±5.12	19.72±4.52	14.90±3.22	14.46±4.03	21.86±4.41
High school	18.76±3.87	20.64±5.24	24.46±5.19	22.44±5.00	15.62±4.74	14.21±4.34	22.75±5.23
University	18.46±3.97	20.25±4.43	25.27±3.20	23.74±2.72	15.06±3.83	11.93±3.57	22.86±4.27
<i>P values</i> [†]	0.082	0.000	0.024	0.001	0.001	0.000	0.482
Occupation							
Working	18.50±4.27	13.64±4.01	24.24±5.57	21.88±5.14	15.87±4.02	13.64±4.01	23.00±4.83
House wife	18.64±5.24	15.74±4.60	23.37±4.82	21.95±4.47	16.46±5.17	15.74±4.60	22.94±4.84
Student	18.13±3.29	12.30±3.18	24.88±4.92	23.25±4.18	15.39±4.18	12.30±3.18	21.88±4.46
<i>P values</i> [†]	0.823	0.000	0.822	0.186	0.037	0.004	0.787
Perception of income							
Low	18.35±5.20	21.20±4.88	23.90±4.38	22.95±4.06	18.95±4.88	17.12±4.98	23.70±3.50
Middle	18.64±4.66	19.98±5.26	23.76±5.05	21.80±4.65	15.82±4.58	14.41±4.27	22.62±4.57
Good	18.37±4.72	19.94±5.05	23.91±5.40	22.35±4.81	15.51±4.63	14.10±4.26	22.74±5.61
<i>P values</i> [†]	0.865	0.376	0.973	0.317	0.000	0.001	0.442
Living region							
Village	17.73±5.24	19.71±6.01	22.97±4.22	21.08±5.01	18.14±4.94	15.93±4.54	22.65±5.20
Town	18.79±4.68	20.29±5.44	23.74±5.15	22.60±4.83	15.25±4.49	14.08±3.78	22.50±4.63
City	18.66±4.63	20.20±4.84	24.07±5.23	22.24±4.44	15.91±4.66	14.54±4.59	22.94±4.74
<i>P values</i> [†]	0.429	0.078	0.400	0.198	0.004	0.078	0.804
Marital status							
Married	18.63±4.90	19.65±5.20	23.41±5.14	21.90±4.83	16.33±4.74	15.06±4.58	22.93±4.97
Single	18.17±4.13	21.92±4.59	25.34±4.47	22.92±3.72	15.46±4.77	13.28±3.68	22.34±4.02
<i>P values</i> [†]	0.499	0.002	0.007	0.076	0.194	0.002	0.393
Husband's education level							
Illiterate	17.83±3.04	20.00±3.76	21.75±4.43	19.33±5.14	19.50±4.23	18.75±4.13	21.00±5.47
Primary school	17.87±5.66	20.07±5.17	23.57±4.18	21.54±4.84	17.50±5.28	16.00±4.07	22.93±4.71
Secondary school	18.92±5.41	19.58±5.86	22.26±6.18	21.34±5.88	15.90±4.57	14.56±5.07	23.14±5.55
High school	18.40±4.48	19.58±5.86	23.49±5.36	22.10±4.30	15.81±4.47	15.31±4.64	22.87±5.11
University	20.31±4.27	19.56±5.36	24.63±4.86	23.43±4.00	15.58±4.62	13.19±4.02	23.14±4.53
<i>P values</i> [§]	0.084	0.981	0.204	0.056	0.035	0.000	0.704

[†]One-Way ANOVA, [‡]t test, [§]Kruskal Wallis test, SD; Standard deviation

The barriers to exercise scores of women who were older ($p=.000$), housewives ($p=.037$); with a primary school education ($p=.001$); with low income ($p=.000$); who were living in a village ($p=.004$), whose husband's education level was lower ($p=.035$), who were menopausal ($p=.000$) and who had experienced a hip fracture in the past ($p=.011$) were higher than other women's scores,

and the differences were statistically significant. The barriers to calcium subscale scores of the women who were older ($p=.002$), were housewives ($p=.004$), had lower education level ($p=.000$), had low income ($p=.001$), were married ($p=.002$), whose husbands' education level was lower ($p=.000$), who were overweight ($p=.041$) and menopausal ($p=.003$) were higher than other

women's scores and the differences were statistically significant (see Table 4-5).

Health motivation subscale scores of women who were 36 years of age and older (p=.007), menopausal (p=.004) and who had been screened for bone density measurements (p=.030) were

higher than other women's scores, and the differences were statistically significant (see Table 4-5).

Table 5. Comparisons and scores of OHBS subscales according to women's some characteristics (n=29)

Women's characteristics	Susceptibility	Seriousness	Benefits of exercise	Benefits of calcium	Barrier to exercise	Barrier to calcium	Health motivation
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
BMI groups)							
Lower than 18.5	18.10±4.54	13.15±4.43	22.78±5.42	21.15±5.34	16.21±4.46	13.15±4.43	22.47±5.37
18.5-24.9	17.94±4.57	14.43±4.90	23.53±5.40	22.05±5.21	15.80±4.97	14.43±4.80	22.48±5.24
25-29.9	19.53±4.70	14.83±4.02	24.79±5.00	22.83±3.61	15.93±4.64	14.83±4.02	23.58±3.76
Higher than 30	18.78±5.20	15.72±3.99	23.50±5.35	21.54±3.95	17.45±4.27	15.72±3.99	22.60±4.65
<i>P values</i> †	0.282	0.041	0.423	0.272	0.066	0.041	0.575
Menopausal status							
Yes	21.48±5.23	20.66±5.87	24.78±4.08	23.05±3.75	18.78±5.45	16.18±4.67	24.38±3.98
No	17.78±4.31	20.00±4.96	23.58±5.26	21.88±4.81	15.48±4.32	14.30±4.33	22.40±4.89
<i>P values</i> ‡	0.000	0.375	0.102	0.083	0.000	0.003	0.004
Getting information about osteoporosis							
Yes	19.49±5.16	19.54±5.28	21.41±5.05	23.10±4.38	16.87±4.77	14.73±4.61	23.54±4.49
No	18.13±4.51	20.38±5.09	23.58±5.06	21.71±4.68	15.85±4.73	14.66±4.41	22.50±4.88
<i>P values</i> ‡	0.024	0.198	0.200	0.019	0.092	0.902	0.089
History of osteoporosis							
Yes	23.90±5.47	17.85±5.85	25.52±4.40	24.85±3.05	16.09±4.88	15.14±4.90	24.4±5.33
No	17.66±4.53	20.04±5.03	23.70±5.18	21.69±4.78	15.96±4.61	14.70±4.34	22.51±4.89
I don't know	19.20±4.02	20.93±5.11	24.19±4.98	22.43±4.38	16.59±5.08	14.51±4.67	23.07±4.31
<i>P values</i> ‡	0.000	0.072	0.735	0.002	0.532	0.793	0.099
Bone density measurement							
Yes	21.41±5.85	19.52±6.08	24.06±5.26	22.67±4.83	17.26±5.24	15.60±4.28	24.21±4.05
No	18.00±4.32	20.25±4.97	23.78±5.03	22.02±4.59	15.94±4.64	14.51±4.48	22.54±4.87
<i>P values</i> ‡	0.000	0.446	0.730	0.383	0.085	0.127	0.030
History of hip fracture in family							
Yes	20.50±5.02	21.03±4.73	25.36±4.09	22.83±3.16	16.26±4.66	13.86±4.43	24.06±3.43
No	18.31±4.67	20.03±5.19	23.65±5.14	22.04±4.76	16.13±4.77	14.77±4.46	22.66±4.90
<i>P values</i> ‡	0.016	0.317	0.079	0.378	0.890	0.290	0.129
History of fracture in herself							
Yes	18.25±2.36	18.50±5.19	25.50±2.51	23.25±2.62	21.75±2.06	17.50±3.87	21.25±2.06
No	18.53±4.77	20.16±5.16	23.80±5.09	22.10±4.65	16.07±4.73	14.64±4.46	22.82±4.81
<i>P values</i> ‡	0.962	0.463	0.514	0.859	0.011	0.145	0.149
Bone density treatment							
Yes	23.94±5.50	18.50±5.75	2.33±4.53	24.05±3.50	16.61±4.88	15.44±4.98	24.00±5.49
No	18.18±4.48	20.24±5.10	23.85±5.10	22.00±4.67	16.12±4.75	14.63±4.43	22.73±4.73
<i>P values</i> ‡	0.000	0.241	0.452	0.042	0.806	0.448	0.126

†Kruskal Wallis test, ‡ t test, §Mann-Whitney U test, SD; Standard deviation

Discussion

The current study examined women's osteoporosis health beliefs and osteoporosis self-efficacy. Results of the women's OHBS subscales average scores were as follows: perceived susceptibility, 18.53±4.74; perceived seriousness, 14.68±4.46; benefits of exercise; 23.82±5.06; benefits of calcium intake, 22.12±4.63, barriers to exercise, 16.15±4.75; barriers to calcium intake, 14.68±4.46; health motivation, 22.80±4.7, and the total OHBS scale average score, 138.27±17.93. In

addition, women's perceived benefit scores were higher than their barrier scores. When the perceived benefit of certain behaviors is deemed positive to one's health, this can be the impetus for women to adopt new behaviors which would protect their osteoporosis health (Kılıç and Erci, 2007). Altın and colleagues (2014) found that women's susceptibility average score was 16.8±5.0; seriousness average score, 17.6±5.4; benefits of exercise average score, 24.4±3.7; benefits to calcium intake average score, 21.7±3.5; barriers to exercise average score,

14.1±4.5; barriers to calcium intake average score, 12.4±3.9; and health motivation average score was 21.3±4.2. Aslan and Kılıç (2017) indicated that the total OHBS scale average score was 145.65±13.58. The results of this study are similar to the literature (Altın et al., 2004; Kılıç and Erci, 2007; Aslan and Kılıç, 2017).

A previous study found similar scores regarding health beliefs and statistically significant differences in the degree of susceptibility, seriousness, health motivation, family income, and in the degree of barriers to exercise according to education (Altın et al., 2014; Shin and Kang, 2002). In a review study reported that individuals generally have low to moderately high health beliefs about osteoporosis (McLeod and Johnson, 2011). This means that some women may believe that they do not have much control over their osteoporosis status, while others are firm in the belief that they can indeed positively influence their osteoporosis health (McLeod and Johnson, 2011). In this study, the results are also similar to the findings of earlier studies (Altın et al., 2014; Shin and Kang, 2002).

This study revealed that women's total OSES average score was 790.64±260.96. The OSEES subscale average was 361.38±162.72, and OSECS subscale was 429.25±147.57. This study indicated that increasing exercise self-efficacy reduced both the exercise and calcium intake barriers scores. In addition, there was a positive effect on the women's health motivation and seriousness regarding osteoporosis self-efficacy. Furthermore, when women became totally committed to osteoporosis self-efficacy, exercise barriers and calcium intake barriers decreased. In the previous study found that there was a statistically significant correlation between calcium intake behavior and health motivation among the osteoporosis health beliefs (Song and So, 2000). Other study noted that a positive correlation between calcium intake and health motivation with high levels of calcium intake was associated with a high motivation to become healthy and improve osteoporosis health (Edmonds et al., 2002). Swaim et al. (2008) found that self-efficacy of both exercise and calcium had significant positive correlations with calcium intake behavior. Furthermore, a woman's self-efficacy of exercise was significantly and positively related to actual exercise behavior (Swaim et al., 2008). Contrary to the findings of this study, in previous study found that a positive correlation between osteoporosis self-efficacy and barriers to exercise and a negative correlation between osteoporosis self-efficacy and health motivation (Shin and Kang,

2002). This study's results showed significantly better osteoporosis self-efficacy of women with a higher education level, "good" income perception, information about osteoporosis, and no past history of hip fracture. A previous study found a positive correlation between education level and regular exercise in the OSEES scores (Arslan et al., 2015). Similarly, there was a positive correlation between the OSEES score and education level and regular exercise. There was a positive correlation between OSECS average scores and education level, but there was no significant correlation between OSECS average scores and doing regular exercise (Arslan et al., 2015).

It is very important that individuals become informed regarding their actual as well as perceived susceptibility to osteoporosis as these factors have been shown to be a strong indicator of health behavior (Nayak et al., 2010). The current study revealed that several factors affected a woman's susceptibility to osteoporosis: if she were older, menopausal, knowledgeable about osteoporosis, had a history of past hip fracture, previous screening for bone density measurement, a family history of hip fracture, and presently receiving treatment for bone density. Similarly, an earlier study revealed that a personal and family history of osteoporosis, being female, and undergoing testing for osteoporosis were factors affecting osteoporosis susceptibility (Nayak et al., 2010). This study found that the seriousness scale scores were higher for osteoporosis in women who were housewives, single, overweight, and who had a higher education than other women. A previous study related to severity of osteoporosis revealed that older ages, family history of osteoporosis, and testing for osteoporosis were significantly associated with osteoporosis severity (Nayak et al., 2010). The results of this study differed from those in the literature (Nayak et al., 2010). These differences may be due to the fact that participants were solely women, different measurement tools were used, and there was a difference in the average age of the individuals in this study.

The current study investigated factors affecting the barriers to exercise and barriers to calcium intake of OHBS. Affecting factors for women on barriers to exercise were being older, being menopausal, being a housewife, having a low education level, having a low-income perception, living in a village, having a past hip fracture, and having a husband with a low education level. In addition, affecting factors on barriers to calcium intake were older ages, being a housewife,

menopausal, low education level, low income perception, being married, low education level of husband, and being overweight. In a study was found the health belief scale scores of women to be higher than men (Altın et al., 2014). This situation is thought to be associated with a woman's family history of osteoporosis or with her own personal health history. These findings are consistent with the literature.

Limitations of the study are that it was a convenience sample and a small sample size confined to specific Turkish women. The data were collected only a public hospital in the northern region of Turkey; therefore, further studies are needed in order to determine whether these findings can be generalized to participants in other areas. As the findings are based on data from a cross-sectional design, data from prospective survey are needed to infer causal effects.

Conclusions

The results of this study revealed that the levels of health beliefs and self-efficacy regarding osteoporosis of women were low. Nevertheless, women's perceived benefits scores were found higher than perceived barriers. This is encouraging news. When women can clearly understand the perceived benefits of taking care of their osteoporosis, they may become more motivated to do all possible to achieve positive outcomes.

The help to work towards these goals should come from nurses, doctors and other health care professionals who should be educated about osteoporosis and fully informed in the osteoporosis health beliefs and self-efficacy of their patients. Nurses, in particular, should have a thorough knowledge regarding bone health throughout a person's entire life. They can be instrumental in educating the public about life-long bone health, and they can also provide information about how to prevent osteoporosis and fracture risk.

In conclusion, when women can access reliable and up-to-date information and education about osteoporosis, they may then become more motivated to develop self-efficacy in the prevention of this very common and sometimes debilitating disease.

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Ethical considerations: Approval for this study was obtained written permission from the institution to do research before initiation of the study. Information about the purpose of the research before starting the study were given to participants. If the participants agreed, the researcher provided detailed information regarding the study, and received written informed consent from volunteered to participate in the study. Confidentiality and anonymity of data of participants were guaranteed. The study was carried out a proper research to Helsinki Declaration Principles.

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RESEARCH ARTICLE

Evaluation of Fundoscopic Abnormalities in Patients with Coronary Artery Disease

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Abstract

Objective: Coronary artery disease (CAD) is the leading cause of death in the world. There has been recent interest to microvasculature changes that are involved in systemic conditions associated with CAD. Retinal microvascular changes which can be easily detected noninvasively may be also a marker for cardiovascular diseases. Our aim in this study was to evaluate the relationship between the retinal findings and CAD by performing fundoscopic examination in patients diagnosed with CAD.

Methods: This study enrolled 100 patients (72 female, mean age: 59.3±7.1 years) diagnosed with CAD, along with 100 controls (75 female, mean age: 57.8±8.2 years) who were proved to have normal coronary arteries by coronary angiography. Bilateral fundoscopic examination was performed in all study population. Fundoscopic findings and risk factors for CAD were compared between the groups.

Results: There was no significant difference between the groups in terms of clinical, demographical and laboratory characteristics of the patients. The prevalence of atherosclerotic changes was significantly higher in patients with CAD than controls (87 vs 58 %, p<0.001). Hypertensive retinopathy was observed more frequently in CAD group as compared to controls (95 vs 60 %, p<0.001). The prevalence of diabetic retinopathy, retinal vein occlusion, retinal collateral vessels, increased retinal tortuosity, Drusenoid bodies and Hollenhorst plaques were similar between the groups.

Conclusion: The atherosclerotic and hypertensive retinal findings were more frequently observed in patients with CAD. Therefore, fundoscopic examination may be useful in the evaluation of such patients with CAD.

Key words: Coronary artery disease, fundoscopic examination, atherosclerosis.

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Introduction

Currently, coronary artery disease (CAD) is the leading cause of death in our country and in the world (Bonow et al., 2002). Hypertension, dyslipidemia, diabetes mellitus, obesity, and smoking are traditional risk factors that were accused to cause CAD in most cases (Wilson et al., 1998; Smith 2006). However, 15-20% of those with CAD have no identified traditional risk factors (Humphrey et al., 2008). There has been recent interest to microvasculature changes that are involved in systemic conditions associated with

CAD. Blood flow disturbances and vascular changes in ocular circulation in patients with CAD can lead to abnormal retinal findings. Retinal microvascular abnormalities which can be easily detected noninvasively reflect cumulative microvascular injury and may indicate the relationship between microvascular pathologies and cardiovascular diseases (Goto et al., 1975). Potential links between retinal findings and CAD would have important clinical implications, as individuals with abnormal findings in the retinal microvasculature could be screened or monitored for development of CAD. In this study, we aimed to evaluate the relationship between the retinal findings and CAD by performing fundoscopic examination in patients diagnosed with CAD.

Methods

Study design and subjects

This single-center study enrolled 100 patients (72 female, mean age: 59.3±7.1 years) diagnosed with CAD, along with 100 controls (75 female, mean age: 57.8±8.2 years) who were proved to have normal coronary arteries by coronary angiography. The blood pressure values were measured following a resting period of ten minutes in the sitting position from the right arm using an appropriate cuff size. The patients who had a systolic blood pressure of ≥140 mmHg and/ or diastolic blood pressure of ≥90 mmHg and who were using antihypertensive medication were considered as hypertensive (Tedeschi-Reiner et al., 2005). Diabetes mellitus was diagnosed if subjects were on drug treatment for diabetes (insulin or oral antidiabetic agents) and/or fulfilled the criteria laid down by the World Health Organization Consulting Group report (i.e., a fasting venous blood glucose level of >126 mg/dL and/or a 2-h postglucose value of >200 mg/dL) (Alberti and Zimmet 1988). The coronary risk factors were evaluated separately in the patients who were included in the study. All fundoscopic and demographic parameters including traditional risk factors for CAD were recorded into a dataset and compared between CAD patients and controls. All patients provided a written informed consent and the study protocol was approved by the local ethics committee of the hospital in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Fundoscopy examination

The patients were evaluated in the Ophthalmology Retina Outpatient Clinic. Fundoscopic examination was performed in both

eyes by the same ophthalmologist using Zeiss FF 450 Plus IR fundus camera (Carl Zeiss, Meditec Inc. Jena, Germany). The ophthalmologist did not know any data about the subjects, particularly their coronary artery condition. Before the procedure, both pupils were dilated using Tropicamide 1% eye drop. The extent and severity of atherosclerotic vascular lesions in the retinal arteries were classified according to the Scheie classification (Scheie 1953). Grade 1 is a broadening of the light reflex from the artery, with scanty or no arteriovenous compression (earliest sign of retinal artery atherosclerosis). Grade 2 is the same as stage 1, but more prominent. In Grade 3, the arteries have a “copper wire” pattern, the arteriovenous compression is much greater and severe atherosclerotic changes of the retinal arteries are seen. In Grade 4, the arteries have a “silver wire” pattern and the arteriovenous crossing changes are the most serious (Hubbard et al., 1999; Wong et al., 2001).

Coronary angiography

Coronary angiography was performed by clinical indications such as abnormal stress test results, positive treadmill test, dobutamine stress echo, typical chest pain, or signs of ischemia during myocardial perfusion scintigraphy. All study population underwent selective coronary artery angiography after appropriate patient preparation. Femoral artery and sometimes radial or brachial artery cannulation was used for the arterial access site and a Judkins system was applied for cannulation of the left and right coronary arteries. Coronary angiographies were evaluated by at least two independent interventional cardiologists. Presence of 25% or more stenosis in the major epicardial arteries on coronary angiography was considered CAD (Baim and Grossmann 2000). Presence of less than 50 stenosis in the epicardial coronary arteries and/or lateral CAD (having a diameter of less than 2 mm and supplying a small myocardial area) was considered non-critical CAD.

Laboratory analysis

In order to perform complete blood count and blood chemistry panel, venous blood samples were collected after 12-hours of fasting by a clean puncture of an antecubital vein from all patients. Complete blood countings, fasting blood glucose, urea, creatinine, HbA1c, serum reactive protein (CRP), erythrocyte sedimentation rate (ESR), total cholesterol (TC), high-density lipoprotein (HDL), and triglyceride (TG) levels were measured. Low-density lipoprotein (LDL), was calculated using the

Friedewald formula [LDL (mg/dL) = TC - (HDL + TG/5)] (Friedewald 1972).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0. (IBM Corp. Armonk, NY). The variables were investigated using analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk test) to determine whether or not they were approximately normally distributed. Descriptive statistics were reported as mean with standard deviation for continuous variables with normal distribution, median and 25th -75th percentile values for continuous variables without normal distribution, and frequencies with percentages for the categorical variables. Group comparisons for continuous variables were tested using Student t test when data distribution was normal and using Mann-Whitney U test when data distributions were not normal. Comparisons for categorical variables were evaluated by chi-square test. Significance level was accepted as $p < 0.05$ in all statistical analyses.

Results

The clinical, demographical, laboratory characteristics and medications of patients with and without CAD were presented in Table 1. There was no significant difference between the groups in terms of age, gender, frequency of diabetes mellitus, hypertension, dyslipidemia, smoking status and family history of CAD. Body mass index, systolic and diastolic blood pressures were also similar between the groups. Upon comparison of laboratory parameters between CAD group and controls, there was no significant difference in terms of hemoglobin, fasting blood glucose, urea, creatinine, HbA1c, CRP, ESR, TC, HDL, LDL, and TG levels between the groups.

Retinal findings which were found during fundoscopic examination were presented in Table 2. Atherosclerotic changes were observed in 87% of the patients with CAD and in 58% of the controls. Among patients with CAD, Grade I atherosclerosis was found in 54%, grade II atherosclerosis was found in 32% and grade III atherosclerosis was found in 1%. Grade IV atherosclerosis was not found. However, among control group, Grade I atherosclerosis was found in 39% and grade II atherosclerosis was found in 19%.

Table 1: Comparison of baseline demographic characteristics, laboratory findings and medications between patients with CAD and controls

Demographic Characteristics	CAD Group (n=100)	Controls (n=100)	P value
Gender (female)	72 (72)	75 (75)	0.631
Age (years)	59.3±7.1	57.8±8.2	0.165
Hypertension, n(%)	70 (70)	59 (59)	0.104
Diabetes Mellitus, n(%)	26 (26)	20 (20)	0.313
Dyslipidemia, n(%)	39 (39)	29 (29)	0.136
Smoking Status, n(%)	21 (21)	14 (14)	0.193
Familial history of CAD*, n(%)	22 (22)	18 (18)	0.480
BMI* (kg/m ²)	29.1±4.4	28.7±3.6	0.829
SBP* (mmHg)	133.1±17.7	129.7±15.6	0.488
DBP* (mmHg)	77.7±12.3	80.4±17.5	0.257
Laboratory Parameters			
Glucose (mg/dL)	109.8±48.9	113.1±44.8	0.643
Urea (mg/dL)	35.5±18.3	36.2±13.1	0.795
Creatinine (mg/dL)	1.04±0.43	1.03±0.41	0.868
HbA1c (%)	6.42±1.31	6.27±1.23	0.682
Total cholesterol (mg/dL)	173.8±43.6	171.4±42.9	0.698
HDL* (mg/dL)	40.8±9.9	39.1±8.3	0.170
LDL* (mg/dL)	102.5±33.8	105.5±32.9	0.522
Triglyceride (mg/dL)	153.8±77.5	141.3±59.9	0.202
CRP* (mg/L)	0.3 (0.2-0.8)	0.4 (0.3-0.8)	0.214
Sedimentation (mm/hour)	12 (8-23)	12 (8-15)	0.427
Hemoglobin (mg/dL)	13.2±2.3	13.7±2.6	0.16
Medications			
Clopidogrel, n(%)	20 (20)	12 (12)	0.123
Acetylsalicylic Acid, n(%)	81 (81)	72 (72)	0.133
B-blockers, (%)	77 (77)	68 (68)	0.154
ACE* inhibitors, n(%)	46 (46)	35 (35)	0.113
ARB*, n(%)	24 (24)	19 (19)	0.389
CCB*, n(%)	31 (31)	23 (23)	0.203
Statins, n(%)	28 (28)	25 (25)	0.631
OAD*, n(%)	20 (20)	17 (17)	0.585
Insulin, n(%)	9 (9)	6 (6)	0.421

ACE*: Angiotensin Converting Enzyme, ARB*: Angiotensin Receptor Blocker, BMI*: Body Mass Index, CAD*: Coronary Artery Disease, CCB*: Calcium Channel Blocker, CRP*: C-

Reactive Protein, DPB*: Diastolic Blood Pressure, HDL*: High Density Lipoprotein, LDL*: Low Density Lipoprotein, OAD*: Oral anti-diabetic drug; SBP*: Systolic Blood Pressure

Table 2: Comparison of fundoscopic examination findings between patients with CAD and controls

Fundoscopy Findings	CAD Group (n=100)	Controls (n=100)	P value
Atherosclerosis, n (%)			
Grade I	54 (54)	39 (39)	<0.001
Grade II	32 (32)	19 (19)	
Grade III	1 (1)	0 (0)	
Grade IV	0 (0)	0 (0)	
Hypertensive Retinopathy, n (%)			
Grade I	53 (53)	33 (33)	<0.001
Grade II	30 (30)	20 (20)	
Grade III	12 (12)	7 (7)	
Grade IV	0 (0)	0 (0)	
Diabetic Retinopathy, n (%)	8 (8)	6 (6)	0.579
Retinal Vein Occlusion, n (%)	10 (10)	6 (6)	0.297
Retinal Collateral Vessels, n (%)	10 (10)	5 (5)	0.179
Retinal tortuosity, n (%)	65 (65)	57 (57)	0.246
Hollenhorst plaques, n (%)	3 (3)	1 (1)	0.312
Drusenoid bodies, n (%)	52 (52)	42 (42)	0.157
CAD: Coronary Artery Disease,			

Grade III and IV atherosclerosis was not found. The prevalence of atherosclerotic changes was significantly higher in patients with CAD ($p < 0.001$). Hypertensive retinopathy (HR) was found in 95% of the CAD patients and 60% of the controls which was also significantly different ($p < 0.001$). Among patients with CAD, Grade I HR was found in 53%, grade II HR was found in 30% and grade III HR was found in 12% of the patients. Grade IV HR was not found. However, among control group, Grade I HR was found in 33%, grade II HR was found in 20% and grade III HR was found in 7% of the patients. Grade IV HR was not found. Diabetic retinopathy was found in 8 patients with CAD and in 6 controls ($p = 0.579$). HbA1c levels were significantly higher in patients with diabetic retinopathy ($p < 0.001$). There was no significant difference in terms of retinal vein occlusion (10 vs 6%, $p = 0.297$), retinal collateral vessels (10 vs 5%, $p = 0.179$), and increased retinal tortuosity (65 vs 57%, $p = 0.246$) between the groups. Drusenoid bodies were found in 52 patients with CAD and in 42 controls ($p = 0.157$). Hollenhorst plaque was found in three patients with CAD and one among controls ($p = 0.312$) (Figure 1).

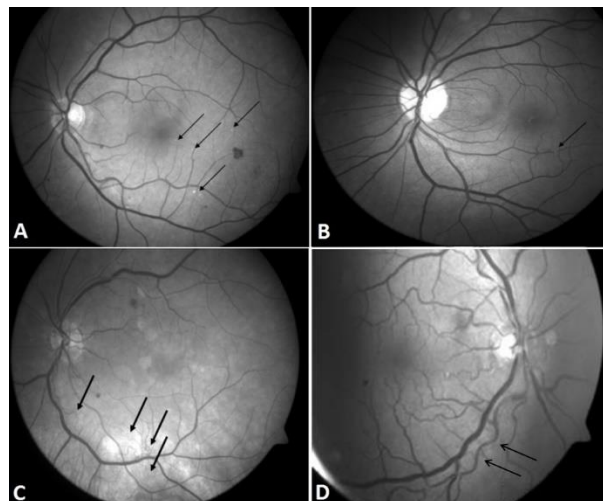


Figure 1. A: Drusenoid Bodies, B: Hollenhorst plaque, C: Venous collaterals, D: Retinal vascular tortuosity

Among fundoscopic findings, drusenoid bodies were found with a significantly higher rate in patients who were smokers ($p < 0.001$). Similarly, drusenoid bodies were found with a statistically significantly higher rate in patients who were not using clopidogrel compared to the patients who were using clopidogrel ($p < 0.001$).

Discussion

In this study we have focused on the relationship between the retinal findings and CAD by performing fundoscopic examination in patients diagnosed with CAD. The atherosclerotic and hypertensive retinal findings were more frequently observed in patients with CAD than the controls with similar risk factors. Therefore, fundoscopic examination may be useful in the evaluation of such patients with CAD.

Many studies have proposed that atherosclerotic changes found in the retina may be a marker of the prevalence of CAD (Tedeschi-Reiner et al., 2005). In a large-scale study, it was found that the risk of congestive heart failure was increased by three-fold in patients with retinopathy who had no CAD and hypertension (Torpy et al., 2005). In another study, the relationship of retinal vascular changes with left ventricular mass, left ventricular volume and concentric remodeling was investigated and it was stated that microvascular disease contributed to formation of cardiac remodeling by correlating with the risk factors of CAD (Cheung et al., 2007). In our study, Scheie classification was used in evaluation of atherosclerotic and hypertensive retinopathy (Scheie 1953). Our results showed that atherosclerotic and hypertensive retinopathy were closely related with the presence CAD similar to previous studies. Besides, the distribution of atherosclerotic retinopathy was similar to the

distribution of hypertensive retinopathy in this study.

Point opacities were observed on the retinal surface in 52% and 42% of CAD patients and controls respectively. When fundus camera was used, it was thought that these opacities were drusenoid bodies (Figure 1A). It was thought that the drusenoid bodies which were found with a high rate in our study might be small drusens associated with age-related macula degeneration (ARMD) and/or particles located in the retina by way of extravasation of intravascular cholesterol crystals. ARMD is the most common reported cause of blindness in the population aged over 65 years old (Klein 1999). In all studies, the prevalence of ARMD has shown an increase with age. Atherosclerosis in the carotid vascular bed, presence of systemic hypertension, smoking and dyslipidemia are risk factors for development of ARMD (Klein et al., 1993; Smith et al., 1996). Similarly, drusenoid bodies were found with a statistically significantly higher rate in patients who were smokers in our study.

The frequency of clopidogrel usage is increasing in the cardiovascular area. In previous studies, ASA and the other non-steroid antiinflammatory drugs were not shown to decrease the risk of ARMD (Christen et al., 2001). Similarly, no significant difference was found between the patients who were and were not using ASA in terms of drusenoid bodies in our study. However, these bodies were observed with a significantly higher rate in the patients who were not using clopidogrel compared to the patients who were using clopidogrel. If these bodies are considered drusen bodies related with ARMD, it may be thought that clopidogrel decreases development of ARMD in patients with a high risk in terms of CAD. In a study conducted by Cymerman et al. with young patients who had CAD, it was found that reticular macular disease which is a subtype of ARMD was observed commonly in middle-aged patients with CAD (Cymerman et al., 2016). In contrast to our study, it was emphasized that there was no significant correlation between CAD and drusen bodies. It was emphasized that the relationship of reticular macular disease with CAD was related with subretinal drusenoid deposits found between the retinal pigment epithelium and internal segment ellipsoid region similar to the lipid mechanism in atherosclerosis (Cymerman et al., 2016). More and extended studies are needed to elucidate the relationship between reticular macular diseases and CAD.

As known, increased tortuosity in the arteries occurs as a result of aging or pathological changes

in vascular elastic material (Ertugrul 1967; Soikkonen et al., 1991; Dobrin et al., 1998; Zegers et al., 2007). It has been reported that atherosclerosis, hypertension and aging play a role in development of arterial tortuosity (Leipzig and Dohrmann 1986; Weibel and Fields 1965; Del Corso et al., 1998). Increased tortuosity in the retinal arteries occurs as a result of aging or pathological changes in vascular elastic material (Zegers et al., 2007; Del Corso et al., 1998). Increased tortuosity may also be observed in the retinal arteries. It is known that this is observed frequently especially in retinal pathologies including diabetic retinopathy, retinal vein occlusion and retinal vasculitis. In a previous study, a relationship was shown between increased cholesterol (especially increased triglyceride level) and blood pressure (risk factors for CAD) in the first 10 years of the childhood and tortuosity in the retinal arteries (Owen et al., 2011). Although the difference was not significant, the presence of retinal tortuosity in 65% of patients with CAD in our study supports this study.

One of the findings examined in our study was Hollenhorst plaques. Hollenhorst plaques are one of the most frequent causes of retinal emboli (Brown and Magargal 1982). These are orange, refractile cholesterol crystals with a length of 10-250 μ m and constitute the fundoscopic finding of Cholesterol Embolization Syndrome (CES) (David et al., 1963; Hollenhorst et al., 1962). In our study, Hollenhorst plaques were found in three patients with CAD. One of these patients had a history of thrombolytic treatment and the other one had a history of coronary bypass graft surgery. All three patients were hypertensive. Patients with Hollenhorst plaques on ophthalmologic examination are in the high risk group in terms of morbidity and mortality. The most appropriate mechanism explaining CES syndrome related with thrombolytic agents includes dissolving of protective thrombin coagulum with thrombolytic agents and release of cholesterol crystals because of subintimal hemorrhage (Scolari et al., 1996).

The primary limitation was that our study was a nonrandomized and single center study with a relatively small number of patients. Secondly, the severity of CAD was not evaluated quantitatively in patients with scoring systems such as Syntax or Gensini Scores. Comparison of the CAD severity with the prevalence of abnormal retinal findings would be clinically more meaningful.

Conclusion

The atherosclerotic and hypertensive retinal findings were more frequently observed in patients with CAD than the controls with similar risk factors. Fundoscopic examination is a non-invasive method which can be performed easily in patients with CAD. Therefore, fundoscopic examination may be useful in the evaluation of such patients with CAD. Collaboration of cardiologists and ophthalmologist in the evaluation of such patients with cardiovascular risk factors may provide a more efficient approach in diagnosis and treatment of CAD.

Ethics Committee Approval: Ethics committee approval was received for this study from Clinical Research Ethics Committee of Uludağ University Faculty of Medicine (2009-1/70).

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RESEARCH ARTICLE

Comparison of Antibiotic Sensitivity Pattern of *Escherichia coli* which Produce Extended Spectrum Beta-Lactamase Strains Isolated from Various Clinical Specimens in Intensive Care Unit

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Abstract

Objective: A retrospective analysis of the widely used antibiotics all susceptibility testing results from *Escherichia coli* (*E. coli*) cultured from clinical specimens' private hospital (from January 2017 to November 2018) was performed.

Methods: The VITEK 2 Compact automated microbiology system (bioMérieux) is designed for automated rapid antimicrobial susceptibility testing and identification of clinically relevant bacteria. Minimum inhibitory concentration (MIC) results previously obtained in recent clinical isolates with well-defined in isolates with well-characterized resistance mechanisms with the microdilution method were re-interpreted for the susceptible, intermediate and resistant categories using the 2018 EUCAST breakpoints. Clinical samples are most commonly isolated from blood, sputum and urine samples.

Results: The results of resistance pattern of *E. coli* isolates in our locality to antimicrobial agents showed that the 64 *E. coli* strains tested against fifteen antimicrobial agents. *E. coli* isolates were highly resistant to piperacillin, ceftazidime and aztreonam 98%, 61% and 61% respectively. The most sensitive antibiotics were colistin, tigecycline, imipenem and meropenem. In the present study, 73% (47) of the isolates were resistant to at least three to fourteen antibiotics. All the isolates showed resistance to at least one antibiotic. Thirty-nine per cent of *E. coli* isolates were extended spectrum beta-lactamase (ESBL) producers.

Conclusion: Considering the antibiogram, imipenem and meropenem should be preferred drugs for *E. coli* infection isolated from clinical samples.

Key words: *Escherichia coli*, antibiotic sensitivity, clinical specimens, intensive care unit

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Introduction

Escherichia coli is a diverse group of facultative anaerobic Gram-negative bacilli of the genus *Escherichia* in the family Enterobacteriaceae, and contains a variety of strains ranging from commensal organisms to highly pathogenic variants especially the intestine and the urinary tract (Mos al., 2010).

The extended spectrum beta-lactamase (ESBL) enzymes are predominantly found in *E. coli* and *Klebsiella spp.* however, may also be found in other

species of *Enterobacteriaceae* (Khanfar et al., 2009). Fluoroquinolones, aminoglycosides and trimethoprim-sulfamethoxazole are used for treatment of infections caused by ESBL-producing bacteria (Falagas and Karageorgopoulos., 2009).

The aim of this study was to determine the characteristics and patterns of antibiotic resistance among isolates of *E. coli* recovered from clinical specimens in Giresun province.

Methods

Bacterial isolates

Ethical approval is were taken before study. Because of retrospective analysis, we did not patient approval. The sixty four *E. coli* were isolated from clinical specimens from intensive care unit of internal medicine in private hospital. Bacterial isolates were identified to level of species and subspecies by using the morphological and traditional biochemical tests and automatic diagnostic systems currently present in the market and commonly used for AST (Antimicrobial Susceptibility Testing) in clinical laboratories will therefore have to incorporate these criteria in their instruments to meet the needs of European microbiology laboratories according to standard methods described by (MacFaddin., 2000). In total, 64 *E. coli* were isolated from various clinical samples and detected by the VITEK 2 (bioMérieux) at the microbiology laboratory of our hospital between from January in 2017 to December in 2018. The VITEK 2 Compact Automated Microbiology System (bioMérieux) is designed for the rapid bacterial identification at the species level and determination of AST of clinically significant human bacterial pathogens (Ling et. al., 2001).

Antibiogram profile of E. coli

MIC results previously obtained in recent clinical isolates with well-defined in isolates with well-characterized resistance mechanisms with microdilution method were re-interpreted for the susceptible, intermediate and resistant categories using the 2018 EUCAST breakpoints. Fifteen different antibiotics were used. Antibiotics tested in AST-N326 (bioMérieux) card included piperacillin (PIP), ceftazidim (CAZ), aztreonam (ATM), levofloxacin (LEV), cefepime (FEP), trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), tazobactam/piperacillin (TZP), netilmicin (NET), gentamicin (GEN), colistin (CT), amikacin (AK), imipenem (IPM), meropenem (MEM), tigecycline (TIG).

Detection of ESBL

VITEK 2 system with the antimicrobial susceptibility extend card AST-N326 (bioMérieux) card was designed to perform both screening and confirmatory tests for phenotypic detection of ESBL on the same plate. VITEK 2 system has two different ESBL detection procedures. The first one uses specific computer software called advanced expert system (AES), that performs analyzes and interpretation of MIC of the antibiotics used. The use of several antimicrobial agents increases the sensitivity of ESBL detection (Sorlózano et. Al., 2005) thus the second procedure was based on ESBL test on same AST-N326 card, where the antibiotic susceptibility of the isolates to FEP and 3rd generatin cephalosporin: cefotaxime (CTX) and ceftazidime (CAZ) with or without clavulanic acid were evaluated (Drieux et al., 2008).

Multiple Antibiotic Resistance (MAR) index

For all isolates, MAR index values were tested according to Matyar et al., (2008).

Results

The results of resistance pattern of *E. coli* isolates in our locality to antimicrobial agents showed that the 64 *E. coli* strains tested against fifteen antimicrobial agents in Table 1. *E. coli* isolates were highly resistant to PIP, CAZ and ATM 98%, 61% and 61% respectively. Resistance rate of CIP was showed in 52%. When we compared to resistance of TZP, *E. coli* isolates showed 38% resistance rate. Among the aminoglycosides group, GEN resistance rate was 28%. In respect of resistance rate of CT, it was 11%. The most sensitive antibiotics were CT, TIG, IPM and MER, as is illustrated in Table 1 and Table 2 shows the antimicrobial susceptibility of all *E. coli* isolated from urine, blood, and sputum. Of the total *E. coli* isolates, 25 (39%) isolates were ESBL producers and 39 (61%) isolates were non-ESBL producers in Table 2.

Escherichia coli which Produce ESBL Strains Isolated From Clinical Specimens

Table 1. Antibiotic resistance pattern of 64 *E. coli* isolated from clinical specimens in intensive care unit.

Antibiotics	Resistance	Intermediate	Sensitive
PIP	63 (98%)	-	1 (2%)
CAZ	39 (61%)	2 (3%)	23 (36%)
ATM	39 (61%)	3 (15%)	22 (34%)
LEV	36 (56%)	-	28 (44%)
FEP	34 (53%)	6 (9%)	24 (38%)
SXT	34 (53%)	1 (2%)	29 (45%)
CIP	33 (52%)	2 (3%)	29 (45%)
TPZ	24 (38%)	37 (58%)	3 (4%)
NET	22 (34%)	2 (3%)	40 (63%)
GEN	18 (28%)	1 (2%)	45 (70%)
CT	7 (11%)	-	57 (89%)
AK	7 (11%)	10 (16%)	47 (73%)
IPM	5 (7%)	9 (14%)	50 (78%)
MEM	4 (6%)	9 (14%)	51 (80%)
TIG	4 (6%)	4 (6%)	56 (88%)

Abbreviation; PIP, Piperacillin, CAZ; Ceftazidim, ATM; Aztreonam, LEV; Levofloxacin, FEP; Cefepime, SXT; Trimethoprim sulfamethoxazole, CIP; Ciprofloxacin, TPZ; Tazobactam/Piperacillin, NET; Netilmicin, GEN; Gentamicin, CT; Colistin, AK; Amikacin, IPM; Imipenem; MEM; Meropenem, TIG; Tigecycline.

Discussion

In our study, when we compared to resistance of PIP, *E. coli* isolates showed high antibiotic resistance with 98% PIP. Some researchers have reported resistance rate PIP from 100% to 17.2% to *E. coli* in clinical samples (Kafilzadeh and Farsimadan., 2016; Batarseh et al., 2013). Our results were lower than Batarseh et al., (2013) who also reported that resistance rate of PIP with 100%.

When it comes to resistance of CAZ, *E. coli* isolates showed high antibiotic resistance with 61% CAZ. Some researchers have reported that CAZ resistance rate from 7.3% to 98.9% to *E. coli* in clinical samples (Ozsahin et al., 2005; Al-Mijali et al., 2017). Our results were lower than Al-Mijali et al., (2017) who also reported that resistance rate of CAZ with 98.9%.

In our study, when we compared to resistance of ATM, *E. coli* isolates showed high antibiotic resistance with 61% ATM. Some researchers have reported that ATM resistance rate from 89% to 98.9% to *E. coli* in clinical samples (Akter et al., 2012; Al-Mijali et al., 2017). Our results were lower than Akter et al., (2012) who also reported that resistance rate of ATM with 89%.

Table 2. Distribution of 64 *E. coli* clinical samples, Sexuality, source, MAR Index and ESBL Producers

Name of Clinic	Number of samples	Source of isolates	Sexuality F/M	ESBL Producers	MAR Index
Anesthesia and Reanimation	34	5 Sputum 29 Urine	18F 16M	21- 12+	0.07(8isl);0,14(2isl);0.2(4isl); 0.27;0.33;0.4(7isl);0.47;0.53(3isl);0 .87;0.67;0.6(2isl); 0.8(2isl); 0.93
Internal medicine	9	9 Urine	9F	6+ 3-	0.07; 0.14; 0.47; 0.53 (3 isl) 0.6; 0.67(2isl)
Chest diseases	6	2 Sputum 4Urine	4F 2M	2- 4+	0.2;0.27;0.33(2);0.6;0.67
Neurology	7	2 Sputum 5Urine	3F 4M	5- 2+	0.07;0.27; 0.4; 0.47; 0.53(2); 0.67
Infectious Diseases	2	2Urine	1M 1F	2-	0.07(2 isl)
Cardiology	3	1Blood	3M	1+ 2-	0. 0.4;0.93
Gynecology	1	1Urine	1F		0.07
General Surgery	1	1Urine		1-	0.8
Brain and Nerve Diseases	1	1 Sputum	1F	1-	0.07
Total	64	53 Urine, 10 Sputum 1 Blood		25+ (39%) 39- (61%)	

MAR, Multiple Antibiotic Resistance Index, isl; isolates, +; ESBL Producing, -Non-ESBL Producing F; Female, M; Male

In our study, when we compared to resistance of LEV, *E. coli* isolates showed high antibiotic resistance with 56% LEV. Some researchers have reported resistance rate LEV from 63,23% to 82% (Sohail et al., 2015; Al-Mijali et al., 2017). Our results were lower than Al-Mijali et al., (2017) who also reported that resistance rate of LEV with 63.23% to *E. coli* in clinical samples.

As for the resistance rate of FEP to *E. coli* isolates it showed high resistance with 53%, Some researchers have reported resistance rate from 4,1% to 47.5% FEP to *E. coli* in clinical samples (Albayrak and Kaya, 2009; Batarseh et al., 2013). Our results were higher than Batarseh et al., (2013) who also reported that resistance rate of FEP with 47.5% to *E. coli* in clinical samples.

As for the resistance rate of AK, it was 11%. Some researchers have reported that AK resistance rate from 21.2% to 91% to *E. coli* in clinical samples (Albayrak and Kaya, 2009; Sohail et al., 2015). In other studies which conducted in Italy (Tinelli et al., 2012), Brazil (Abreu et al., 2011), and Nepal (Chander et al., 2013), the resistance rates were lower compared to our results.

Being a highly beta-lactamase stable carbapenem, with an unusual property of causing a post antibiotic effect on Gram negative bacteria resistance to IPM was found to be very low (7%). On the other hand, higher resistances were shown by (Jafri et al., 2014) and (Sabir et al., 2014) were 43.3% and 32.5% respectively. Some researchers have reported that IPM resistance rate to *E. coli* in clinical samples (Al-Mijali et al., 2017).

Carbapenems, especially MEM, resistance rate of MEM was showed in 6 % (table1). Some researchers have reported that MEM from 3% to 1.20% resistance rate to *E. coli* in clinical samples (Sohail et al., 2015; Al-Mijali et al., 2017). Our results were higher than Sohail et al., (2015) who also reported that resistance rate of MEM with 3%.

In our study, when we compared to resistance of TIG, *E. coli* isolates showed antibiotic resistance with 6% TIG. Some researchers have reported that TIG from 6.59% to 9.8% resistance rate to *E. coli* in clinical samples (Batarseh et al., 2013; Al-Mijali et al., 2017). Our results were equivalent to Al-Mijali et al., (2017) who also reported that resistance rate of TIG with 6,59%.

As for the ESBL producers, our results were similar to El Sayed et al. (2017) who also reported that out of 100 isolates of *E. coli*, 36 were detected as ESBL producers and 64 were non-ESBL producers. In studies performed throughout the world, the frequency of ESBL positive. *E. coli* was

from 0.2% to 95.4% (Shadid et al., 2008; Kaftandzhieva et al., 2009). For example, in a study Tasli ve Bahar, in Turkey producing ESBL enzymes in *Escherichia coli* strains of 17%, in the study Villegas, in Colombia 3.3-4.7% (Villegas et al., 2004), in the study Duttaroy and Mehta (2005), in India 29.1% in study Lavigne et al., (2004), in France 16.2%, have been reported.

On the other hand, study of Zhou, in Shanghai show that 47.4% of *E. coli* isolated from patients were ESBL producers (Zhou., 2001), in another study by the Wu, be was conducted in Taiwan hospitals, a rate of 18.18% of ESBL-producing *E. coli* (Wu et al., 2003), While in Lebanon the amount of at 28.1 percent, respectively (Daoud and Hakime, 2003).

In the present study, 73% (47) of the isolates showed Multiple Antibiotic Resistance three to fourteen antibiotics. All of the isolates showed resistance to at least one antibiotics.

The antimicrobial resistance of bacteria is a problem of global concern. There is a correlation between antibiotic use and subsequent resistance (Jensen et al., 2009). In the present study, it was observed that the isolates of *E. coli* showed different degree of resistance to different antimicrobials. The samples were isolated from different clinical specimens. Maximum numbers of isolates were collected from urine indicating that urinary tract is more prone to infection by *E. coli* which corresponds to the findings of other researchers (Sharafi et al., 1996; Paterson and Bonomo., 2005; Kumar et al., 2014).

Conclusion

Considering the antibiogram, CT, TIG, IPM and MER should be preferred drugs for *E. coli* infection isolated from clinical samples from Giresun region.

Ethics Committee Approval: Patients' consent was obtained in the use of microbiological data.

Peer-review: Externally peer-reviewed.

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REVIEW

The Challenge of Pathological Diagnosis for Precancerous Cervical Lesions

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Abstract

Cervical cancer is the third most common cancer after breast and colorectal cancers worldwide, and the second most common gynecological malignancy after endometrial cancer. Cervical cancer screening was first described by Papanicolaou in 1941 using the PAP smear test. The incidence of invasive cervical cancer clearly reduced with the common use of PAP smear in developed countries. The basic methods used for diagnosis of premalignant lesions of the cervix are determination with colposcopy, biopsy and HPV DNA typing. Cervical premalignant lesions cannot be observed with the naked eye, other than exophytic or papillary lesions of condyloma acuminatum. Condyloma acuminatum are simultaneously LSIL. LSIL and HSIL differentiation cannot be made with colposcopy. Due to better repeatability and interobserver compliance, the World Health Organization (WHO) recommends a 2-layer HSIL/LSIL system. In the 3-layer CIN system, CIN1 is equivalent to LSIL, while CIN3 equivalent is HSIL. The lesions are frequently encountered in routine biopsies, and in some cases, differential diagnosis may be difficult. Basal cell hyperplasia, atrophy, reactive and repair-induced atypia and immature squamous metaplasia may mimic precancerous lesions. Although histomorphology is gold standard, P16 and Ki-67 are beneficial immunohistochemical ancillary testes. However, it should be kept in mind that p16 can be positive in LSIL, and negative in HSIL.

Key words: Cervix, premalignant lesions, pathology

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Introduction

Cervical cancer is observed in 3rd place after breast and colorectal cancers in the world in general and is the 2nd most common gynecological malignancy after endometrial cancer (Eser, 2010). In countries around the world, cervical cancer comprises nearly 12% of all cancers in women (Ferlay et al., 2015). In Turkey according to Ministry of Health Turkish Public Health Organization data, this rate is 2.7% (Sencan I et al., 2014). For more than 90% of cervical cancer and cervical intraepithelial neoplasia (CIN) cases, the main factor in development of cancer is human papilloma virus (HPV) (Walboomers et al., 1999).

Precancerous lesions of the cervix are named CIN1/CIN2/CIN3 linked to the degree of effect on

the epithelium. CIN1 is also known as low grade intraepithelial lesion (LSIL), while CIN2 and CIN3 are known as high-grade intraepithelial lesion (HSIL). Lesions beginning as CIN1 may transform to CIN2 or may develop “de novo” without progression to CIN2 and CIN3 (Gupta & Basavaraj, 2018). The progression potential of these types of lesions has been researched in many studies. According to the study by Ostor et al., 60% of CIN1 lesions regress, 11% transform to carcinoma in situ (CIS) and only 1% result in invasive cancer. For CIN2, 40% regress and 33% of CIN3 regress. For CIN2, 5% transform into invasive cancer, while 12% of CIN3 transform to invasive cancer (Ostor, 1993).

Adenocarcinomas are 2nd most common cervical cancers after squamous cancers. Precursors of adenocancers are adenocarcinoma in situ (AIS) or glandular lesions. Glandular lesions may be multifocal. AIS is associated with HPV at rates of 90% (Quint et al., 2010).

Screening Method

Cervical cancer screening was first described by Papanicolaou in 1941 using the PAP smear test. The incidence of invasive cervical cancer clearly reduced with the common use of PAP smear in developed countries, with regression in cervical cancer incidence falling to sixth or even tenth place in some countries (Eser, 2010; Ferlay et al., 2015). According to Republic of Turkey Ministry of Health records, in Turkey cervical cancer incidence is in 9th place (Sencan I et al., 2014). In recent years, the HPV test has been used as a screening method. Although screening test is not suggested before 21 years of age, it is recommended to have a pap smear test every 3 years in the 21-29 age range, and a pap smear test every 3 years or co-test (HPV and PAP smear test combination) every 5 years after the age 30 years old. (Saslow et al., 2012).

The Bethesda system, developed for standardization of PAP smear reports, standardized a diagnostic approach for cervical cytology and was most recently updated in 2014 (Nayar et al., 2015). In this system, cervical epithelial lesions are classified as atypical squamous cells, atypical squamous cells with undetermined significance (ASC-US) and atypical squamous cells not excluding high-grade cervical intraepithelial lesions (ASC-H) (Table 1) (Nayar et al., 2015). ASC-US diagnosis is reported for up to 5% of cervical smears with low repeatability between pathologists. When these cases are monitored, just as intraepithelial lesions or malignancy may not be encountered, varying rates of CIN may be observed (Edebal et al.,

2017). A study by Katki et al. (2013) identified that patients with ASC-H identified on PAP smear had CIN2 prevalence of 35%, CIN3 prevalence of 18% and cervical cancer incidence rates of 2.6% after colposcopy and biopsy.

Table 1. Classification of squamous cell abnormalities with the Bethesda system

SQUAMOUS CELLS	
• Atypical squamous cells	
- Undetermined significance (ASC-US)	
- Cannot exclude HSIL (ASC-H)	
• Low-grade squamous intraepithelial lesion (LSIL)	
- (HPV/mild dysplasia/CIN1)	
• High-grade squamous intraepithelial lesion (HSIL)	
- (Moderate/severe dysplasia/CIN2/CIN3/CIS)	
• Squamous cell carcinoma	

Diagnostic methods

The basic methods used for diagnosis of premalignant lesions of the cervix are determination of cervical lesions with colposcopy, biopsy and HPV DNA typing. Though the Bethesda system was developed for use in description of cervical cytologic samples, it is still used for histologic diagnosis. For biopsy material, the most common classifications are the CIN classification and the Bethesda system (Table 2).

Table 2. Comparison of Bethesda and CIN classifications

CIN1: Dysplasia of lower 1/3 of epithelium	LSIL
CIN2: Dysplasia of 2/3 of epithelium/koilocytosis	HSIL
CIN3: Dysplasia of more than 2/3 of epithelium	HSIL

P16

P16 is a protein coded on the 9th chromosome of the CDKN2A gene in humans, which acts as a G1 control point regulator and cyclin-dependent kinase inhibitor tumor suppressor. It accumulates in the cytoplasm and nuclei of cells infected with HPV and with loss of control of the cell cycle (Wentzensen et al., 2007; Tsoumpou et al. 2009). P16 is used as a sensitive and specific marker for determination of cervical cancer and precursors (Wentzensen et al., 2007; Cuschieri et al., 2008; Gustinucci et al., 2012). The use of P16 and Ki-67 together increases the diagnostic sensitivity (Sun et al., 2018). According to LAST (lower anogenital squamous terminology standardization project) project results, it is recommended that CIN2 showing over expression of P16 should be classified as HSIL and treated accordingly for lesions associated with HPV. If CIN2 lesions do not show P16

overexpression, they may be assessed as LSIL with low risk of progression (Darragh et al., 2013).

HPV

HPV infection is shown to be a critical precursor for squamous and adenocancers of the cervix (Moore et al., 2010). HPV transmitted by sexual routes infects the basal layer of the cervical epithelium in the transformation zone. Proliferation of the virus causes changes in the lower 1/3 of the epithelium, enlargement of the nuclei, hyperchromasia and koilocytosis. These changes are named CIN1 or LSIL. Natural immunity clears 90% of HPV infections and the lesion disappears. In 10% of infected women, persistent oncogenic HPV infection causes inactivation of tumor-suppressing genes (p53, pRB) due to viral oncoproteins of E6 and E7. Thus, control of the normal cell cycle is lost. Without natural control mechanisms, proliferation of cells causes formation of high-grade lesions (Doorbar et al., 2012).

Terminology

At the beginning of the 20th century, terms like “surface carcinoma, intraepithelial carcinoma or carcinoma in situ” were used for cells with carcinoma features in situations which had not exceeded the basal membrane. Diagnosis of carcinoma in situ (CIS) determined by 2 clinical approaches. While those without CIS did not require a hysterectomy, those with CIS had hysterectomy performed. After a duration of over 100 years, the basic approaches are still the same. In the 1950s, pathologists defined lesions with less severity than CIS. The term “atypical hyperplasia” described a lesion with less severity than CIS and was later changed to dysplasia. Dysplasia is classified as mild/moderate/severe. While those with CIS diagnosis continue to have hysterectomy performed, severe dysplasia began to be treated with more conservative methods like conization. In 1956 Kos and Durfee defined koilocytes (from the Greek meaning cave). Definition of the association between koilocytes and HPV was made 20 years later. In 1969 Richard revealed the concept that there may be a spectrum in cervical cancer varying from mild dysplasia to CIS. This spectrum determined the CIN term. Mild dysplasia is called CIN1, moderate dysplasia is CIN2 and severe dysplasia is called CIN3. For CIN treatment, hysterectomy is only recommended for women without expectations of child-bearing.

From 1980 to 2000, the development of molecular biology led to an understanding of HPV and cervical carcinogenesis. CIN1/mild

dysplasia/koilocytic atypia were defined as histological and cytological equivalents of HPV infection. These lesions have low progression risk, most regress during surveillance and treatment is accepted as clinical observation. Contrary to this, CIN2/CIN3 and CIS are morphological equivalents of cell transformation linked to the HPV oncogene. These lesions have persistent character and have greater tendency toward progression and invasive tumor development. As a result, they are accepted as being high grade. These concepts greatly affected classification of cervical PAP cytology and pioneered the Bethesda system. LSIL and HSIL are terminology recommended for all intraepithelial neoplasia associated with HPV in the lower anogenital region, and not just for CIN (Keating et al., 2001; Lysandra et al., 2016).

Macroscopy

Cervical premalignant lesions cannot be observed with the naked eye, other than exophytic or papillary lesions of condyloma acuminatum. Condyloma acuminatum are simultaneously LSIL. LSIL and HSIL differentiation cannot be made with colposcopy (Stoler et al., 2014).

Histopathology

Due to better repeatability and intraobserver compliance, the World Health Organization (WHO) recommends a 2-layer HSIL/LSIL system. In the 3-layer CIN system, CIN1 is equivalent to LSIL, while CIN3 equivalent is HSIL. CIN2 is the group with lowest repeatability. For these cases, classification as HSIL or LSIL according to immunohistochemical data is recommended (Stoler et al., 2014).

LSIL

LSIL is a morphologic sign of HPV virion production in host squamous cells (Stoler, 2000). It is characterized by proliferation of cells in the parabasal/basal-like cells in the lower 1/3 of the epithelium. The normally-observed garden-fence like sequence of basal cells is lost. Mitosis is limited to this area. Koilocytic atypia characterized by increased nucleus/cytoplasm rates, perinuclear halo and grapeseed-like disrupted nuclear contours is typical of LSIL. Koilocytosis is mostly observed in the upper portion of the epithelium. At the surface parakeratosis or hyperkeratosis may be observed (Koss & Durfee, 1956). Most koilocytosis is observed in HSIL; however, not in all. Histomorphological findings are the gold standard. Immunohistochemistry may be beneficial for cases where definite decision cannot be made. Clear

atypical cells and atypical mitosis presence does not comply with LSIL. In these situations, it is more appropriate to make HSIL diagnosis. Most LSIL cases regress within 1 year. The treatment protocol for LSIL is based on surveillance (Stoler et al., 2014).

HSIL

In HSIL, there are hyperchromatic atypical cells with loss of maturation and large nuclei affecting more than 1/3 of the epithelium (Figure 1). Mitosis has reached the upper layers of the epithelium and atypical mitosis may be observed. There is strong staining with P16 (Figure 2 and 3). According to histomorphological appearance, it may be typed as:

-Thin HSIL (less than 10 cell thickness)

-Keratinized HSIL (abnormal keratinization on the surface, dyskeratotic cells in the epithelium and atypia)

-Condylomatous HSIL (condyloma-like) (Darragh et al., 2013; Stoler et al., 2014).

HSIL treatment is applied with cryotherapy thermal ablation, LEEP or conization. It is important to fully remove the transformation zone (Darragh et al., 2013).

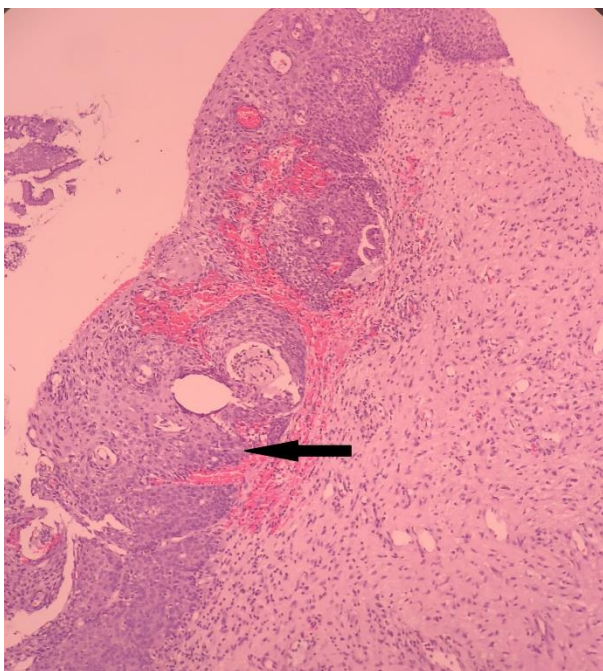


Figure 1. HSIL: dysplasia of more than 1/2 of epithelium(arrow) (H&E, X20).

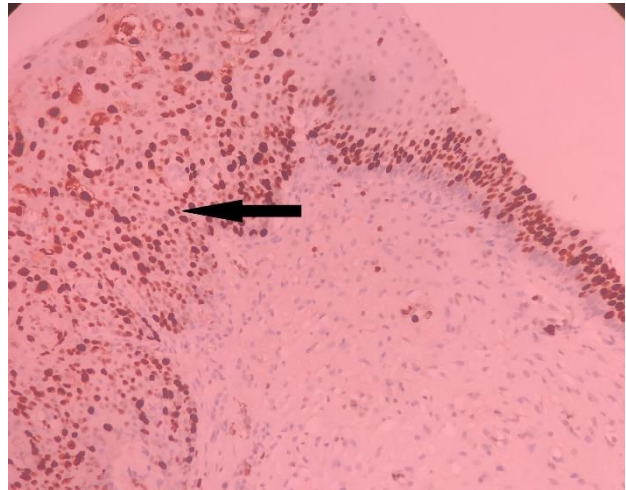


Figure 2. HSIL; Ki 67 immunohistochemical staining increases throughout full epithelium (arrow) (X20).

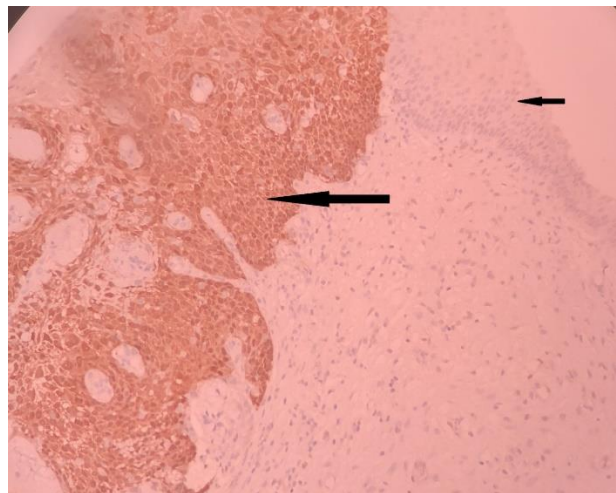


Figure 3. HSIL; p16 immunohistochemical study (long arrow). Normal epithelium is observed on the right side of the figure (short arrow) (X20).

Differential Diagnosis

Precancerous lesions of the cervix are frequently encountered in routine biopsies, but differential diagnosis of cases may be difficult. Basal cell hyperplasia, atrophy, reactive and repair-linked atypia and immature squamous metaplasia may mimic precancerous lesions.

In atrophy, maturation loss linked to hormonal insufficiency may be observed in multilayered squamous epithelium. Atrophy may be observed as typical atrophy, partial maturation atrophy and postmenopausal squamous atypia. In typical atrophy, the epithelium is thin, and maturation of cells is completely lost. The nucleus/cytoplasm ratio is increased; however, it is uniform, and mitosis is rare. Postmenopausal squamous atypia involves perinuclear cytoplasmic clearing (pseudokoilocytosis), nuclear hyperchromasia, mild nuclear enlargement (up to two times) and double

nuclei; however, chromatin distribution is normal. Atrophy with partial maturation observed has cells with large dark nuclei containing cytoplasmic glycogen, with rare mitosis (Wright & Ferenczy 2001; Malpica & Eucher, 2009). In situations where SIL cannot be differentiated with hematoxylin eosin, immunohistochemical studies may be beneficial. Ki-67 only stains parabasal cells in atrophic epithelium, while p16 is negative (Keating et al., 2001).

Basal cell hyperplasia is characterized by basal and parabasal thickness increases. The cell nuclei have large oval shapes and display vertical arrangement. Pleomorphism and hyperchromasia are not observed, with normal maturation of cells in the upper layers; however, in basal cells the typical “fence-like” arrangement is lost. Basal cell hyperplasia may be observed reactively in pregnancy, repair and inflammation (Wright & Ferenczy, 2001).

Reactive and repair atypia may be specific or non-specific with acute or chronic infections. Reactive changes include mild enlargement of the nucleus and hyperchromasia. In some cases, prominent atypia may be observed; however, mitosis is rare. Spongious presence may be helpful for differentiation. In some reactive cases, there may be intermittent Ki-67 staining in the upper two thirds of the epithelium; however, p16 is negative (Keating et al., 2001).

LSIL may be mimicked by squamous papilloma. Squamous papilloma does not involve koilocytosis and has fibrovascular cores in the center which is not typical of condyloma (Stoler & Schiffman, 2001).

It may be difficult to distinguish HSIL in situations with immature squamous metaplasia and atrophy and confusion may occur. In these situations, there are high nucleus/cytoplasm ratios in cells; however, in squamous metaplasia and atrophy, contour irregularity of the nucleus membrane is not observed. Mitotic figures may be observed in the basal layer; however, they are not observed in the upper half. For undecided cases, immunohistochemical staining with p16 is beneficial (Stoler et al., 2014). In some cases where definite diagnosis cannot be made due to reasons such as section errors, small sample pieces and cautery artifacts, there may be indecision between LSIL and HSIL and these cases may be called unidentified-grade SIL.

Conclusion

Cervical biopsies are common in routine practice. However, there are sometimes diagnostic difficulties. It is important to distinguish between HSIL and LSIL due to differences in treatment. Although histomorphology is gold standard, P16 and Ki-67 are beneficial immunohistochemical ancillary tests. However, it should be kept in mind that p16 can be positive in LSIL, and negative in HSIL.

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