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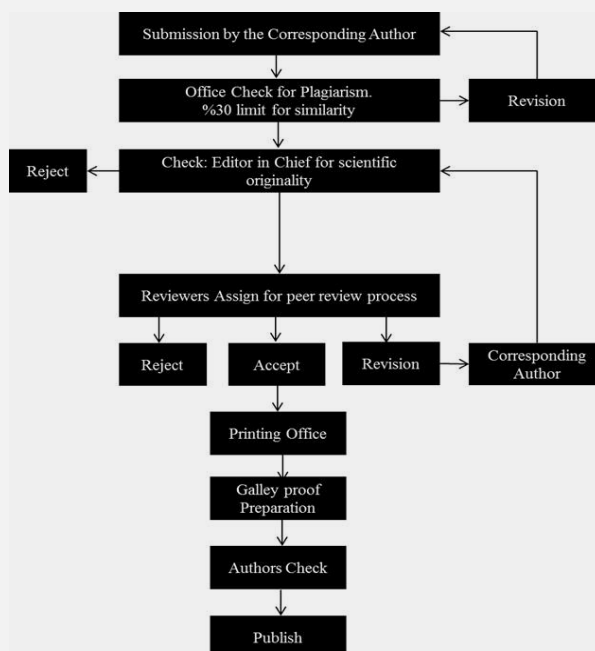
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Contents

Research Articles

[Demographic and clinical characteristics of traumatic shoulder dislocations in an eastern Anatolian city in Turkey: A retrospective single-centre analysis of 181 patients](#)

Ömer Cengiz, Ferdi Dırvar/ 298-305

[A Comparison of vitamin D deficiency with neutrophil lymphocyte ratio and CRP levels in Covid-19 patients](#)

Aslıhan Dilara Demir, Zeynep Hulya Durmaz/306-309

[Is There A Relationship Between The Umbilical Cord Coiling Index And Oxidative Stress Markers And SGA Fetuses?](#)

Gul Nihal Buyuk, Zeynep Asli Oskovi Kaplan, Umit Yasemin Sert, Inci Halilzade, Salim Neselioglu, Ozcan Erel, Huseyin Levent Keskin/ 310-314

[Determination of scatter radiation to the breast during lumbosacral x-ray examination using thermoluminescence dosimeter](#)

Chinenye Evangeline Eyisi-Enuka, Christian Chukwuemeka Nzotta , Ebbi Donald Robinson, Akintayo Daniel Omojola, Thomas Adejoh/315-321

[Clinical Significance of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Liver Transplantation](#)

Ahmet Atlas/322-328

[Do we need to enlarge emergency services or new emergency hospitals?](#)

Ensar Durmuş, Fatih Güneysu/329-333

Case Reports

[A rare cause of breast masses in childhood: ALK positive anaplastic large cell lymphoma](#)

Mustafa Özey, Zuhale Keskin, Sare Şipal, Zerrin Orbak, Handan Alp/334-337

[Geophagia: A cause of distal large bowel obstruction in a Sudanese woman.](#)

Khalid Yousif abu aagla, Osama Mohamed Elsanousi/338-340

[Articulating Os Intermetatarsium with painful ganglion cyst](#)

Celestie Yaacoub , Ahmad Kanj, Malak Eljebai, Georges Rouhana , Ali Kanj/341-344

Demographic and clinical characteristics of traumatic shoulder dislocations in an eastern Anatolian city in Turkey: A retrospective single-centre analysis of 181 patients

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ABSTRACT

Objective: This study aims to investigate demographic and clinical characteristics of traumatic shoulder dislocations in an Eastern Anatolian city (Muş) in Turkey.

Material and Methods: Digital patient database was reviewed to identify the glenohumeral shoulder dislocations admitted to the emergency department between January 2017 and December 2018. Incidence, demographics, recurrence, associated injuries, and mechanism of injury were evaluated.

Results: One hundred and eighty-one patients (140 males, 41 females; mean age: 39.98±20.41 years) experienced traumatic shoulder dislocation during the study period. The incidence was 18,9 per 100,000 person-years. Age distribution peaked between 21 and 30 (94.5% male) and between 61 and 70 years. Primary shoulder dislocation occurred in 153, recurrent dislocations in 28, and anterior dislocations in 177 patients. The mechanism of injury included falls in 144 and sports injuries in 18 cases. The reduction was achieved in 154 patients in the emergency department.

Conclusion: The incidence of traumatic shoulder dislocations in Muş was higher than the study conducted in Turkey but similar to those in Europe, the UK, and the USA. Risk factors included young age (21-40) and participation in sports in men but fall and being in the 6th decade in women.

Keywords: Glenohumeral joint, shoulder dislocation, incidence.

INTRODUCTION

Shoulder dislocations and related instabilities are common causes of chronic shoulder pain and limitation of joint functions. Shoulders are the biggest joints with the highest dislocation frequency in the osteoarticular system in the human body. The majority of shoulder dislocations are anterior dislocations. Less frequently, posterior and inferior dislocations occur respectively (1).

It has been reported that the incidence of shoulder dislocation varies between 8.2-56.3 per 100,000 person-years (2,3). In the literature, there is a limited number of studies conducted on the Turkish population. Although there are many studies on this subject in the world, the majority of them are European and American studies.

We think that demographic and clinical features of shoulder dislocations in the literature show differences in both Turkish populations and in the region due to socio-cultural characteristics, behavioural changes in sports activities and lifestyle differences.

In this retrospective study, demographic and clinical characteristics of shoulder dislocation in an Eastern Anatolian city in Turkey will be discussed and compared with available literature.

Research Article

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MATERIAL and METHODS

Muş, located in the Eastern Anatolian region of Turkey, has a population of 407,992 according to 2018 census (4) (**Figure1**). There is only one state hospital in Muş city centre, Muş State Hospital which provides treatment for effectually all traumatic injuries in the city. Since this study is based on non-invasive and retrospective clinical research, ethics committee approval could not be taken; however, administrative permission certificate related to the study was obtained from the hospital and all the conditions of the Helsinki Declaration were respected during the course of the study.

Patient data from January 2017 to December 2018 were reviewed retrospectively. The data of a total of 306 patients were obtained from the database with the diagnosis in the ICD-10 classification system including M24.3 (Pathological dislocation and subluxation of joints, not elsewhere classified), M24.4 (Recurrent dislocation and subluxation of joint), S43.0 (Dislocation of shoulder joint), S43.3 (Dislocation of other and unspecified parts of shoulder girdle) and S43.4 (Sprain and strain of shoulder joint). The radiological images and epicrisis information of the patients recorded in the PACS system (picture archiving and communication system) were examined one by one. 125 patients with no radiological imaging of shoulder dislocation were excluded from the study. During the examination, the data of 181 patients were examined and the demographic characteristics of the patients, the type of dislocations, the presence of additional injuries, the etiology of the dislocations, the presence of recurrent dislocations, the length of hospital stay, and the place of dislocation reduction were evaluated. The patients with suspicious information in their records were contacted to confirm the data. Radiographic images and epicrisis information of the patients were evaluated by two orthopaedic surgeons. The patients were grouped as under 20 years of age and over 80 years of age and were evaluated as decades between 20-80 years of age.

Statistical Analyzes: Statistical analyses were performed using SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The conformity of the numerical variables to the normal distribution was performed using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/ShapiroWilk tests). While the descriptive statistics for the numerical variables which showed normal distribution in the comparisons were given by mean and standard deviation, the descriptive statistics of the numerical variables not showing normal distribution were given with median and interquartile values. Descriptive statistics of categorical variables were given using numbers and percentage values. The Mann-Whitney U test was used to compare two groups with at least one non-normal distribution. Chi-square or Fisher tests were used according to the smallest expected value and the expected value in the comparison of two categorically independent groups. Kruskal-Wallis test was used to compare three groups with at least one not showing normal distribution. Statistical significance level was accepted as $p < 0.05$.

RESULTS

There were 140 (77.3%) male and 41 (22.6%) female patients with a mean age of 37.2 ± 21.3 . The median age was 39.9 (range: 12 to 93) years. More than half of patients (59.6%) were under 40 years of age. The average age of the male and female patients was 66 ± 25.5 , and 28 ± 20.7 , respectively ($p < 0.0001$). Incidence according to age peaked at two points; age 21 to 30 years (94.5% male) and 61 to 70 years (50% female). The male/female ratio was 3.4/1. The overall incidence of shoulder dislocations during the study period was 22.4 per 100,000 person-years (male: 17.3 per 100,000 person-years, female: 5.1 per 100,000 per person-years). The incidence of primary shoulder dislocations was 18.9 per 100,000 person-years (male: 14.4 per 100,000 person-years, female: 4.4 per 100,000 person-years). One hundred and fifty-three patients (84.5%) had primary shoulder dislocations, while 28 patients (15.4%) had recurrent shoulder dislocations (**Figure2**). The mean number of previous episodes of dislocations was 3.2 ± 1.9 (range: 2 to 8). Patients with recurrent shoulder dislocations were younger than those with primary dislocations (mean age, 29.86 ± 13.93 and 41.84 ± 20.9 , respectively; $p = 0.004$). The distribution of gender among patients with primary and recurrent dislocations was similar ($p = 0.072$) (**Table 1**).

There were 177 (97.7%) anterior dislocations, 3 (1.65%) posterior dislocations and 1 (0.55%) inferior dislocation (luxatio erecta) (**Figure 3**). Dislocations occurred in the right shoulder in 95 (52.5%) cases and in the left shoulder in 85 (46.9%). The simultaneous bilateral anterior dislocation was identified in 1 (0.55%) case. There was no significant difference in the incidence of dislocations in the right and left extremities ($p > 0.05$). Considering the months when the patients were admitted to the hospital and grouped according to the seasons, 51 (28.1%) patients were admitted to the hospital in spring, 51 (28.1%) in summer, 41 (22.6%) in autumn and 38 (20.9%) in winter (**Figure 4**). No statistically significant difference was found between the seasons ($p > 0.05$). The mechanism of injury was falling in 144 (79.5%) cases, sports injuries in 18 (9.9%), traffic accidents in 16 (8.8%) and epileptic seizure in 3 (1.6%) cases. The injury mechanism was similar between age groups ($p = 0.786$), but statistically different between genders ($p = 0.008$) (**Table2**). 156 patients (86.1%) presented with isolated shoulder dislocation. In addition to shoulder dislocation, 3 (1.6%) patients had proximal humerus fracture, 18 (9.9%) had fracture of the greater tuberosity (**Figure 5**), 1 (0.55%) had scapula fracture, 1 (0.55%) had clavicle fracture, 1 (0.55%) had acromion fracture and 1 (0.55%) had coracoid fracture. Of 18 cases with fractures of the greater tuberosity, 13 (72.2%) were older than 50 years of age. The fracture of the greater tuberosity was more common in the older age groups ($p = 0.0001$). The mean age of patients with isolated dislocation was found to be younger ($p = 0.009$). Initially, the reduction was attempted in the Emergency Department (ED) under conscious sedation in all patients. A successful reduction could be achieved in 154 patients (85.1%). However, 27 patients (14.9%) required general anaesthesia for reduction. The success rate in the ED was similar between primary and recurrent dislocations ($p = 0.283$).

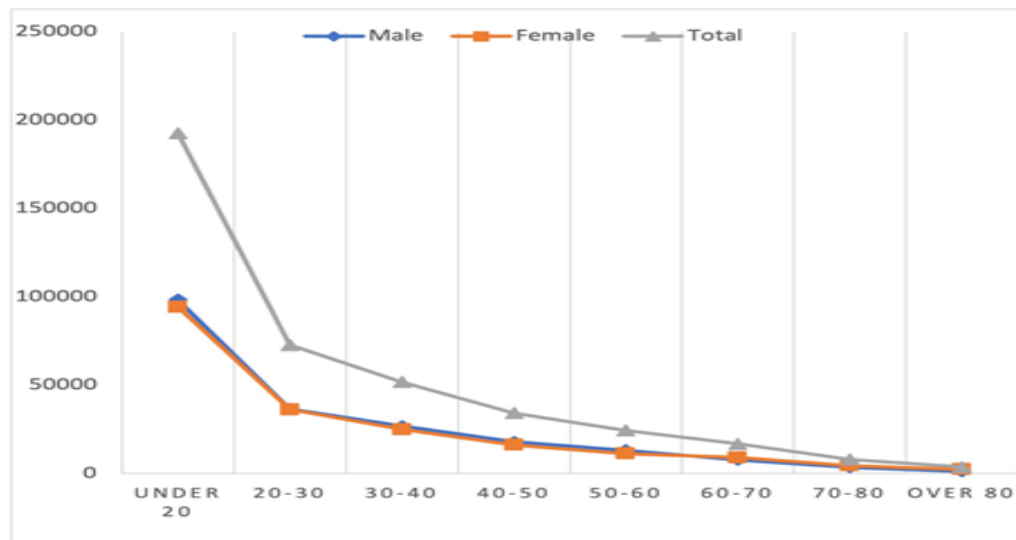


Figure 1. Demographic data of Muş in 2018.

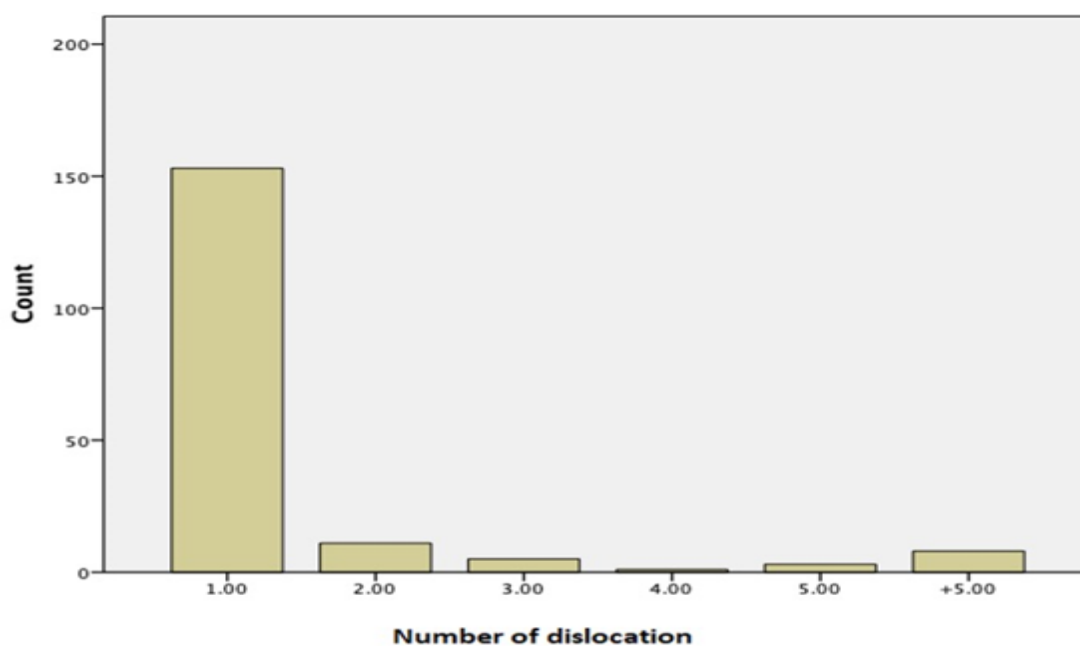


Figure 2. Distribution of the patients according to the number of dislocations.

Table 1. Distribution dislocations according to the age groups.

Age Groups	Recurrent Dislocation		First Dislocation		Total
	Male	Female	Male	Female	
Under 20	4	2	18	0	24
Between 20-30	12	1	40	2	55
Between 30-40	4	1	22	2	29
Between 40-50	0	0	17	5	22
Between 50-60	2	0	4	1	7
Between 60-70	1	1	11	11	24
Between 70-80	0	0	4	9	13
Over 80	0	0	1	6	7
Total	23	5	117	36	181
Average age (year)±SD	29,86±13,93		41,84±20,9		



Figure 3. Inferior shoulder dislocation of a 75-year-old female patient after falling.

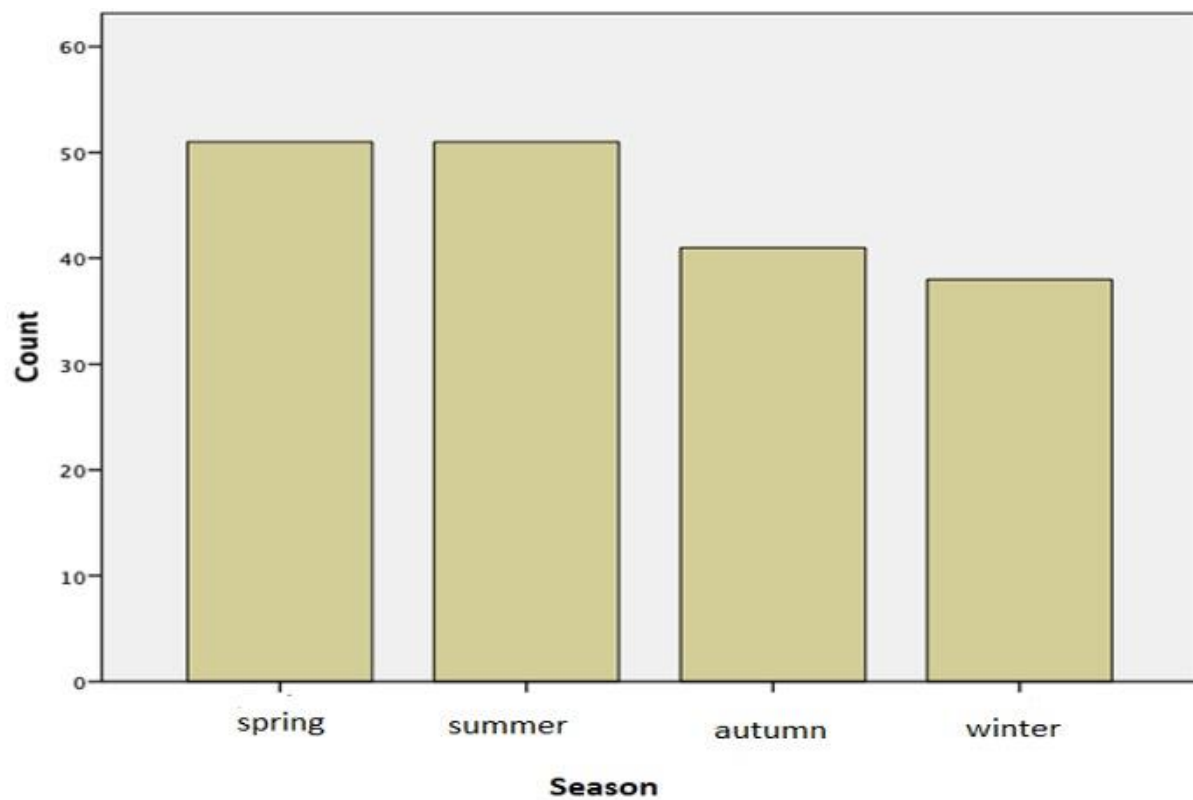


Figure 4. Distribution of patients according to seasons.



Figure 5. Tuberculum majus fracture and shoulder dislocation of a 20-year-old male patient after falling.

DISCUSSION

This study aims to determine the demographic and clinical characteristics of shoulder dislocations in an Eastern Anatolian city in Turkey. There is only one study reported in the literature on the incidence and demographic characteristics of shoulder dislocations on the Turkish population (5). However, the majority of the studies in the literature were conducted on American, British, and European populations.

In a study conducted in the United States, 124 patients were included in the study using the data between 1970 and 1979, the incidence of shoulder dislocation was found as 11.2/100,000 person-years (2). In another study conducted in the USA by Zacchilli et al. (6), a total of 8940 shoulder dislocations were included in the study using the data from 2002 to 2006 and the incidence of shoulder dislocation was 23.9/100,000 person-years. Szyluk et al. (7) reported the incidence of shoulder dislocation between the years 2010 and 2015 as 26.69/100,000 person-years. In a study in Denmark by Kroner et al. (8), the incidence of shoulder dislocation between 1980-1984 was 17/100,000 person-years.

In a study in Norway by Liavaag et al. (3), the shoulder dislocation incidence between 2009 and 2010 was 56.3/100,000 person-years. The incidence of shoulder dislocation between 2008 and 2010 in a study conducted in Turkey by Tafi et al. (5) was 5.3/100,000 person-years. The 22.4 per 100,000 person-years incidence of traumatic shoulder dislocations in our study was much higher than the previous study conducted in Turkey but similar to European and American studies.

Gender and age have been shown as the two most significant risk factors for traumatic shoulder dislocations. Shoulder dislocation can occur in all age groups. A study conducted by Hazmy et al. (9) revealed that reproductive age (21-40 years) and participation in sports were risk factors in men and being over 40 years of age and falls were the risk factors to develop shoulder dislocation in women. Owens et al. (10) carried out a study in predominantly young male military personals and the incidence of shoulder dislocations was found 169 per 100,000 person-years. The incidence rate is higher in physically active young males who are more frequently exposed to trauma. In our study, shoulder dislocations had a bimodal distribution with two peaks of incidence (Figure 6).

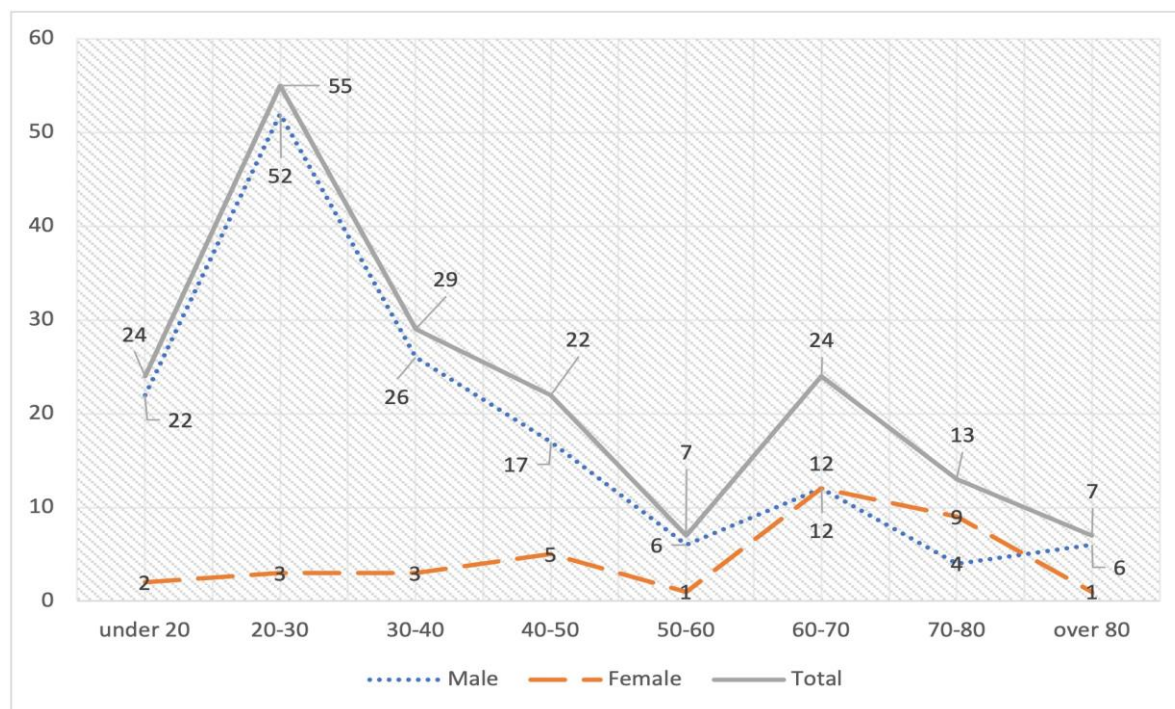


Figure 6. Distribution of shoulder dislocation according to age and gender.

Table 2. Distribution of dislocation mechanism according to the age groups.

Age Groups	Falling		Traffic Accident		Sports Injury		Epilepsy		Total
	M	F	M	F	M	F	M	F	
Under 20	18	2	1	0	3	0	0	0	24
Between 20-30	39	2	3	0	9	0	1	1	55
Between 30-40	19	2	1	0	5	1	1	0	29
Between 40-50	13	5	4	0	0	0	0	0	22
Between 50-60	5	1	1	0	0	0	0	0	7
Between 60-70	7	12	5	0	0	0	0	0	24
Between 70-80	3	9	1	0	0	0	0	0	13
Over 80	1	6	0	0	0	0	0	0	7
Total	144		16		18		3		181

Males constituted the majority of the cases in the 3rd decade of life and females in the 6th decade. This particular pattern has been identified in nearly all previously conducted studies (2,3,5,6,8). Nevertheless, the age range in the second peak was lower in our country. The second peak of incidence was seen in patients older than 80 years in Norway (3) and between 80 to 89 years of age in Zacchilli's study in the USA (6). This diversity can also be explained by the differences in the population pyramid and the lower average life expectancy in our country. A study conducted in Denmark (8) and another study in a large population-based cohort of 16,763 patients aged 16–70 years in the UK during 1995–2015 (11) identified the bimodal age distribution of incidence and also specifically noted that older people most frequently dislocated their shoulder at home by falling on their arm, whereas young people most frequently suffered a shoulder dislocation while playing sports.

The reason behind the second peak of incidence in elderly women in the general population is not so clear. Nordqvist et al. (12), Tafi et al. (5) and Liavaag et al. (3) proposed that the increased incidence of falls in this age group is the major reason behind the second peak. Shoulder dislocations in the elderly are generally associated with rotator cuff tears and fractures with following loss of function as well as instability. However, further work is needed to analyze the reasons that may support this increased risk of shoulder dislocations in aging women. Possible reasons include biological differences between aging men and women such as differences in joint proprioception, soft tissue tendon quality, protective muscle size, or whether there is a difference in the incidence of falls between men and women (11). Falls were responsible for 79.5% of all cases in our study. There was a distinct variation between genders regarding the mechanism of injury. In females, falls were responsible for nearly all cases. In addition to falls, sporting activities and traffic accidents were other significant causes of shoulder dislocation in males (Table 2).

In Muş, because of the sociocultural structure of the community, a large proportion of women are housewives. Hence, the relatively low participation of women in the workforce and sporting activities may explain the differences in the mechanism of injury in males and females. Similarly, Zacchilli & Owen reported that males had a significantly higher proportion of sports or recreation-related dislocations than females and that younger age groups had a significantly higher proportion than the older age groups (6). On the other hand, Krøner et al. could not show any difference in the mechanism of injury between genders (8).

Several studies have revealed that the age at the time of primary dislocation is the most important prognostic factor in determining the risk of recurrence (13,14,15,16). te Slaa et al., in their study, found a radiolocation rate of 64% for cases under the age of 20 and 4% for those over 40 (14). In a retrospective analysis of 488 cases with a follow-up duration of 20 years, Rowe reported 83% recurrence rate for cases below the age of 20 and 16% for those above the age of 40 (17). Hovelius et al. followed up 255 patients with 257 primary shoulder dislocations for two years in a multicentre study in Sweden and reported 47% recurrence rate in patients with 22 years of age or younger (8). The study conducted by Tafi et al. (5) in Turkey revealed that recurrent dislocations constituted 17% of 208 patients and patients with recurrent dislocations were reported to be younger than those with primary dislocations (mean age, 29.7 ± 14.5 and 38.8 ± 22.2 , respectively). In our study, recurrent dislocations constituted 15.4% of the cases. Patients with recurrent shoulder dislocations were younger than those with primary dislocations (mean age, 29.86 ± 13.93 and 41.84 ± 20.9 , respectively; $p=0.004$).

Analysis of incidence figures in particular months of the year shows a significantly higher incidence in the winter months, with a peak in January (7). On the contrary, in our study, 38 (20.9%) patients were admitted to the hospital in the winter season. In our opinion, adverse weather conditions and economic difficulties in rural areas in Muş prevent people from accessing health services in winter. Also, we think some of the patients with dislocated shoulders were treated by traditional bonesetters. Hovelius et al. (16) stated that nearly 50% of the people with primary dislocations never visited hospitals nor were treated by a physician. Therefore, we explain the low rate of shoulder dislocations in winter due to not reaching the hospital in Muş.

The majority of studies showed an overall predominance of anterior directionality, followed by posterior and inferior directions (8, 19, 20). Krøner et al. (8), Rowe (17), Owen et al. (20) and Tafi et al. (5) reported anterior shoulder dislocations by 97.2%, 98%, 94% and 93.4%, respectively. Similar to the literature, anterior dislocations constituted 97.7% of cases in our study. te Slaa et al. and Hovelius et al. reported that bilateral dislocations composed 12% and 9% of all the cases, respectively (14, 19). Contrary to this finding, bilateral anterior dislocation was identified in only 1 case (0.5%) in our study.

In a study of 500 shoulder dislocations, fractures of the shoulder girdle, being more common in older population, were associated with dislocation in 122 (24%) and with fractures of the greater tuberosity in 75 (15%) cases. In the

same study, other fractures (surgical neck, clavicle, scapula and acromion) were associated with dislocation in 10 (2%) cases (17). Tafi et al. (5) reported that 10.6% of cases had fractures of the greater tuberosity which were more common in the older population. In our study, the majority of shoulder dislocations (86.1%) were isolated dislocations without an accompanying fracture. In addition to shoulder dislocation, 3 (1.6%) patients had proximal humerus fracture, 18 (9.9%) had tuberculum majus fracture and 4 (2.2%) had other fractures similar to Rowe's study (17) and were more common in the older population of our study.

All patients included in our study were diagnosed with shoulder dislocations verified by radiographs and clinical records. The radiographs were determined by two orthopaedic surgeons. This enabled eliminating any inappropriate clinical records or misdiagnosis. The data obtained in the study provided detailed information about several characteristics of shoulder dislocations such as the direction of dislocations, recurrence, associated injuries, and etiology. Yet, our study had some limitations as well. First, our findings cannot be generalized to Turkey due to the distinct demographic characteristics of the region where the study was conducted. Secondly, a tiny decrease in annual incidence might be expected in a real situation as additional patients with shoulder dislocations might have been coded with a false ICD-10 code in our clinical databases. Finally, there is only one private hospital in Muş that usually provides treatment for a small number of patients with shoulder dislocations.

CONCLUSION

In conclusion, the overall incidence of primary shoulder dislocations was 22.4 per 100,000 person-years in Muş. Our findings were similar to the European and American studies but different from the other study conducted in Turkey. Age and gender-specific distribution of shoulder dislocations showed two peaks of incidence in young males and elderly women. The incidence in males, which constituted the majority of the cases, was 3.4 times that of females. We believe that the current study will provide additional knowledge and outline the demographic characteristics of primary shoulder dislocations in Turkey. Consequently, it is required to study changes in the incidence of shoulder joint dislocations over time with regular updates and to monitor this problem in the general population to make our understanding more accurate.

Author contributions: ÖC, FD; Literature search and study design, Data collection, patient examination and therapy ÖC; Writing article and revisions

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Ethical issues: All authors declare originality of research.

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Comparison of vitamin d deficiency with neutrophil lymphocyte ratio and crp levels in covid-19 patients

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ABSTRACT

Objective: Objective: We aimed to evaluate the association of neutrophil-lymphocyte ratio (NLR) and C reactive protein (CRP), ferritin, sedimentation levels with vitamin D concentrations in Covid-19 patients and to investigate their effect of levels on Covid-19 patients.

Materials and Methods: Forty-six patients aged 18-85 were included in our study. Our study is a retrospective study. Patients were divided into 2 groups with the first group consisting of those with vitamin D level 20 and below and 2nd group consisting of those with vitamin D level above 20. After Vitamin D, CRP, neutrophil, and lymphocyte values were retrospectively investigated with the hospital database, vitamin D levels were compared to CRP and neutrophil/lymphocyte ratio.

Results: A positive correlation between CRP and SED, CRP and ferritin, NLR, and ferritin was observed in Covid-19 positive patients with Vitamin D level > 20. A positive correlation between NLR and CRP was observed in Covid-19 positive patients with Vitamin D level ≤ 20.

Conclusion: In patients with Vitamin D levels >20, there was a significant correlation between vitamin D and NLR and a moderate correlation between Vitamin D and CRP. In patients with Vitamin D levels <20, there was a positive correlation of Vitamin D with CRP and NLR.

Keywords: Covid-19, Vitamin D, Neutrophil Lymphocyte Ratio, CRP, SARS-CoV-2

INTRODUCTION

The world's first cases of a highly contagious, deadly new type of coronavirus infection were identified in December 2019. There have been applications to the hospital with cases of pneumonia with serious complications. The cause of which is unknown, and it was later understood that this is a new type of coronavirus infection (1). The World Health Organization reported 11,125,245 cases and 528,204 deaths worldwide as of July 6, 2020 (2).

Coronavirus was first described by Tyrell and Bynoe in 1966. They are enveloped positive single chain RNA viruses. Although it has 7 subgroups that can infect people, beta coronavirus makes the deadliest, most serious disease. SARS-COV-2 is one of these beta coronavirus (3).

Coronaviruses have been found to be responsible for 2 diseases affecting the entire world in recent years; Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) (4). The genetic sequence of the new type of coronavirus is similar to the genetic sequence of SARS co-V at 80% and MERS at 50% (5).

Vitamin D is produced on the skin from 7-dehydrocholesterol by the effect of UVB rays. It converts to 25(OH)D in the liver and then 1.25(OH)2D metabolites in the kidney (6). Vitamin D has a protective effect on many viral infections. It reduces viral replication. By reducing proinflammatory cytokines, it shows an anti-inflammatory effect. A study has shown that vitamin D reduces the risk of colds and viral infections in cold patients, both by its effect on the immune system and by its physical effect on tight junctions (7, 8).

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Neutrophil lymphocyte ratio and CRP are our routine laboratory tests. They are easily accessible, inexpensive, routine biochemical parameters. CRP is an acute-phase protein synthesized from the liver. In cases of acute infection and inflammation, the amount in the blood increases (9). Neutrophil lymphocyte ratio is also a marker that reflects inflammation.

We aimed to evaluate the relationship of neutrophil-lymphocyte ratio and CRP level with vitamin d concentrations, evaluate the relationship of Vitamin D deficiency with the disease. We wanted to investigate the deficiency of vitamin d and the relationship with the disease.

MATERIAL and METHODS

This study was approved by the Committee of Tokat Gaziosmanpaşa University, Education and Research Hospital with Decision No. 20-KAEK-218 in the scientific meeting which was held on 13.08.2020. Patients diagnosed with Covid-19 in our hospital were taken to the study. Forty-six patients aged 18-85 were included. These patients were retrospectively examined. Patients admitted with cough, fever, or upper respiratory tract complaints and followed up with Covid-19 diagnosis according to PCR and tomography results were included in the study. Examinations of patients were obtained through the hospital database. After Vitamin D values, also CRP, neutrophil, and lymphocyte values were retrospectively obtained from the hospital database; Vitamin D levels and CRP and neutrophil and lymphocyte values were compared. Being under 18 and over 85 are the criteria for being excluded from the study.

Neutrophil and lymphocyte values were studied with Sysmex XN 1000 hemogram device in our hospital. A laser optical method is used.

CRP is studied with Roche Cobas 8000 device by the Turbidimetric method. Vitamin D is studied by the chemiluminescence method with Siemens Advia Centaur XP hormone device.

Statistics: GraphPad Prism version 7.00 was used for statistical analysis (GraphPad Software, La Jolla California USA). After calculating quantitative data, the existence of the relationship between variables was investigated by applying the Spearman correlation test. Correlation coefficient (r) was evaluated as weak from 0.00 to 0.24, medium from 0.25 to 0.49, strong from 0.50 to 0.74, very strong from 0.75 to 1.00. The parameters measured in Covid-19 positive male and female patients were compared with the non-parametric test (Mann-Whitney test).

Results were obtained at a 95% confidence interval and a statistical significance level of $p < 0.05$.

RESULTS

There was a positive strong correlation between n/L and CRP, and a moderate positive correlation between CRP and age, n/L and age, sed and age, sed and CRP, sed and n/L, fer and n/L. A weak positive correlation between fer and age, fer and CRP, fer, and sed was noted.

* The correlation coefficient (r) shows that the relationship between parameters is statistically significant ($p < 0.05$).

There was a very strong positive correlation between CRP and sed, CRP and fer, n/L and fer, and a strong positive correlation between age and n/L, age and sed, CRP and n/L, n/L and sed, sed and fer, age and CRP, and moderately positive correlation between age and fer.

* Correlation coefficient (r) shows that the relationship between parameters is statistically significant ($p < 0.05$).

Table 1. Independent t-test results between biochemical results of Covid-19 patients with Vitamin D levels ≤ 20 and > 20

Parameters	Vit d ≤ 20 (n=33) (13.06 \pm 1.10)	Vit d > 20 (n=13) (27.12 \pm 1.76)	p value*
Age	52.61 \pm 2.415	44.62 \pm 6.19	0.3612
Crp	23.36 \pm 6.49	28.96 \pm 14.20	0.9185
n/l	2.69 \pm 0.42	2.64 \pm 0.62	0.7770
Sed	34.42 \pm 4.67	27.08 \pm 5.0	0.5344
Fer	126.3 \pm 19.59	151.6 \pm 47.49	0.9089

* Those with a p-value of less than 0.05 were considered statistically significant.

Table 2. Inter-parameter correlation analysis in Covid-19 positive patients with Vitamin D level ≤ 20

Parameters		age	CRP	n/l	sed	fer
age	r	1	0.421*	0.313	0.367*	0.246
CRP	r	0.421*	1	0.650*	0.495*	0.124
n/l	r	0.313	0.650*	1	0.334	0.252
sed	r	0.367*	0.495*	0.334	1	0.090
fer	r	0.246	0.124	0.252	0.090	1

Correlation coefficient (r) was evaluated as weak from 0.00 to 0.24, medium from 0.25 to 0.49, strong from 0.50 to 0.74, and very strong from 0.75 to 1.00.

Table 3. Correlation analysis between parameters in Covid-19 positive patients with Vitamin D level > 20

Parameters		age	CRP	n/l	sed	fer
age	r	1	0.392	0.535	0.609*	0.417
CRP	r	0.392	1	0.694	0.862*	0.801*
n/l	r	0.535	0.694*	1	0.538	0.774*
sed	r	0.609*	0.862*	0.538	1	0.704*
fer	r	0.417	0.801*	0.774*	0.704*	1

Correlation coefficient (r) was evaluated as weak from 0.00 to 0.24, medium from 0.25 to 0.49, strong from 0.50 to 0.74, very strong from 0.75 to 1.00.

DISCUSSION

Our study is a retrospective study with 46 patients. Patients with vitamin D >20 had a strong correlation between vitamin D and NLR, and a moderate correlation between vitamin D and CRP. In other words, the increased vitamin D level of the patients did not show itself in the form of a decrease in inflammation and a decrease in the parameters indicative of this. It was increasing in correlation with Vitamin D.

Patients with Vitamin D <20 also had a positive correlation between Vitamin D and CRP and NLR. This means that in patients with low Vitamin D levels, the infection is expected to be more severe and reflected in the form of high NLR and CRP, but the opposite happens, and NLR and CRP also fall.

NLR and CRP are important markers of increased inflammation and sepsis. Vitamin D reduces the apoptosis of alveolar cells, increases surfactant synthesis, and has been shown in many studies to be protective in respiratory infections with its anti-inflammatory role (10). Many studies conducted so far showed that vitamin D deficiency increases the risk of Covid-19, and its supply is protective (11).

In Indonesia, Raharus P and friends (12) studied with 780-person and noted that low vitamin D levels were associated with increased mortality in Covid-19 patients.

But in some recent studies, they have not found an association between Vitamin D levels and Covid-19 severity, as in our study. Hastie C.E and friends (13) could not show an association between Vitamin D concentration and Covid-19 in a large-scale study involving 502,604 participants aged 37-73 through UK Biobank. We did not see an increase in CRP and NLR as expected in people with vitamin D below 20 who were expected to have more serious infections. On the contrary, we observed a decline in them with a positive correlation. Sabetta J.R and friends (14) conducted a large-scale study to examine the relationship between Covid-19 risk and serum vitamin D and found no significant relationship.

Despite this, Mardani R (15) noted that low serum vitamin D levels increased hospitalization rates in Covid-19 and they observed higher neutrophil-lymphocyte ratio and vitamin d levels in Covid-19 patients compared to the control group. They found a statistically significant difference.

In a study with 348 598 UKBiobank participants, Hastie C.E and friends did not reach any findings indicating a relationship between the risk of infection and vitamin D level (16).

CONCLUSION

Our study was retrospective, so we did not know about the socioeconomic levels of patients, their living conditions, whether they had a sedentary lifestyle, or their ultraviolet exposure. While evaluating the deficiency of vitamin D, it should be considered the contribution of this situation to occurrence of the covid-19 disease or as a result of covid-19 disease. For the purpose of clarifying the subject, we believe that studies with a larger number of groups will be useful. In addition, the fact that we did not show a direct relationship in our study, it does not mean that patients are deprived of vitamin D supplements. Vitamin D support is required and should be done as needed.

Author contributions: ADD, ZHD; Literature search and study design, Data collection, patient examination and therapy ADD; Writing article and revisions

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Is there a relationship between the umbilical cord coiling index and oxidative stress markers and SGA Fetuses?

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ABSTRACT

Objective: We aimed to investigate the relationship between umbilical coiling index and thiol/disulfide balance in SGA newborns to compare with AGA newborns.

Material and Methods: Fetal umbilical cord serum samples were collected during labour and the thiol/disulfide homeostasis was measured. After birth, umbilical cords were collected and cord parameters were examined including, length, number of coils, umbilical cord index.

Results: Significant decrease in native thiol, total thiol, and a significant increase in disulfide, disulfide/native thiol ratio and disulfide/total thiol ratios were observed in the study group while native thiol/total thiol ratio levels of the two groups did not reach to a statistical significance.

Conclusion: The results of this study showed that SGA babies had altered thiol homeostasis in favor of oxidative stress.

Keywords: Oxidative Stress, SGA, Thiol/disulfide, Coiling, Index

INTRODUCTION

A small for gestational age (SGA) fetus is defined when the fetal weight is <10th percentile (1). SGA fetuses carry higher risk for adverse outcomes, such as impaired performance of cognitive and sensorimotor functions (1). Although most SGA infants will catch up growth during the early childhood, in obstetric practice, the increased risk of perinatal morbidity and mortality is a matter of concern (2).

Umbilical cord is the bond of life between the fetus and the placenta, which is believed to be simple in both structure and function (3, 4). Umbilical coiling index (UCI) defines the umbilical coil structure, and it is calculated by dividing number of coils to the cord length. An increased fetal risk is present in cases of hypercoiling (UCI>0,3 spiral/cm) and hypocoiling (UCI<0,1 spiral/cm) (5, 6). A relationship has been reported between the fetal chromosomal anomalies, fetal growth restriction, fetal death, preterm labor, abnormal fetal heart trace, fetal distress and abnormal coiling index (7). A higher risk for intrauterine growth restriction was reported in cases with hypercoiling (8). Hypocoiling was reported to be associated with meconium stained amniotic fluid and higher rates of admission to the neonatal intensive care unit (9).

Oxygen is essential for life, however, the excessive amounts of oxygen causes production of free radicals which are toxic to the protein structures of cell membranes, enzymes and neurotransmitters (10, 11). Antioxidant defense systems prevent the formation of these oxidants and their harmful effects. When this redox homeostasis is tipped toward an overbalance of free radicals, then oxidative stress occurs. Thiols are compounds that contain sulfur and are the most important part of the antioxidant defense system (11). In 2014, Erel and Neselioglu developed a method for detecting total thiol/disulfide homeostasis (12).

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Thiol/disulfide homeostasis represents the oxidative stress and indirectly reflects the anti-oxidative defense, and is previously reported to have an association in the pathogenesis of various acute and chronic diseases (11, 12).

To the best of authors' knowledge, an analysis of oxidative stress markers and its relationship between the umbilical cord coiling and SGA fetuses have not been reported yet. This study was designed to investigate the relationship between umbilical coiling index and thiol/disulfide balance in full term SGA newborns to compare with appropriate for gestational age (AGA) newborns.

MATERIAL and METHODS

This prospective study was performed between May 2019 and August 2019 in a tertiary obstetric care center. Ethical approval was obtained from the Zekai Tahir Burak Educational and Research Hospital Ethics Committee with the number (No: 02-37/2019). A verbal and written informed consent was obtained from all participants. A total of 160 women with term (>37 weeks), singleton pregnancies and vertex presentation who delivered at term, either by an elective cesarean section or a spontaneous vaginal delivery were included.

High-risk pregnancies (gestational diabetes, hypertension, oligohydramnios, polyhydramnios, multiple pregnancies); fetuses with single umbilical artery, congenital anomalies, or fetal growth restriction and women with chronic systemic diseases were excluded. Pregnancies of assisted reproductive techniques were also excluded from the study. Gestational age was determined by the last menstrual period or by adjustment regarding the ultrasound measurements in the first trimester.

Maternal demographic characteristics, age, BMI, parity, gestational age, fetal gender, mode of delivery, admission to neonatal intensive care unit (NICU), Apgar scores and arterial blood pH were recorded. An Apgar score of <7 at the 5th min was considered low. Birth weights <10th percentile were accepted as small for gestational age and >90th percentiles were accepted as large for gestational age according to Ballard's chart (1).

The umbilical cord of patients were cut and collected after delivery. The following cord parameters were examined: the cord length and number of coils. Umbilical cord index (UCI) was also calculated as a demonstrator of the ratio of the number of coils and the cord length. Blood from umbilical artery was drawn after the fetal cord was clamped, centrifuged at 5000 r.p.m for ten minutes and stored at - 80 OC until the analysis.

The blood samples were analyzed in the biochemistry laboratory of the Yıldırım Beyazıt University Medical School. Thiol/disulfide homeostasis tests were measured by an automated spectrophotometric method described by Erel et al. (12). Native (NT) and total thiol levels (tNT), disulfide levels (D), disulfide/total thiol ratios (D/tNT), disulfide/native thiol ratios (D/NT) and native thiol/total thiol ratios (NT/tNT) were calculated (Cobas 501, Roche, Mannheim, Germany).

The patients were divided into two groups regarding the fetal growth, 41 women formed with a fetus <10th percentile formed the SGA group and 119 women with appropriate for

gestational age fetuses formed the control group. The two groups were compared regarding the maternal characteristics, neonatal outcomes, oxidative stress markers and the coiling of the umbilical cord.

Statistical analysis: Statistical analysis was performed by SPSS (Statistical Package for the Social Sciences) 24 (SPSS Inc., Chicago, IL). The distribution of parameters was assessed by visual (histograms, probability plots) tests and Kolmogorov Smirnov normality test. Descriptive analyses were reported using medians and minimum-maximum levels for the non-normally distributed and categorical variables and mean and standard deviation for the normally distributed variables.

Independent samples t-test were used for the normally distributed data and Mann-Whitney U-test was used for non-normal distributed data in two independent groups. The comparison of categorical variables was performed by the chi-square test. P values <0.05 were considered statistically significant. P values <0.05 was considered statistically significant. Pearson correlation coefficient was used to determine the correlation between presence of hypercoiled umbilical cord index and fetal umbilical cord thiol/disulfide homeostasis values.

RESULTS

A total of 160 term, singleton pregnant women were enrolled in the study; 41 pregnancies with SGA newborns formed the study group and were compared with 119 AGA fetuses in the control group.

The two groups were similar in terms of maternal age, gestational week, parity, mode of delivery and the fetal gender. In Table 1 main characteristics of the two groups are compared. The mean 1st and 5th minute Apgar scores were significantly lower in SGA infants (p: 0.003 and p:<0.001, respectively). The need for neonatal intensive care unit was higher in SGA deliveries than AGA fetuses (33.3% vs. 7.1% respectively; p<0.001). The mean umbilical cord pH was also lower in the SGA group (p<0.001).

In Table 2 the umbilical cord coiling findings were compared between the two groups. The rate of normal UCI index was more common in neonates with appropriate gestational age than SGA group (85.5 vs 53.6% respectively; p=0.036). The rate of hypocoiling was similar between groups while hypercoiling was more common in SGA group than controls (41.6% vs. 10% respectively; p=0.021).

Oxidative stress measures are presented in Table 3. Significant decrease in native thiol (p:0.021), total thiol (p:0.041), and significant increase in disulfide (p:0.035), disulfide/native thiol ratio (p:<0.001), and disulfide/total thiol ratios (p:<0.001) were observed in the study group while native thiol/total thiol ratio levels of the two groups did not reach to a statistical significance. No significant correlation was observed between presence of hypercoiled umbilical cord and fetal umbilical cord thiol/disulfide homeostasis values (Table 4).

Table 1: The participant characteristics and clinical outcomes for groups.

	SGA Group (n:41)	Control Group (n:119)	P values
Age (years)	28.2±2.3	27.8±2.6	0.560
Gestational week (weeks)	39.8±0.9	39.5±0.7	0.879
Parity	1.2±0.7	1.5±0.8	0.128
Birthweight (grams)	2893±783	3293±535	0.001*
Mode of delivery	6(14.6%)	17(14.2%)	0.536
1 minute Apgar	6.7±1.3	7.5±1.1	0.003*
5 minute Apgar	8.8±1.1	9.5±0.7	<0.001*
NICU	(33.3%)	(7.1%)	<0.001*
Umbilical cord Ph	7.26	7.38	<0.001

* P<0.05, significant. NICU: Requirement of neonatal intensive care unit. SGA: Small for gestational age

Table 2: The distribution of small and normal for gestational age neonates by antenatal umbilical cord coiling.

	SGA Group (n:41)	Control Group (n:119)	P values
hypocoil	2(4.8%)	5(4.2%)	0.648
normocoil	22(53.6%)	102(85%)	0.036*
hypercoil	17(41.6)	12(10%)	0.021*

* P <0.05, significant.

Table 3: The thiol/disulfide homeostasis parameters of the groups.

	SGA Group (n:41)	Control Group (n:119)	P values
Native thiol (Imol/l)	271.8±49.3	296±44.3	0.021*
Total thiol (Imol/l)	316±52.7	340.1±48.9	0.041*
Disulfide (Imol/l)	26.2±8.5	21.9±8.6	0.035*
Disulfide/native thiol (%)	10.3±5.5	7.5±3.1	<0.001*
Disulfide/total thiol (%)	8.5±3.4	6.4±2.3	<0.001*
Native thiol/total thiol (%)	86.7±16.9	87.2±4.6	0.789

*p<0.05, significant.

Table 4. Correlations of thiol-disulfide levels with coiling index

	Native thiol (Imol/l)	Total thiol (Imol/l)	Disulfide (Imol/l)	Disulfide/native thiol (%)	Disulfide/total thiol (%)	Native thiol/total thiol (%)
Coiling	r:-0.49	r:-0.030	r:0.142	r:0.162	r:0.167	r:0.087
index	p:0.320	p:0.701	p:0.072	p:0.031	p:0.031	p:0.271

The correlation between the two variables was a weak correlation of -0.5 < r < 0

DISCUSSION

Hypercoiled umbilical cord has been reported to have an association with SGA fetuses, however a relationship with oxydative stress has not been analyzed yet. In current study, we have demonstrated that SGA newborns had altered thiol homeostasis in favor of oxidative stress. To the best of authors knowledge, this is the first report on the association between thiol/disulfide balance and hypercoiling of the umbilical cord. Higher levels of disulfide, disulfide/native thiol ratio and disulfide/total thiol ratio were found in the SGA group compared to the AGA group. Concurrent with previous studies in SGA group, an increase in the coiling index was observed. Ezimokhai et al. showed that hypercoiled cords were correlated with poor perinatal outcomes such as low birthweight and meconium stained amniotic fluid at birth, and fetal growth retardation (13).

Laat et al. reported an increased risk for the need of operative deliveries in patients with hypercoiled umbilical cord structure in SGA fetuses (14). Concurrent with their results; hypercoiled structure was higher in SGA group, however, no increased risk was observed for operative delivery in our study. This findings suggested that hypercoiling of the umbilical cord may result in compression of the umbilical vein and consequent compromise of the placento-fetal blood flow.

Abnormal umbilical cord coiling is associated with adverse perinatal outcomes; however, the etiology of the umbilical coiling pattern is poorly understood. Numerous studies have demonstrated relationships between aberrancies in coiling and adverse perinatal outcomes including abnormal fetal heart rate patterns in labor and an increased incidence of perinatal morbidity and mortality (15, 16).

In a study by Mittal et al, it was revealed that hypercoiling (UCI higher than 0.30) was associated with intrauterine death and an inverse correlation was found between the UCI and the gestational age of intrauterine death (17). In our study, Apgar scores and the cord blood pH were significantly different between the two groups. Similarly, the need for neonatal intensive care unit admission was higher than the control group.

Several oxidative stress markers were used to determine the oxidative stress in SGA fetuses (18). Gupta et al. showed that SGA newborns had double the concentration of malondialdehyde as compared to AGA controls indicating significant oxidative damage that there is evidence of oxidative stress in SGA births as evidenced by increased lipid peroxidation (19). Dede et al. showed oxidative stress markers were increased while levels of antioxidant were decreased in SGA neonates when compared with normal weight newborn infants (20). Similarly Lindeman et al. studied the total radical trapping capacity of the antioxidants in plasma (TRAP) and compared the TRAP level in the preterm and term baby (cord blood) with that in adults. The concentrations of various known antioxidants were measured and the theoretical contribution of these antioxidants to the TRAP was calculated. They showed that measured and calculated TRAP were higher in the newborn babies than the adults (21).

Thiol-disulfide homeostasis is an essential for the antioxidant system. Oxygen bound thiols with many disulfide bonds are accepted to be a sign of oxidative stress (22). Since thiol/disulfide homeostasis is a novel, available, easily calculated and relatively cheap marker for oxidative stress, it was used to evaluate fetal oxidation and obstetric outcomes in pregnancies complicated by SGA in present study. We observed significant differences in thiol/disulfide homeostasis markers when the SGA and AGA fetuses were compared. Thiol/disulfide homeostasis was found to shift towards disulfide formation in SGA group. Higher levels of disulfide in umbilical cord blood of SGA newborns show that these babies suffered from lipid peroxidation and more pronounced oxidative stress than the AGA newborns. Our study has shown onset of oxidative stress during birth in SGA infants, as was observed already by other researchers using different analytical methods.

The weakness of our study were that it had a moderate patient number and not determine the number of coils with antenatal ultrasound. The strength of our study is that it is a prospective study and a single observer was involved, thus eliminating the inter-observer bias.

CONCLUSION

This is the first study on the association between thiol/disulfide balance and hypercoiling of the umbilical cord. In light of our findings, SGA newborns had altered thiol homeostasis in favor of oxidative stress. SGA newborns had increased frequency of hypercoiled cords. According to our results that there was no significant correlations between the hypercoiled umbilical cord and thiol/disulfide balance.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all parturient individuals and their spouses included in the study.

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This research did not receive and specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical issues: All authors declare originality of research.

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Determination of scatter radiation to the breast during lumbosacral x-ray examination using thermoluminescence dosimeter

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ABSTRACT

Objective: Exposure to ionizing radiation during radiographic examination is associated with some biological effects. The study was aimed to determine the amount of scatter radiation to the breast during lumbosacral x-ray examination.

Materials and Methods: The study was a prospective, cross-sectional study carried out among 60 women referred for Lumbosacral spine radiography from September 2019 to December 2019. Ethical approval was granted by the hospital ethical committee. A single-phase mobile X-ray unit was used to dispense the radiation while a thermoluminescent dosimeter (TLD) chip was used to measure the radiation dose. The TLD chip was attached to the peri-areolar region of the left breast and held in place by a transparent adhesive tape. The TLD was carefully enclosed in a black polythene sachet before and after the investigation to shield it from background radiation. After the investigation the TLDs were sent to the Centre for Energy Research and Training (CERT) for readout.

Results: The mean age and BMI of participants were 55.32 ± 12.35 years and $29.70 \pm 7.09 \text{ kg/m}^2$ respectively. The cumulative mean (\pm SD) ESD to the breast was $3.87 \pm 0.87 \text{ mGy}$. The highest scatter radiation dose was observed in the age group 60-69 years. Pearson's correlation showed a weak correlation between age and ESD.

Conclusion: The study showed that there were scatter radiations to the breast during lumbosacral X-Ray investigations which was lowest among the age group 50-59 years. No significant difference was seen between AP and lateral positions. The cancer risk was approximately 1 in 2,155 indicating that there might be a need to shield the breast while performing lumbosacral X-ray.

Keywords: Scatter Radiation, Breast, Lumbosacral X-Ray Thermoluminescence Dosimeter

INTRODUCTION

There are naturally occurring and man-made sources of radiation, with the latter being used largely for medical diagnosis and therapy (1). The exposure of man to radiation for medical practices arises from diagnostic and therapeutic procedures which constitute the largest component of radiation doses to the population from artificial sources (1). Since the discovery of x-ray in 1895, there has been a marked growth in the installation of x-ray machines and in the frequency of diagnostic x-ray examinations (2). Although radiation doses from fluoroscopy and computed tomography are much higher than that of x-ray (3), the main concern about patient dose relates to stochastic effects which have no threshold to induce cancer and hereditary changes (4).

Evidence abounds for radiation-induced cancer risks from exposure to x-ray in the course of diagnosis (5).

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Persons exposed early in life have high relative risks for cancers. Although the dose from the x-ray procedure is well below 10mSv which poses no challenge in deterministic effects, stochastic effects which can occur even with a low dose continue to present a challenge (6). Exposure to the minute amount of radiation has lifetime attributable risk to cancer which varies according to patient age and gender, with risk doubling in individuals 20years or younger and 2.22 times higher in women (7). These Dose increases have consequently raised concerns in the literature (1).

Therefore, the use of x-ray requires strict adherence to the principles of radiation protection to ensure that the risk to patients does not outweigh the benefit gained from the procedure (8). The international commission on radiological protection (ICRP (9)) is involved in radiation protection and has recommended that all medical exposures be subjected to radiation safety principles of justification, optimization and limitation (9). Optimization of patient protection requires that the magnitude of radiation doses be as low a reasonably achievable (ALARA) (9,10). One anatomical region often examined with high radiographic radiation doses is the lumbosacral spine because of its high anatomical density. Higher exposure settings and dense anatomical regions increase the tendency for scattered radiation (11).

The scatter radiation reaches the breast as entrance skin dose which could increase the risks of stochastic effects (11-13). Stochastic effects of radiation can be induced by any amount of radiation dose since it has no threshold. The breast, a high radiosensitive organ, often receives scattered radiation during x-ray examination of distant organs like the lumbosacral spine and head (12,13). Radiation exposure of the breast is the predominant factor in risk considerations since it contributes more than 98% to the effective dose of the thoracic region (12-14). At present, it is generally assumed that, with regard to cancer induction by ionizing radiation, the glandular tissue is the most vulnerable part of the breast. Glandular tissues trap scattered radiation to the breast (14).

Developing low-resource countries have faulty radiation protection culture, with most radiology facilities using older and secondhand equipment (15). Patient doses can be controlled through appropriate investigation of its quantity in order to predict risk, and thereafter recommending appropriate measures to reduce this risk.

Many researchers have estimated entrance surface dose and the absorbed dose to the breast using mammography locally, but none has estimated scatter radiation arising from lumbosacral examination, hence the need to determine the scatter radiation to the female breast during lumbosacral x-ray examination using thermoluminescence dosimeter. This will help to predict risks and guide the formulation of radiation protection policies as well as open more windows for research.

MATERIAL and METHODS

The study was a prospective, cross-sectional study carried out from September – December 2019, in the Radiology Department of Federal Medical Centre (FMC) Asaba, Delta State of Nigeria among 60 women who were referred to the radiology department for radiographic examination of the Lumbosacral Spine.

Ethical considerations

Ethical approval was granted by the hospital ethical committee of Federal Medical Centre Asaba Delta State. Signed informed consent was also obtained from every participant. Ambulant, adult female patients referred for lumbosacral x-ray examination without any history of preexisting breast lesion who granted consent participated in the study.

Taro Yamani formula as quoted by Uzoagulu (2011) (16), was used to calculate and obtain the sample size. A sample population of seventy (70) (17) being the number of female patients referred for lumbosacral radiography from September to December of the previous year was used to determine the sample population resulting in a sample size of sixty (60).

The sample size (n) was obtained using the equation below.

$$n = \frac{N}{1 + N(e)^2}$$

Where n = sample size

N= Sample population (known)

e = error limit/alpha value (5%; 0.05)

$$n = \frac{70}{1.175}$$

$$n = 59.57 \approx 60$$

Equipment: A single-phase mobile X-ray unit having a kilovoltage range of 40-150kVp (Table 1), was used for the study. The x-ray unit is adapted to radiographic couch and a stationary grid.

A thermoluminescent dosimeter (TLD) chip (TLD-100) with an active ingredient of Lithium-Fluoride, doped with Magnesium and Titanium (LiF: Mg, Ti) was used to measure the patients' entrance surface dose (ESD). All the TLD chips were annealed at the Centre for Energy Research and Training (CERT) in Kaduna, Nigeria, which is a Secondary Standard Dosimetry Laboratory (SSDL). The TLD chips were carefully enclosed in a black radiolucent polythene sachet before and after x-ray irradiation to shield them from background radiation.

Methods: Patients for lumbosacral x-rays were identified from the reception area using their radiological request forms. Before the commencement of the examination, the nature of the investigation was explicitly explained to the participants and an informed consent form was filled by each participant. Prior to the radiographic examination the patient's age (years), weight (kilogram) using a weighing balance and height (meters) were obtained. The weight and height were then used to calculate the BMI of participants.

The lumbosacral X-ray examination was done using a standard radiographic procedure based on patient weight and thickness. Each patient was in a supine position at a film-focus-distance (FFD) of 90 – 100 with a grid system in place. Two views involving anteroposterior (AP) and lateral were

obtained. The TLD chip was placed at the peri-areolar region (been the most central aspect) of the left breasts during the examination. Immediately after the exposures the TLD's were carefully removed and labeled with the patient's identity. The TLD's were then placed in a cellophane bag having the patient's identity written in the abbreviation for patient's confidentiality.

They were then placed inside a black bag in other to prevent the exposure of the TLD's to spurious background radiation and later sent to the radiation dosimetric laboratory of the Regional Centre for Energy Research and Training for reading.

The effective dose (E) arising from scatter radiation was calculated using the mathematical relation:

$$\text{Effective dose (E)} = \Sigma [\text{Tissue weighting factor (W}_T\text{)} \times \text{Equivalent dose (H}_T\text{)}] \quad (1)$$

The tissue weighting factor (W_T) was determined using the International Commission on Radiological Protection (ICRP) report 103 and the equivalent dose (H_T) was determined from the product of the absorbed dose and radiation quality factor for X-ray.

$$\text{Similarly, Equivalent dose (H}_T\text{)} = \text{Quality factor (Q)} \times \text{Absorbed dose (D}_T\text{)} \quad (2)$$

In this case the radiation quality factor (Q) for X-ray \equiv 1.

Method of data analysis: The data was analyzed with the aid of Statistical Package for Social Sciences (SPSS) version 20.0. The ESD values for the two views (antero-posterior and lateral) were collated and summed to obtain the cumulative ESD to the breast. Descriptive and inferential statistics were used in the data analysis. The relationship between parameters was accessed using Pearson's correlation method. Results were presented in tables. Statistical significance was to be set at $p \leq 0.05$.

RESULTS

The majority of the participants are within the age group 50-59years which accounts for 28.33%, followed by the age group 60-69years (26.67%), whereas 80 years and above were the least (1.67%) as shown in **Figure 1**. The mean (\pm SD) age and BMI of participants were 55.32 ± 12.35 years and 29.70 ± 7.09 kg/m² respectively (**Table 3**). However, concerning the BMI, age group 40-49years and 50-59years were obsessed, with a BMI of 31.78 ± 5.12 kg/m² and 31.65 ± 8.87 kg/m² respectively (**Table 3**).

The cumulative mean (\pm SD) scatter radiation reaching the breast was 3.87 ± 0.87 mGy but the lowest amount of scatter radiation was demonstrated among the age group 50-59years (3.62 ± 0.97 mGy) as also illustrated in table 2. According to **Table 3**, the mean ESD AP (mSv) was 2.20 ± 0.70 and the ESD Lat (mSv) was 1.70 ± 0.40 mSv. The mean exposure factor in respect to the kVp Lat was 78.00 ± 4.00 with a rand of 70 to 86 kVp while the mean mA AP 236.00 ± 29.00 with a range of 180 to 320.

A Pearson correlation analysis to ascertain statistical significance and strength of the relationship between Scattered radiation reaching the breast with age revealed that, there was no significant between scatter radiation and age ($p = 0.767$), while there was a weak relationship with a Pearson correlation coefficient of 0.039 ($r = 0.039$).

Similar findings were seen between scatter radiation with BMI (where the $p = 0.975$ and $r = 0.004$), showing no statistical significance and weak relationship (**Table 4**). The scatter plots show uneven distribution along the midline between age and breast effective doses as well as BMI and breast effective dose as shown in **Figure 2** and **3**.

A comparison of means for scattered radiation reaching breasts from antero-posterior and lateral dimensions was done using paired sample t-test. Results indicate that there was no significant difference in mean (**Table 5**). This is an indication that the direction of scattered radiation didn't influence the ESD.

As shown in table 6, the mean dose to the breast in the index study when compared with other related studies revealed that the result obtained in the present study was higher than that obtained in Slovenia, and United Arab Emirates (**Table 6**).

A One-Sample t-test shows that there was no statistically significant difference in the mean dose to the breast among the 4 studies that were compared ($P = 0.224$).

The lifetime risk of cancer incidence in this study was 4.5×10^{-4} and 5.2×10^{-4} (for HPA and ICRP 103 report respectively). When compared to the Health Protection Agency (HPA) and the ICRP 103 report, the risk was 1 in 2,155.56 for HPA and 1 in 2,153.85 for ICRP 103 report as demonstrated in **Table 7**.

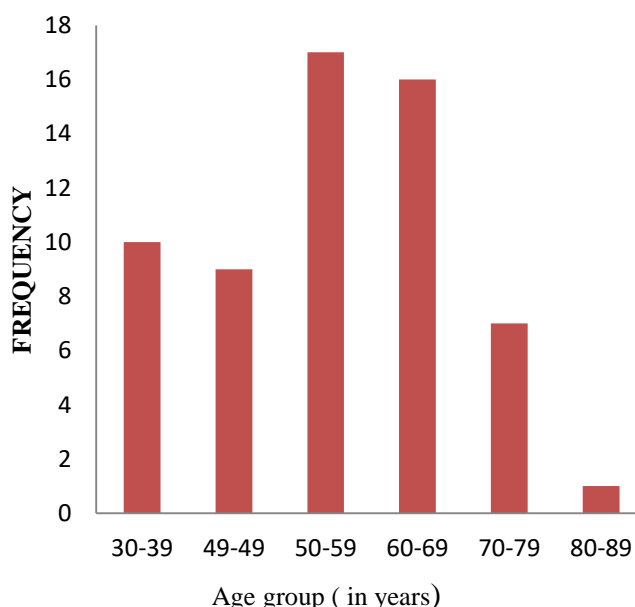


Figure 1: Age group distribution of participants

Table 1. Device specification

Mobile Radiography Device specifications	
Manufacturer	STEPHANIX
Type	Mobile Unit
Serial Number	8K1545
Machine Model	MOVIX 16 E ⁺
Power Capacity	32kW
kVp Range	40-150kVp
mAs Range	0.1-500mAs
Maximum Current	3.5-1.6A
Total Filtration	3.3mmAl
Focal Spot	1.0/0.3
Total Filtration	3.3mmAl
Line Voltage	110-240V
Phase	1, 50/60Hz
Target	Tungsten
Manufactured Date	September 2018

Table 2: showing the distribution of age BMI and ESD following age group classification.

Age Group	Frequency (N)	Age (Years)	BMI	Esdose (Mgy)
30-39	10 (16.67%)	35.90±3.04	28.66±4.95	3.76±0.74
49-49	9 (15%)	44.89±3.10	31.78±5.12	3.93±0.68
50-59	17 (28.33%)	55.76±2.56	31.65±8.87	3.62±0.97
60-69	16 (26.67%)	63.94±3.19	30.42±6.38	4.20±0.95
70-79	7 (11.67%)	72.14±2.67	23.24±5.67	3.70±0.80
80-89	1(1.67%)	80.00±0.00	22.10±0.00	4.67±0.00
TOTAL	60 (100%)	55.32±12.35	29.70±7.09	3.87±0.87

Table 3: Showing the minimum, maximum, Mean and Standard error of variables

Variable	n	Min	Max	Mean ± SD	SE Mean
Age (years)	60	31	80	55.30 ± 12.40	1.60
Weight (kg)	60	42	146	79.30 ± 20.00	2.60
Height (m)	60	1.45	1.77	1.61 ± 0.10	0.01
BMI (kg/m ²)	60	13.5	58.5	30.00 ± 7.10	0.92
ESD AP (mSv)	60	1.02	3.61	2.20 ± 0.70	0.09
ESD Lat (mSv)	60	1.02	2.80	1.70 ± 0.40	0.05
ESD Total (mSv)	60	2.22	5.73	3.87± 0.87	0.11
kVp AP	60	68	88	77.00 ± 4.00	0.52
kVp Lat	60	70	86	78.00 ± 4.00	0.53
mA AP	60	180	320	236.00 ± 29.00	3.80
mA LAT	60	175	320	214.00 ± 31.00	4.00
mAs AP	60	40	80	48.00 ± 9.00	1.20
mAs Lat	60	35	80	58.00 ± 10.00	1.32

Table 4: Showing Pearson Correlation of Scattered radiation with age and BMI

	Correlation	AGE	BMI	ESD
AGE	Pearson Correlation	1	.005	.039
	Sig. (2-tailed)		.967	.767
	N	60	60	60
BMI	Pearson Correlation	.005	1	.004
	Sig. (2-tailed)	.967		.975
	N	60	60	60
ESD	Pearson Correlation	.039	.004	1
	Sig. (2-tailed)	.767	.975	
	N	60	60	60

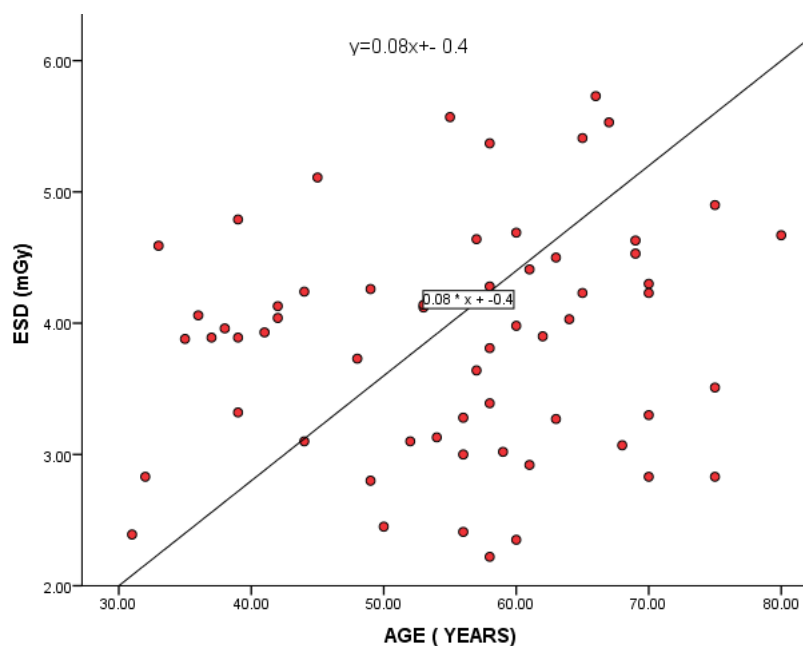


Figure 2: Scatter plot showing the distribution of scatter radiation reaching the breast in relation with age.

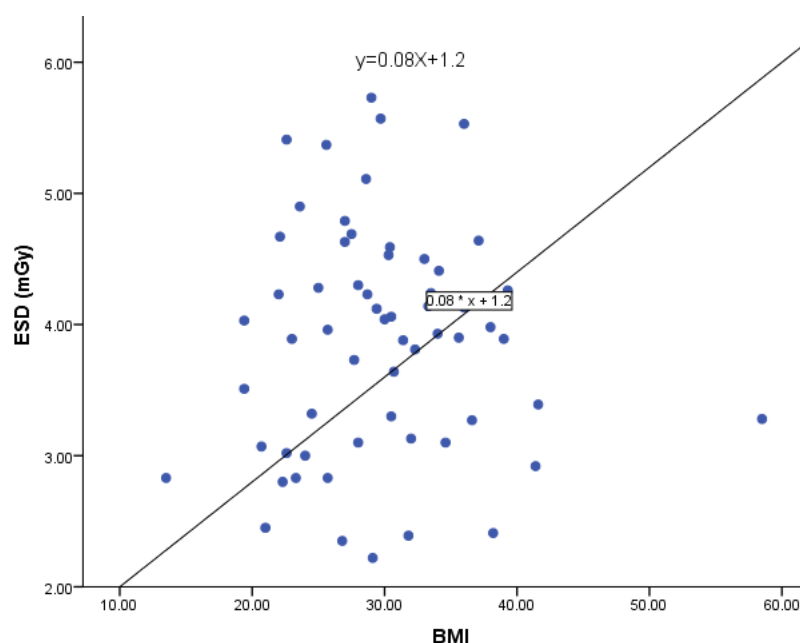


Figure 3: Scatter plot showing the distribution of scatter radiation reaching the breast in relation with BMI

Table 5. An independent sample t test to compare mean difference in scatters to breasts in AP and lateral dimensions

	Position	N	Mean \pm SD ESD (mSv)	t (Statistics)	p	Remarks (Distribution)
Independent Sample T-test	AP	60	2.20 \pm 0.70	0.738	0.462	No significant difference exists
	Lateral	60	1.70 \pm 0.40			

Table 6. Comparison of this study mean breast dose with other studies

Authors	Year	Detector/Patient type	Location	Mean ESD \pm SD (mGy)
Present work	2020	TLD/Real patients	Nigeria	3.87 \pm 0.87
Mekis et al	2013	TLD/Phantom	Slovenia	0.36 \pm 0.13
Elshami et al	2020	*Solid state /Phantom	UAE	0.0008 \pm 0.0003
Jecl et al	2015	**Solid state/Phantom	Slovenia	0.35 \pm 0.37

*The solid state detector used was a Piranha (RTI electronic AB, Sweden), ** solid state detector used was Unfors (Raysafe AB, Sweden)

Table 7. Lifetime risk of cancer incidence for the breast based on HPA and ICRP report

Report	lifetime risk of cancer incidence (%per Sv)
This study	4.5×10^{-4}
HPA (UK)	0.97
This study	5.2×10^{-4}
ICRP 103	1.12

DISCUSSION

Ionizing radiation exposure to the breast following radiographic investigation may vary significantly with reference to the type of examination, exposure factors, and patient habitus. The index study estimated scatter radiation doses to the breast from lumbar-spine X-ray examination (AP/lateral) using TLD chips was conducted using 60 participants. The mean (\pm SD) age of participants was 55.32 ± 12.35 years and the majority of the participants are within 50-59 years. One of the commonest investigations for patients presenting with low back pain (LBP) is the lumbosacral spine radiography (18). It can then be deduced that LBP is relatively commoner among patients within age group 50-59 years. This is closely in accordance with the finding in the study to assess various lumbosacral spine abnormalities which revealed that the peak incidence of low back pain (LBP) was in the fourth and fifth decade of life (19). The mean (\pm SD) scatter radiation reaching the breast was 3.87 ± 0.87 mGy but the lowest amount of scatter radiation was demonstrated among the age group 50-59 years (3.62 ± 0.97 mGy). This finding is higher than the values obtained by Mekis et al (20) where the ESD without a lead shield was 0.45 ± 0.25 mGy and 0.26 ± 0.14 mGy on the right and left breasts respectively. Factors like the type of the detector, FFD and field size may have contributed to the difference in variation. The index study is a real patient evaluation while the study by Mekis et al (20) was a phantom study. This may have caused the significant difference seen which is characterized by the scatter properties of both media (real patient and phantom). According to the International Commission on Radiological Protection (ICRP, 2017) (9), there is up to 30-40% in dose variation and uncertainty with the use of phantoms.

In another study to evaluate the efficacy and feasibility of breast shielding during abdominal fluoroscopic examinations with sixty-six women revealed that the mean radiation to the skin of the unshielded breast was 119 mR which is equivalent to 1.19 mGy (21). The value in their study (21) is also higher than that of the index study. The variation may be attributed to the kind of examination, the field of view and the exposure factors used. The mean dose to the breast in the index study when compared with other related studies also revealed that the result obtained in the present study was higher than that obtained in Slovenia and United Arab Emirates (20-23). A One-Sample t-test shows that there was no statistically significant difference in the mean dose to the breast among the 4 studies that were compared ($P = 0.224$).

The mean ESD (\pm SD) for the antero-posterior (AP) and lateral (Lat) views were 2.20 ± 0.70 mGy and 1.70 ± 0.40 mGy respectively. A comparison of means for scattered radiation reaching breasts from antero-posterior and lateral dimensions was done using paired sample t-test. Results indicate that there was no significant difference in mean.

This is an indication that the direction of scattered radiation didn't influence the ESD. The variation in ESD for lumbosacral X-ray for AP and lateral views was 18%, this was lower compared to a study by Elshami et al, 2020 (22), where the variation in ESD from cervical X-ray for AP and lateral positions was 34%. The reason for the difference may be due to the type of examination where their study (22) is cervical spine radiograph while the index study was a lumbosacral spine. It may also be attributed to the type of detector, FFD and field sizes that were used for the study.

There was no significant statistical relationship but there was a weak correlation between scatter radiation and age as well as scatter radiation and BMI, which was also evident by the uneven distribution in the scatter plot. The lifetime cancer risk in this study was compared to the Health Protection Agency (HPA) and the ICRP 103 report. The risk from this study was 1 in 2,155.56 for HPA and 1 in 2,153.85 for ICRP 103 reports. The study was subject to some limitation such as sizes of the breast, and only one breast was evaluated instead of the two, the exact mid-point of the breast could not be ascertained, and the field size for individual examination was not recorded. Notwithstanding the limitations, the study shows that there were scatter radiations to the breast during lumbosacral X Ray investigation.

CONCLUSION

The study shows that there were scatter radiations to the breast during the lumbosacral X-Ray investigation. The lowest amount of scatter radiation was demonstrated among the age group 50-59 years. The study also revealed that there was no difference in ESD when the patient lies in AP and lateral positions. The cancer risk was approximately 1 in 2,155 indicating that there might be a need to shield the breast while performing lumbosacral X-ray.

Recommendations: Based on the findings and conclusion from this study, the study recommends that patient bio-data and machine parameters should be properly documented for every procedure. This will ensure a dose audit and any point in time. The use of protective devices for lumbosacral X-ray is necessary as this will reduce the amount of radiation that reaches the breast with the need to optimize the lumbosacral protocol to reduce patient doses.

Author contributions: CEEE, CCN, EDR, ADO, TA, AAA: Study design and Literature search, Measurements and data collection, statistical analyzes EDR: Writing article and Revisions.

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discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all participant individuals and their spouses included in the study.

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical issues: All authors declare originality of research.

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Clinical significance of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in liver transplantation

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ABSTRACT

Objective: Liver transplantation has been reported to be a predictor of patient survival in acute coronary syndrome and various malignancies, including hepatocellular carcinoma (HCC). In a previous study, it was demonstrated that high Platelet-to-Lymphocyte Ratio (PLR) values before treatment are an independent prognostic factor predicting poor survival in patients with large HCC. We aimed to investigate whether preoperative neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and thrombocyte count are prognostic factors for post transplantation mortality or graft function in patients who underwent liver transplantation in the clinic.

Material and Methods: The data of 40 patients who underwent liver transplantation in the clinic during January 2018–December 2020 were retrospectively analyzed and included in the study.

Results: The mean age of the 40 patients included in the study was 51.1 ± 11.7 years. Of these, 27 (67.5%) were male, and 13 (32.5%) were female. Living-donor liver transplantation was performed in 33 patients, whereas cadaveric liver transplantation was performed in seven patients. The mean ejection fraction (EF) was $56.7\% \pm 3.2\%$, and the mean model for end-stage liver disease score was 22.4 ± 5.4 . After one year of follow-up, 10 out of 40 patients (25%) died after orthotopic liver transplantation. The mean preoperative neutrophil count was found to be $5.7 \pm 2.4 \times 10^9/l$ in non-surviving patients and $3.1 \pm 2.05 \times 10^9/l$ in surviving patients. It was found that mortality increased in patients with high preoperative neutrophil values ($NLR > 3.7$, $p < 0.001$) and preoperative platelet count ($< 79.52 \times 10^9/L$, $p < 0.001$).

Conclusion: Preoperative neutrophilia, thrombocytopenia and high NLR values may predict poor prognosis in patients undergoing OLT.

Keywords: liver transplantation, neutrophil-to-lymphocyte ratio, thrombocytopenia

INTRODUCTION

Liver transplantation in humans was first performed in 1963. Since then, orthotopic liver transplantation (OLT) is considered the only definitive treatment in patients with end-stage liver disease (1). In the USA and Western Europe, genetic disorders such as liver cirrhosis, alcoholic cirrhosis, hepatocellular carcinoma, or hemochromatosis due to viral hepatitis B or C are the main indications for OLT (2). In Turkey, liver cirrhosis due to viral hepatitis B (the most common cause) and due to hepatitis C, alcoholic cirrhosis, autoimmune diseases, Wilson's disease, Budd–Chiari syndrome, and cryptogenic liver cirrhosis are the main indications for OLT (3). According to the Unified Network for Organ Sharing, the 1-year and 5-year survival rates of patients who underwent OLT are 85% and 75%, respectively (4).

Neutrophil-to-lymphocyte ratio (NLR) has recently been reported as a simple and useful marker of various inflammatory changes and is calculated based on complete blood count data (5, 6). Increased neutrophils usually indicate that patients have a bacterial infection and that the infection is getting worse.

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Lymphocyte reduction means that immune function is poor (7, 8). It has been reported to be a predictor of patient survival in acute coronary syndrome and various malignancies, including hepatocellular carcinoma (HCC) (9, 10). In addition, it has been reported that high NLR value implies poor prognosis for acute–chronic liver failure after liver transplantation (11).

Platelets may play an important role in indicating post-transplant liver regeneration and dysfunction. Therefore, it has been suggested that platelet count in the acute phase of OLT is a prognostic factor for early post-transplant survival or graft function (12, 13).

Further, platelet-to-lymphocyte ratio (PLR) has recently been suggested to be a predictor of thrombotic and inflammatory conditions and therefore, to be an inflammation-related biomarker for tumors (14). In a previous study, it was demonstrated that high PLR values before treatment are an independent prognostic factor predicting poor survival in patients with large HCC (15). Moreover, PLR values have been shown to predict survival in ovarian, breast, and lung cancers (16–18).

OLT results were analyzed retrospectively in the organ transplant center. The usefulness of preoperative NLR, PLR values and platelet count in predicting prognosis was investigated.

MATERIAL and METHODS

Forty adult patients who underwent OLT at the organ transplant center between January 2018 and December 2020 were included in the study. After obtaining permission from the local ethics committee (Document Date and Number: 19.02.2021-12864), the patient files were retrospectively reviewed. The data of the recipients who underwent liver transplantation were accessed from the hospital information processing system, anesthesia records, intensive care nurse observations, and epicrisis records.

Patients' demographic data, cirrhosis etiology, comorbid diseases, ejection fractions (EF), Child–Pugh scores, model for end-stage liver disease (MELD) scores, and hematological parameters were analyzed. Hematological parameters such as the counts of leukocytes, neutrophils, lymphocytes, and platelets were recorded. NLR and PLR values were calculated based on the measured hematological parameters. Clinical events such as postoperative infectious complications, acute cellular rejection, or relaparotomy resulting in any surgical complications, durations of intensive care unit (ICU) and hospital stay, and mortality rates were analyzed retrospectively.

Anesthesia management

Patients who were admitted to the operating room were monitored using 12-lead electrocardiography, pulse oximetry, noninvasive blood pressure measurement, and bispectral index (BIS) monitoring. Anesthesia was induced with 3–5 mg/kg propofol, 1–2 µg/kg fentanyl, and 0.6 mg/kg rocuronium. After intubation, the patients were ventilated in a volume-controlled mode with breath volume of 8 mL/kg and respiratory rate of 10–12 breaths per min. Anesthesia depth was monitored using a BIS monitor, (Masimo SET® Rainbow, Masimo corp., Irvine, CA) and BIS score was

maintained between 40 and 60. Anesthesia was maintained with a mixture of oxygen/air containing an infusion of 2% sevoflurane, 0.1 mg/kg/h rocuronium, and 0.1–0.2 µg/kg/min remifentanyl. Warming blankets were used to prevent hypothermia. Intravenous fluids were warmed before administration (Hot Line® SIMS Medical System Inc, Rocklan, MA, USA; Fluido® Pressure Chamber, TSCI, Amersfoort, Netherlands). All patients were administered electrolyte solution and 6% hydroxyethyl starch for intravascular volume replacement. Depending on the degree of hypoalbuminemia (<3.0 g/dl), 20% human albumin solution was administered. In cases when the international normalized ratio was >1.5 and prothrombin time was >60 s, the patients were administered 10 ml kg⁻¹ fresh frozen plasma. Platelet suspension was given according to the platelet count (<50000). Erythrocyte suspension was administered to maintain hematocrit values between 25% and 30%. Noradrenaline (0.03–0.15 mcg/kg/min) was initiated if the cardiac index decreased to <2.5 L/min/m² or when the mean arterial pressure (MAP) decreased to <60 mmHg despite adequate fluid resuscitation. Diuretics were administered when oliguria persisted despite adequate fluid resuscitation and vasopressor use. If the mean urine output was <0.5 mL/kg/h, the patients were administered furosemide (0.5–1 mg/kg). If the serum calcium level was <8 mg/dl, patients were administered 10% calcium chloride.

Hemodynamic monitoring: After induction of anesthesia, the pulse co-oximetry probe (Masimo SET® Rainbow, Masimo corp., Irvine, CA) was preferably placed on the index finger of the left hand and covered to prevent the effect of ambient light. Perfusion Index and Pleth variable index (PVI) variables were automatically measured by connecting to the Masimo monitor (Masimo corp., Irvine, CA) installed with PVI software. A 4F-thermodilution catheter (Pulsioath®; Pulsion Medical System, Munich, Germany) was placed in the left femoral artery and connected to the PICCO2® system. A 3-lumen central catheter (20 cm, 7F) was placed in the right internal jugular vein or subclavian vein using Seldinger technique. Body mass index and body surface areas were determined by entering the age, height, and weight information of the patients into the system. With the transpulmonary thermodilution method, cardiac output, cardiac index, systemic vascular resistance index, and volumetric preload parameters were measured by injecting 15 mL of cold saline (at temperature ≤ 8°C) through the central venous line. Saline injections were performed by the same researcher, and the values were obtained by calculating the mean of three consecutive measurements. Besides these parameters, heart rate, MAP, central venous pressure, oxygen saturation, and temperature were monitored.

Surgical technique: For cadaveric liver transplantation, the entire cadaver liver was attached to the same location after the recipient's liver was removed. Hepatectomy was performed on the recipient following laparotomy with an inverted L-shaped incision. Anastomosis between the right and left hepatic veins of the cadaveric liver and the inferior vena cava was performed using the piggyback technique. Subsequently, anastomoses of the portal vein, hepatic artery, and bile duct were performed. Cadaveric liver grafts were prepared using histidine–tryptophan–ketoglutarate solution (Dr Franz Köhler Chemie GmbH, Bensheim, Germany). For living-donor liver

transplantation, the right lobe of the donor liver was attached to the recipient. Hepatectomy was performed in the recipient after the completion of laparotomy with an inverted L-shaped incision. Anastomosis between the right hepatic vein of the donor liver and the inferior vena cava was performed using the piggyback technique, followed by anastomoses of the portal vein, hepatic artery, and bile duct.

Statistical analysis: Statistical analyses of the data were performed using IBM SPSS 24.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). Whether the data showed normal distribution was examined by Shapiro–Wilk test. Mann–Whitney U test was used to compare the non-normal distributed data of two independent groups. Chi-square test was used to investigate the relationship between two categorical variables. P value of <0.05 was considered statistically significant.

RESULTS

The mean age of the 40 patients included in the study was 51.1 ± 11.7 years, of whom 27 (67.5%) were male, and 13 (32.5%) were female. Living-donor liver transplantation and cadaveric liver transplantation were performed in 33 and 7 patients, respectively. The demographic characteristics of these patients are presented in **Table 1**. The most common indication for OLT was liver cirrhosis due to hepatitis B virus (HBV) (57.5%), followed by cryptogenic liver cirrhosis (30%), liver cirrhosis due to hepatitis C virus (HCV) (7.5%), alcoholic liver cirrhosis (2.5%), and Wilson's disease (2.5%). The mean EF value and MELD score were $56.7\% \pm 3.2\%$ and 22.4 ± 5.4 , respectively. In addition, the mean duration of hospital stay was 14.8 ± 6.6 days, whereas that of ICU stay was 6.1 ± 2.8 days. Comorbid diseases of the patients were hypertension in 5 patients, diabetes mellitus in 5 patients, coronary artery disease in 4 patients, chronic obstructive pulmonary disease in 1 patient, and myxoma in 1 patient (**Table 1**).

In the study, 11 patients underwent relaparotomy after OLT 10 due to postoperative bleeding and 1 due to portal vein thrombosis. The patient who developed portal vein thrombosis underwent a second liver transplantation. The most common postoperative complication was bleeding. Biliary stenosis was detected in two patients, and endoscopic biliary drainage was applied to these patients.

After one year of follow-up, 10 out of 40 patients died after OLT (25%). The mean age of these patients was 52.7 ± 11.4 years. The mean MELD score of non-surviving patients was found to be 28.5 ± 4.1 . Mortality was higher in patients with higher MELD scores ($p = 0.011$). The mean preoperative neutrophil count was found to be $5.7 \pm 2.4 \times 10^9/l$ in non-surviving patients and $3.1 \pm 2.05 \times 10^9/l$ in surviving patients. It was found that mortality increased in patients with higher preoperative neutrophil counts ($p = 0.012$). The mean preoperative NLR was 6.8 ± 2.5 in non-surviving patients and 2.5 ± 1 in the surviving patients. The cut-off value of the preoperative NLR was >3.7 with sensitivity and specificity of 100.00% and 92.00% respectively (**Figure 1**). The mortality rate was higher in patients with preoperative NLR of >3.7 ($p = 0.025$). Mean preoperative platelet count was found to be $62.2 \pm 18.3 \times 10^9/l$ in non-surviving patients, and

$119.3 \pm 39.9 \times 10^9/l$ in surviving patients. Preoperative thrombocyte cut-off value was $<79.52 \times 10^9/l$ with sensitivity 88.89%, and specificity 96.00% (**Figure 2**). Preoperative thrombocytopenia was also found to be a sign of poor prognosis in patients who underwent OLT ($p = 0.047$). Mean preoperative PLR was found to be 78.3 ± 26.6 in non-surviving patients and 109.2 ± 40.9 in surviving patients. Decreased PLR was more common in non-surviving patients ($p = 0.062$), although the difference was not significant. The mean duration of surgery in non-surviving patients was 12.3 ± 1.1 h. It was found that prolonged operation time was associated with increased mortality ($p = 0.043$) (**Table 2**).

Mean EF in non-surviving patients was $57.2\% \pm 2.6\%$, and it was found to have no effect on mortality ($p = 0.616$). Mean preoperative hemoglobin values of non-surviving patients and surviving patients were 11.4 ± 1.5 g/dl and 10.7 ± 1.9 g/dl, respectively, whereas the respective mean preoperative leukocyte counts in non-surviving patients and surviving patients were found to be $7.1 \pm 2.3 \times 10^9/l$ and $5.9 \pm 4.8 \times 10^9/l$. Preoperative hemoglobin level and leukocyte count had no effect on mortality ($p = 0.335$, $p = 0.472$, respectively). Preoperative lymphocyte count was $0.9 \pm 0.3 \times 10^9/l$ in non-surviving patients and $1.2 \pm 0.6 \times 10^9/l$ in surviving patients. Preoperative lymphocyte count had no effect on mortality ($p = 0.077$).

Among non-surviving patients, 7 were diagnosed with HBV, 2 with HCV, and 1 with cryptogenic liver cirrhosis. Among the causes of death were multiple organ failure due to cell rejection in 5 patients, sepsis due to infection in 3 patients, portal vein thrombosis in 1 patient, and postoperative bleeding in 1 patient. No significant difference was found between the groups of non-surviving patients and survived after OLT in terms of their duration of ICU stay and hospital stay ($p = 0.321$, $p = 0.063$, respectively). Five of the non-surviving patients were re-operated for postoperative bleeding and one patient due to portal vein thrombosis. Mortality was found to be high in patients who were re-operated ($p = 0.016$). It was observed that the source of the grafts, living donor or cadaver, had no effect on mortality ($p = 0.888$) (**Table 3**).

Table 1. Demographic data of the patients

	Patient (n = 40)
Age (Mean \pm SD)	51.7 ± 11.7
Sex n (%)	
Male	27 (67.5)
Female	13 (32.5)
Comorbid diseases n (%)	
DM	5 (12.5)
HT	5 (12.5)
CAD	4 (10)
COPD	1 (2.5)
Myxoma	1 (2.5)
MELD (Mean \pm SD)	22.4 ± 5.4
Etiology n (%)	
HBV	23 (57.5)
Cryptogenic liver cirrhosis	12 (30)
HCV	3 (7.5)
Alcoholic cirrhosis	1 (2.5)
Wilson's disease	1 (2.5)
EF (Mean \pm SD)	56.7 ± 3.2

CAD: coronary artery disease, COPD: chronic obstructive pulmonary disorder, DM: diabetes mellitus, EF: ejection fraction HBV: hepatitis B virus, HCV: hepatitis C virus, HT: hypertension, M: Mean, MELD: model for end-stage liver disease, SD: Standard deviation

Table 2. Comparison of clinical data of surviving and non-surviving patients

	Surviving (n = 30) Mean \pm SD	Non-surviving (n = 10) Mean \pm SD	OR [95% CI]	p
Age (years)	50.6 \pm 12.1 /	52.7 \pm 11.4	1.02 [0.95 -1.09]	0.642
EF (%)	56.6 \pm 3.45	57.2 \pm 2.6	1.07 [0.83 -1.36]	0.616
MELD	19.8 \pm 3.2	28.5 \pm 4.1	1.93 [1.16-3.21]	0.011 *
Preoperative Hb (g/dL)	10.7 \pm 1.9	11.4 \pm 1.5	1.23 [0.81 -1.88]	0.335
Preoperative leukocyte ($\times 10^9/l$)	5.9 \pm 4.8	7.1 \pm 2.3	1.06 [0.9 -1.26]	0.472
Preoperative neutrophil ($\times 10^9/l$)	3.1 \pm 2.05	5.7 \pm 2.4	1.62 [1.11 -2.37]	0.012 *
Preoperative lymphocyte ($\times 10^9/l$)	1.2 \pm 0.6	0.9 \pm 0.3	0.17 [0.02 -1.21]	0.077
NLR	2.5 \pm 1	6.8 \pm 2.5	10.56 [1.34 -83.1]	0.025 *
Preoperative platelet ($\times 10^9/l$)	119.3 \pm 39.9	62.2 \pm 18.3	0.8 [0.64 -1]	0.047 *
PLR	109.2 \pm 40.9	78.3 \pm 26.6	0.97 [0.94 -1]	0.062
Duration of operation (h)	11 \pm 1.8	12.3 \pm 1.1	1.9 [1.02 -3.53]	0.043 *

EF: ejection fraction, Hb: hemoglobin, M: mean, Max: maximum, MELD: model for end-stage liver disease, Min: minimum, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SD: standard deviation. *Significant at 0.05 level; Binary logistic regression.

Table 3. Relationship of mortality with categorical variables

		Surviving (n = 30) n (%)	Non-surviving (n = 10) n (%)	p
Sex	Male	22 (73.4)	5 (50)	0.220
	Female	8 (26.6)	5 (50)	
Diagnosis	HBV	16 (53.4)	7 (70)	0.106
	Cryptogenic LC	11 (36.7)	1 (10)	
	HCV	1 (3.3)	2 (20)	
	Alcoholic LC	1 (3.3)	0	
	Wilson's disease	1 (3.3)	0	
Relaparotomy	Yes	5 (16.7)	6 (60)	0.016 *
	No	25 (83.3)	4 (40)	
Donor	Living	25 (83.3)	8 (80)	0.888
	Cadaver	5 (16.7)	2 (20)	

HBV: hepatitis B virus, HCV: hepatitis C virus, LC: liver cirrhosis, *Significant at 0.05 level; Chi-square test.

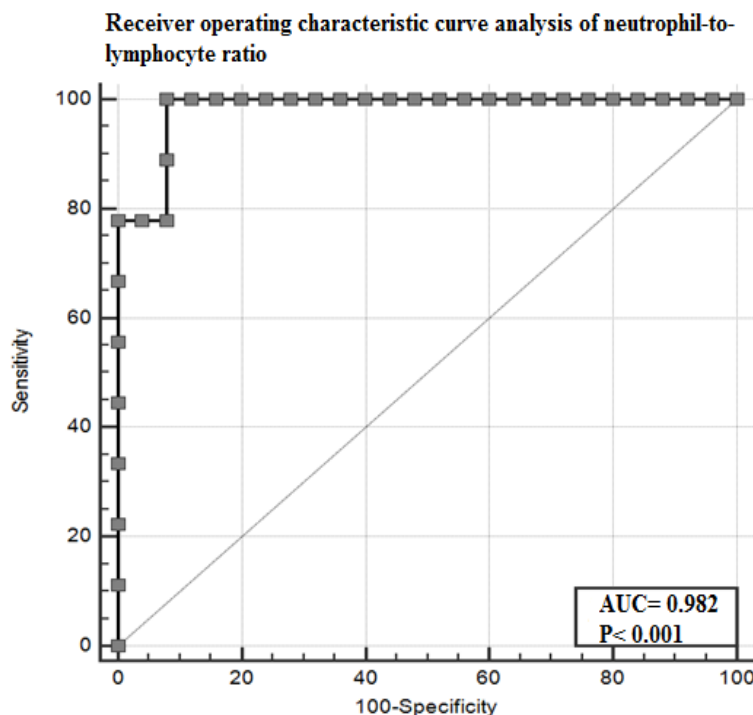


Figure 1: For the preoperative NLR value, it was found that AUC = 0.98 \pm 0.02 and p = 0.001. The recommended optimal cut-off point was >3.7. For values greater than this, sensitivity for mortality was 100% (95% CI = 66.4–100), and specificity was 92% (95% CI = 74%–99%). Sensitivity and specificity were found to be significant since these did not fall within the 50% CI. AUC: area under curve, CI: confidence interval, NLR: neutrophil-to-lymphocyte ratio

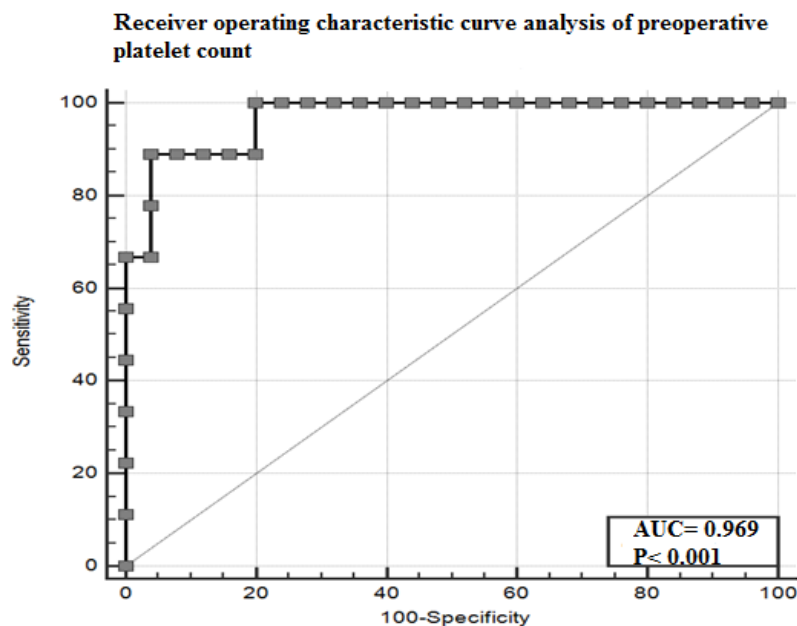


Figure 2: For the preoperative platelet value, it was found that $AUC = 0.97 \pm 0.03$ and $p = 0.001$. The recommended optimal cut-off point was ≤ 79.52 . For values less than or equal to this, sensitivity for mortality was 88.89% (95% CI = 51.8–99.7), and specificity was 96% (95% CI = 79.6%–99.9%). Sensitivity and specificity were found to be significant since these did not fall within the 50% CI. AUC: area under curve, CI: confidence interval

DISCUSSION

This retrospective single-center study investigated one-year graft and patient survival after OLT. Overall, 75% of the patients survived it was one year. It was found that preoperative neutrophilia, thrombocytopenia, and high NLR value correlated with poor prognosis and were successful in predicting mortality in patients who underwent OLT.

Ischemia-reperfusion injury (IRI) is a major cause of morbidity and mortality due to graft rejection after liver transplantation. It is responsible for 10% of early transplant failures (19, 20). During IRI, an intense inflammatory process occurs in the liver. Although this hepatic inflammation begins in the ischemic period, it mainly occurs during the reperfusion phase. Neutrophils are considered to be the main factor involved in the inflammatory process after reperfusion (21, 22). Studies have shown that elimination of increased neutrophils or inhibition of their functions leads to a decrease in liver damage and inflammation (23–25). In the study, the neutrophil count was $5.7 \pm 2.4 \times 10^9/l$ in non-surviving patients, and $3.1 \pm 2.05 \times 10^9/l$ in surviving patients. Consistent with the literature, a higher mortality rate was found in those patients with preoperative neutrophil elevation ($p = 0.012$) in the study.

Lymphopenia has been shown to be a prognostic marker for posttraumatic survival (26). Another study reported that lymphopenia is reported to be a simple prognostic factor for overall survival in patients with metastatic breast cancer, non-Hodgkin's lymphoma, and advanced sarcoma (27). Fernández-Ruiz et al. (28) found that pre OLT lymphocyte count can predict the incidence of infection during two years after OLT.

In the study, preoperative lymphocyte count was found to be $0.9 \pm 0.3 \times 10^9/l$ in non-surviving patients and $1.2 \pm 0.6 \times 10^9/l$ in surviving patients. In the study, a decrease in preoperative lymphocyte count was found to have no effect on mortality.

NLR has been proposed as a new biomarker for systemic inflammation, in which both neutrophil and lymphocyte counts are taken into account (29). Many studies have shown that NLR has a prognostic value in various conditions including sepsis, cardiovascular diseases, and malignant tumors (30–32). Normal NLR values range between 0.78 and 3.53 and are a simple parameter to easily assess a patient's inflammatory status (33). Further, NLR was reported to be an important parameter in predicting recipient prognosis after OLT (34). In the study, the preoperative NLR value was found as 6.8 ± 2.5 in non-surviving patients and 2.5 ± 1 in surviving patients. For the preoperative NLR value, the area under curve (AUC) according to receiver operating characteristic (ROC) curve analysis was found to be 0.98 ± 0.02 , and the corresponding p-value was 0.001. The recommended optimal cut-off point was >3.7 . For patients with values higher than the optimal cut-off points, sensitivity and specificity were 100% [95% confidence interval (CI) = 66.4–100] and 92% (95% CI = 74%–99%), respectively. Mortality was found to be higher in patients who underwent OLT with a preoperative NLR value of >3.7 .

It has been reported that there is a relationship between low platelet count and poor prognosis after OLT (35). Nobuoka et al. (36) reported that thrombocytopenia is the result of sinusoidal endothelial cell damage and decreased thrombopoietin production.

Han et al. (37) found that preoperative platelet count is an important host factor affecting HCC recurrence after living-donor liver transplantation. Platelets have an important role in liver regeneration and dysfunction after transplantation. Therefore, the platelet count in the acute phase of OLT is reportedly a good prognostic factor for survival or graft function after OLT (12). In the study, preoperative thrombocyte count was $62.2 \pm 18.3 \times 10^9/l$ in non-surviving patients, and $119.3 \pm 39.9 \times 10^9/l$ in surviving patients. For the preoperative platelet value, AUC was 0.97 ± 0.03 ($p = 0.001$) and the recommended optimal cut-off point was $\leq 79.52 \times 10^9/l$. For patients with values less than or equal to the optimal value, the sensitivity and specificity for determining mortality were 88.89% (95% CI = 51.8 - 99.7) and 96% (95% CI = 79.6% - 99.9%). Increased mortality was found in patients with preoperative platelet counts $\leq 79.52 \times 10^9/l$.

Recent studies have focused on the correlation of NLR and PLR with tumors. In colorectal cancer and cervical cancer, higher degrees of lymph node metastases have been reported in patients with high PLR (12, 38, 39). Xue et al. (40), observed that high PLR predicts poor prognosis in patients with HCC receiving trans arterial chemoembolization. In the study, the PLR values in non-surviving and surviving patients were found to 78.3 ± 26.6 and 109.2 ± 40.9 , respectively. PLR level was found to be higher in surviving patients. However, this difference was not significant in terms of mortality ($p = 0.062$).

MELD score is used as a scoring tool to assign priority levels to patients on liver transplant waiting lists. It can predict 3-month mortality risk with 83%–87% accuracy. The mortality of patients in waiting lists is directly proportional to the MELD score; a MELD score of <9 is associated with 2% mortality, whereas that of ≥ 40 is associated with a mortality of $\leq 71\%$ (41). Panchal et al. (42), retrospectively analyzed the data of 33,398 patients who underwent the transplant and found that 74% of the recipients had a MELD score of <30 , 18% had MELD score 30 - 39, and 8% had ≥ 40 . Consequently, they showed that overall patient survival was inversely proportional to increasing MELD score. In the study, mean MELD score was 22.4 ± 5.4 respective mean MELD scores of non-surviving and surviving patients were 28.5 ± 4.1 and 19.8 ± 3.2 . The findings were consistent with the literature, and the mortality rate was higher in patients with high MELD scores.

Olthoff et al. (43), examined the results of 385 cases of adult-to-adult living-donor liver transplant recipients in nine healthcare centers and found the mean duration of recipient operations to be 8.5 ± 2.1 h. A previous study in the country evaluated liver transplantation surgery data of 81 patients with end-stage liver disease, 16 of whom received cadaveric transplants, whereas 65 received living-donor transplants; mean operation time was reported as 7.15 ± 1.4 h (44). The mean operation time in the study was found to be 11 ± 1.8 hours, with the mean operation time of 12.3 ± 1.1 h in non-surviving patients. The results show that prolonged duration of the operation is associated with mortality.

The limitations of this study include its retrospective study design and low sample size since the center is a newly founded one.

CONCLUSIONS

Preoperative neutrophilia, thrombocytopenia and high NLR values may indicate poor prognosis in patients undergoing OLT. With these simple indices, high-risk patients can be identified and preventive measures can be taken.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Ethical Committee for Clinical Research of the Harran University (Document Date and Number: 19.02.2021-12864). All authors declare originality of research.

Informed consent: Informed consent was obtained from all parturient individuals and their spouses included in the study.

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Do we need to enlarge emergency services or new emergency hospitals?

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ABSTRACT

Objective: It was aimed to obtain a notion about the needed hospital bed capacity by analyzing the number of hospitalizations and referrals from the ER in this study.

Material and Method: This study is a retrospective, analytical cross-sectional research. Patients admitted to a tertiary hospital's adult emergency service in 2018-2019, hospitalized, or referred to another hospital were analyzed.

Results: Of the patients, 28036 were hospitalized; furthermore, this number corresponded to 38.4 patients per day. Of these cases, 15303 (54.6%) were male, and the mean age was 57.89 (± 19.5); 8438 cases (30.1%) were admitted to the intensive care unit. The department with the most hospitalizations was internal medicine with 6105 patients (21.78%) and cardiology, with 4822 hospitalized, the most intensive care patients; moreover, psychiatry had the most prolonged length of stay service average of 28 days. The number of patients required to be hospitalized from the emergency room was an average of 48.5 patients per day. The average hospital stay was seven days.

Conclusion: Mainly in regions with several emergency admissions, it can be considered to establish emergency hospitals that serve particularly emergency cases to engage the number of patients to be hospitalized from the emergency room.

Keywords: Emergency Room, Hospital, Admission

INTRODUCTION

Emergency services are one of the departments where most patients are examined among the hospital units. According to the National Center for Health Statistics report, several emergency service visits were 130 million (40% of all population) throughout 2018 in the USA, 12.3% of the patients who applied to the USA's emergency department were hospitalized; moreover, 2.3% of them were referred to another hospital (1). According to the Republic of Turkey Ministry of Health data, the just government hospital examination in 2017 was over 90 million in the emergency room; furthermore, this was over 112% of Turkey's population (2).

It is inevitable to undergo density in emergency services where so several cases admit. One of the critical reasons for the emergency services' intensity is that the patients continue to stay in the emergency department due to the lack of suitable empty beds, although the patient's emergency room process is over. It has been reported that each surgical case hospitalized increases the waiting period in the emergency department (3). Also, the decrease in the number of discharges contributes to the emergency department's density, reducing the bed capacity (4). The hospital beds are filled with patients hospitalized from the emergency and elective from the polyclinics (5). Therefore, hospital occupancy causes an increase in emergency room density. The emergency services' density, on the other hand, spreads not only the hospital but also the waiting time of the ambulances, generating the entire emergency health system to be adversely affected. Seeking the solution to expand the emergency service might not present the assumed advantages (6).

The increase in the number of emergency admissions brings together the rise in hospitalizations from the emergency department, necessitates the discussion of whether there are sufficient beds in hospitals.

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Reducing the number of unnecessary patients applying to the emergency department may decrease the emergency department's density. However, it can be thought that people with poor health conditions who need to be hospitalized will continue to apply to the emergency department, and as a result, hospitalizations from the emergency department will continue. Therefore, it is essential to examine hospitalizations and referrals from the emergency department.

It was aimed to contribute to the current medical literature and to obtain a notion about the needed hospital bed capacity by analyzing the number of hospitalizations and referrals from the ER in this study. Thus, the answer to the question asked in the title of the article was endeavored.

MATERIAL and METHODS

Research Type: This study is a retrospective, analytical cross-sectional research.

Definitions: While categorizing the branches in the research, each branch's sub-branch was included in the primary department. Data belonging to general surgery sub-branches such as surgical oncology and gastroenterological surgery were combined with the general surgery branch. The data of hematology, endocrinology, gastroenterology, medical oncology, nephrology, and rheumatology sub-branches were affixed to the internal medicine department's data.

Departments such as otorhinolaryngology, ophthalmology, physical therapy and rehabilitation, and dermatology departments, which the emergency service infrequently consults patients, are assorted under the name of "other branches".

Gynecological oncology data has been included in the gynecology department. The palliative service, which admits patients from the intensive care unit, has been accepted as the anesthesia department's ward.

Inclusion Criteria: Patients aged 18 and over who applied to Sakarya Training and Research Hospital Adult Emergency Service between 01.01.2018-31.12.2019 and were admitted to the hospital's service and intensive care units were included in the research. Moreover, patients who were referred from the adult emergency room to another hospital due to the lack of patient beds were also included in the research.

Exclusion Criteria: Pregnant cases, patients younger than 18 years old, patients admitted to other hospital units, patients with incomplete files were eliminated from the study. The patients left the emergency service by their means, and those who refused treatment were excluded from the study.

Data Collecting: The gender, age, intensive care admission status, the total length of stay in the intensive care unit, wards, and hospital, the departments' name in which the patients were admitted from the emergency department, the mortality data of the patients in the service or intensive care unit were obtained from the patient files and the hospital automation system. Data on patients referred from the SEAH adult emergency department to another hospital due to bed insufficiency was collected.

Statistical Analysis: The data acquired were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) version 21 program. Skewness and Kurtosis values were

required to be in the range of $-2/+2$ for the data's normal distribution (1). Chi-square test was used for comparison of categorical data, and results with $p < 0.05$ were recognized as statistically meaningful. The Mann-Whitney U test was used to compare two independent data groups that were not normally distributed, and the Kruskal Wallis Test was used to analyze more than two independent data groups and results with $p < 0.05$ were regarded significant.

Permission: Approval was obtained from Sakarya Training and Research Hospital Chief Physician's Office on 12.02.2021. Ethical approval was obtained from Sakarya University Medical Faculty, Date: 02.03.2021, No: E71522473-050.01.04-15144-147.

RESULTS

During the research period, the number of examinations performed in the adult emergency department was 762919. The rate of all hospitalizations from the emergency room to the hospital was 3.7%, the rate of admission to intensive care was 1.1%, and the rate of referral from the emergency service to another hospital was 1%. Of the patients, 28036 from the SEAH adult emergency room were hospitalized; furthermore, this number corresponded to 38.4 patients per day. Of these cases, 15303 (54.6%) were male, 12733 of them (45.4%) were female, the mean age was 57.89 (± 19.5), the median age value was 61, and the age range was 18-106.

Of these patients, 8438 cases (30.1%) were hospitalized from the emergency room to the intensive care unit. The department with the most maximum hospitalizations was internal medicine, with 6105 patients (21.78%). The cardiology, with 4822 hospitalized the most patients in intensive care. This number was 17.2% of all emergency hospitalized patients and corresponded to 57.15% of all intensive care hospitalizations. The anesthesia department, which followed 95.7% of its patients in intensive care, had the highest intensive care patients rate.

Considering the mortality status, that was determined that the internal medicine department had the highest number of deaths with 1137, and the anesthesia department had the highest mortality rate, with 70.3%. See **Table 1** for gender, intensive care hospitalization, and mortality status of all departments.

Psychiatry had the most prolonged length of stay in service with an average of 28 days (median 24 days), while the most extended hospitalization time in the intensive care unit belonged to the anesthesia with an average of 24 days (median 11 days). See **Table 2** for the patients' service and intensive care stay periods according to all departments.

Looking at the statistical analysis: There was a significant discrepancy in mortality between the genders; furthermore, 12.8% of men and 10.8% of women died ($p=0.001$). There is a meaningful distinction between genders and intensive care unit admission, with 35.3% of men and 23.8% of women accepted to intensive care ($p=0.001$). There was also a notable variation among genders and hospitalized departments ($p=0.001$). While women were hospitalized more in psychiatry, gynecology, and internal medicine branches, men were hospitalized increased in all other units.

Table 1. Distribution of patients according to the branches

	Gender					ICU State ¹					Mortality Status ²			
	Male		Female		Total	No		Yes		Count	Alive		Ex	
	Count	% ³	Count	% ³		Count	% ³	Count	% ³		Count	% ³	Count	% ³
Internal medicine	2960	48.5%	3145	51.5%	6105	5095	83.5%	1010	16.5%	4968	81.4%	1137	18.6%	
Cardiology	3899	68.5%	1791	31.5%	5690	868	15.3%	4822	84.7%	5087	89.4%	603	10.6%	
General surgery	1958	56.1%	1532	43.9%	3490	3129	89.7%	361	10.3%	3193	91.5%	297	8.5%	
Neurology	1669	51.4%	1580	48.6%	3249	2608	80.3%	641	19.7%	2898	89.2%	351	10.8%	
Orthopedics	1371	58.2%	984	41.8%	2355	2031	86.2%	324	13.8%	2199	93.4%	156	6.6%	
Gynecology	0	.0%	1823	100.0%	1823	1803	98.9%	20	1.1%	1817	99.7%	6	.3%	
Pulmonology	989	60.7%	639	39.3%	1628	1015	62.3%	613	37.7%	1284	78.9%	344	21.1%	
Thoracic surgery	771	78.2%	215	21.8%	986	863	87.5%	123	12.5%	928	94.1%	58	5.9%	
Others branches	587	72.1%	227	27.9%	814	779	95.7%	35	4.3%	764	93.9%	50	6.1%	
Infectious Diseases	384	50.1%	383	49.9%	767	686	89.4%	81	10.6%	685	89.3%	82	10.7%	
Neurosurgery	349	69.0%	157	31.0%	506	399	78.9%	107	21.1%	431	85.2%	75	14.8%	
Psychiatry	106	46.9%	120	53.1%	226	222	98.2%	4	1.8%	222	98.2%	4	1.8%	
CVS ⁴	151	71.2%	61	28.8%	212	92	43.4%	120	56.6%	173	81.6%	39	18.4%	
Anesthesia	109	58.9%	76	41.1%	185	8	4.3%	177	95.7%	55	29.7%	130	70.3%	
Total	15303	54.6%	12733	45.4%	28036	19598	69.9%	8438	30.1%	24704	88.1%	3332	11.9%	

¹The patient's state of admission to intensive care from the emergency department²Mortality status after hospitalization from the emergency department, before discharge from the hospital³Percentage in the relevant branch⁴Cardiovascular surgery**Table 2.** Patients' duration of hospitalization according to the branches

Branches	Length of Stay in Service			Length of Stay in ICU			Total Length of Stay in Hospital		
	Count	Mean	Median	Count	Mean	Median	Count	Mean	Median
Anesthesia	8	9	11	177	24	11	185	25	12
Neurosurgery	399	3	2	107	11	4	506	6	3
Infectious Diseases	686	7	6	81	9	5	767	8	6
General surgery	3129	4	3	361	6	3	3490	5	3
Thoracic surgery	863	7	5	123	4	2	986	8	6
Pulmonology	1015	9	8	613	11	6	1628	12	8
Internal medicine	5095	5	3	1010	8	4	6105	6	4
Gynecology	1803	3	2	20	9	1	1823	3	2
Cardiovascular surgery	92	15	5	120	4	2	212	13	5
Cardiology	868	4	3	4822	3	2	5690	5	3
Neurology	2608	6	5	641	14	5	3249	8	5
Orthopedics	2031	7	5	324	7	3	2355	8	6
Psychiatry	222	28	24	4	17	3	226	28	24
Others branches	779	5	3	35	3	2	814	5	4
Total	19598	5.4	4	8438	6	2	28036	7	4

Table 3. Patients' statistics

	Service Duration	ICU Duration	Total Duration	Gender	ICU Status ¹	Mortality ²	Branches
Gender	p=0.163 ^a	p=0.001 ^a	p=0.001 ^a	N/A	p=0.001 ^b	p=0.001 ^b	p=0.001 ^b
ICU Status	N/A	N/A	p=0.001 ^a	p=0.001 ^b	N/A	p=0.001 ^b	p=0.001 ^b
Mortality	p=0.001 ^a	p=0.001 ^a	p=0.001 ^a	p=0.001 ^b	p=0.001 ^b	N/A	p=0.001 ^b
Branches	p=0.001 ^c	p=0.001 ^c	p=0.001 ^c	p=0.001 ^b	p=0.001 ^b	p=0.001 ^b	N/A

^aMann-Whitney U test results^bPearson Chi-Square test results^cKruskal Wallis test results¹The patient's intensive care unit admission²Mortality status of the patient

A critical relationship was found between mortality and hospitalization in intensive care ($p=0.001$). While 7% of the cases who were not admitted to the intensive care unit died, 23.1% of the patients hospitalized in the intensive care unit died. A significant deviation was found within mortality and departments ($p=0.001$). Thus, anesthesia was perceived to have the most extraordinary mortality rate with 70.3%, pulmonology 21.1%, internal medicine 18.6%, cardiovascular surgery 18.4%.

While gender had no significant impact on hospital stay duration ($p=0.163$), it was observed that it significantly influenced intensive care duration and total days of hospital stay ($p=0.001$).

Hence, men stayed in the intensive care unit and hospital for a more sustained whole time.

Staying in intensive care had a stimulating effect on the whole hospitalization days ($p=0.001$); moreover, the total length of stay in the intensive care unit was prolonged. See **Table 3** for statistical outcomes.

The referring from the emergency department cases' number was 7391 due to insufficient hospital bed capacity. This situation confirmed that an average of 10.1 patients per day was referred to another hospital. It was ascertained that the branch where the highest number of patients were transferred from the emergency department was cardiology, with 2372 cases. See **Table 4** for patient referral data.

Table 4. Adult patient referrals from the emergency department to other hospitals

Branches ¹	Median Age	Referrals From Emergency Room		Total Count
		Male Count	Female Count	
Anesthesia	74	139	123	262
Neurosurgery	58	117	100	217
Infectious Diseases	76	112	146	258
General Surgery	33	258	144	402
Thoracic Surgery	55	22	8	30
Pulmonology	75	698	498	1196
Internal Medicine	72	518	598	1116
Cardiovascular Surgery	56	11	6	17
Cardiology	69	1306	1066	2372
Neurology	72	545	606	1151
Orthopedics	51	66	27	93
Psychiatry	37	165	31	196
Others Branches	39	32	8	40
Emergency Medicine	72	22	19	41
Total	70	4011	3380	7391

¹The branch of the physician decides to refer the patient from the emergency department to another hospital.

Table 5. Number of patients required to be hospitalized

Branches	Referral Count ¹	Inpatient Count ²	Total Count ³	Number Per Day ⁴
Anesthesia	262	185	447	0.6
Neurosurgery	217	506	723	1
Infectious Diseases	258	767	1025	1.4
General Surgery	402	3490	3892	5.3
Thoracic Surgery	30	986	1016	1.4
Pulmonology	1196	1628	2824	3.9
Internal Medicine	1116	6105	7221	9.9
Cardiovascular Surgery	17	212	229	0.3
Cardiology	2372	5690	8062	11
Neurology	1151	3249	4400	6
Orthopedics	93	2355	2448	3.4
Psychiatry	196	226	422	0.6
Gynecology	0	1823	1823	2.5
Others Branches	40	814	854	1.2
Emergency Medicine	41	0	41	0.1
Total	7391	28036	35427	48.5

¹ Number of patients transferred from the emergency department to another hospital

² Number of patients hospitalized from the emergency department

³ Total number of patients requiring hospitalization from the emergency department

⁴ Average number of patients that should be hospitalized from the emergency department per day

Briefly, when the number of patients required to be hospitalized from the emergency room was checked, it was remarked that the cumulative number of cases who were hospitalized and referred from the emergency room was 35427. This number corresponds to an average of 48.5 patients per day. See **Table 5** for a summary of patients requiring the hospitalization.

DISCUSSION

Sultanoglu et al. (7) reported that 6318 (8.4%) of the patients who applied to a tertiary hospital's emergency service within one year were hospitalized, and 0.4% were referred. Erkurun et al. (8) reviewed the emergency room patients and noticed that 2380 of these patients (1.2%) were hospitalized to ICU from the emergency department, and 66 of them (2.8%) died in ICU. On the other hand, Groenland et al. (9) reported that 18.1% of the cases hospitalized from the emergency department to the intensive care unit died. Furthermore, the hospitalization period's prolongation from the emergency department to the ICU was associated with increased patient mortality.

Simpson et al. (10) stated that 26% of the patients hospitalized in intensive care were hospitalized from the emergency room, and the mortality rate could stretch to 46.4% among them.

The medical literature studies reported the density of emergency services and their destructive effects on receiving emergency medical care. Niels et al. (3) found that elective surgical operations and hospital occupancy harmed patients' waiting time in the emergency department. Sun et al. (11) stated that more sick cases were admitted to the emergency department on weekends. Besides, Peter et al. (5) reported that discharge from the hospital on weekends was 50% less than on weekdays. This situation presents us with more severe patients and fewer hospital beds. Emilie et al. (4) similarly stated that patients' discharge from the hospital services reduces emergency room overcrowding.

When all these above researches are assessed together;

In this study, the average number of patients requiring daily hospitalization from the ER was 48.5, and the average hospital stay of all patients hospitalized from the emergency

department was observed to be seven days. Thus, approximately 340 patient beds should be reserved for the patients hospitalized in the emergency department to evade hospital occupancy. Besides, these numbers do not include the patients hospitalized from the pediatric emergency and obstetrics emergency services. Considering that the number of emergency service admissions has risen every year, the number of beds required to suffice the ER hospitalizations suggests that an “emergency hospital” is required separately. Here, an emergency hospital is meant to be a hospital structure where elective hospitalization is not admitted, and all branches work for emergency patients. An increase in the emergency service admissions and the inpatients’ numbers obstruct managing emergency services and elective services together, primarily in regions where emergency admissions are intense. In this case, we will come across two options:

Firstly, emergency hospitalizations will interrupt several elective treatments and operations planned before, and these patients will be disrupted due to the continuous hospitalization of patients from the emergency room. Secondly, the patients who require several urgent interventions will be referred to another hospital or wait for hospitalization in the emergency department while the elective cases are hospitalized. Researches in the current medical literature have also determined that elective patients’ admissions increase the length of stay in the emergency room. The prolongation of the emergency department’s stay will negatively affect the medical care that patients will receive.

The branches with the highest number of hospitalizations from the ER are internal medicine, cardiology, general surgery, neurology, orthopedics, gynecology, and pulmonology; moreover, these have the highest patient rate referred to other hospitals. It is perceived that hospitals should have adequate service and intensive care beds for these branches to provide adequate health care from the ER. Unfortunately, these departments are among the main branches with many outpatients; elective hospitalizations from polyclinics will be confronted with hospitalizations from the ER.

CONCLUSIONS

The number of emergency service admissions increases worldwide and patients hospitalized from the emergency department has a unique place among all inpatients. Mainly in regions with several emergency admissions, it can be considered to establish emergency hospitals that serve particularly emergency cases in order to engage the number of patients to be hospitalized from the emergency room, to prevent unnecessary waiting and intensity in emergency services, and to decrease the referring patients to another hospital. Oppositely, either emergency treatment services or elective treatment procedures may be obstructed.

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A rare cause of breast masses in childhood: ALK positive anaplastic large cell lymphoma

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ABSTRACT

Objective: Non-Hodgkin's lymphomas (NHLs) are the result of malign proliferation of lymphoid cells. According to the morphological, immunological and genetic characteristics of childhood NHLs, they are classified as Burkitt lymphoma (BL), Lymphoblastic lymphoma (LL), diffuse large B-cell lymphoma (DLBCL) and anaplastic large cell lymphoma (ALCL). Anaplastic large cell lymphoma is a distinct form of non-Hodgkin lymphoma (NHL) which accounts for 15% of all childhood lymphomas. We report a girl presented with a breast mass and diagnosed with systemic ALCL.

Case: A 14-year-old girl was referred to our hospital with without a painless mass in the left breast. Physical examination, it was seen two painless mass was found in the left breast. Also, a 2x2 cm, painless lymphadenopathy was found in the left axilla. She had no systemic symptoms In laboratory tests; hemoglobin, white blood cell count, platelet count, liver and kidney function tests, LDH, and uric acid levels were normal. In the imaging and metastasis screenings made to the patient; ultrasound and computed tomography (CT) showed two masses breast region. A large number of lymphadenopathies were detected in the left axillary, which surrounded the paraaortic, the paracaval, and the celiac truncus. She was found to have a hypermetabolic two masses in the breast (SUVmax=33.05) and lymphadenopathies (SUVmax=27.04) in the left axillary, paraaortic, the paracaval, and the celiac truncus on Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) scan. Excisional biopsy of the tumor mass in the breast was done and immunohistochemical analysis showed CD30 and anaplastic lymphoma kinase (ALK) positive ALCL. The patient was diagnosed with stage III anaplastic large cell lymphoma with systemic involvement and she began chemotherapeutic treatment, according to the NHL BFM 1995 protocol. Bone marrow aspirate was normal, and no malignancy was observed in the cerebrospinal fluid. After V-phase, AM block, and BM block treatments evaluation were performed with ¹⁸F-FDG PET/CT according to protocol. In ¹⁸F-FDG PET/CT, it was seen that the lymph nodes in the abdominal and the small mass in the breast were completely retracted, and another lymph nodes had no detected. These results showed that the response to the treatment was complete and the patient's chemotherapy was completed by continuing with the protocol. ¹⁸F-FDG PET/CT taken after the completion of chemotherapy revealed no evidence of mass or lymph node. The patient's controls continue smoothly.

Conclusions: Anaplastic large cell lymphoma should also be considered in the differential diagnosis of children presented with a breast mass. Treatment procedures should be planned according to the involvement site and spread of the disease.

Keywords: Children, Breast, anaplastic large cell lymphoma

INTRODUCTION

Non-Hodgkin's lymphomas (NHLs) are the result of the malign proliferation of lymphoid cells. Malignant lymphomas although usually seen in lymphoid structures such as lymph nodes, Peyer's patches and spleen, can involve the central nervous system, bone marrow and bone. Constitutes for 8-10% of all childhood malignancies and 60% of all lymphomas (1).

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According to the morphological, immunological and genetic characteristics of childhood NHLs, they are classified as Burkitt lymphoma (BL), Lymphoblastic lymphoma (LL), diffuse large B-cell lymphoma (DLBCL) and anaplastic large cell lymphoma (ALCL) (2). Anaplastic large cell lymphoma is a distinct form of non-Hodgkin lymphoma (NHL) which accounts for 15% of all childhood lymphomas. Anaplastic large cell lymphoma is a T or null cell lymphoma characterized by the malignant cell expression of CD30 (Ki-1) (3). The World Health Organization divides ALCL into a systemic form and a primary cutaneous form (4). Systemic ALCL is more common than the cutaneous form and most frequently occurs in the first three decades of life. Clinically, systemic ALCL is characterized by advanced disease at presentation with a high incidence of nodal involvement, frequent association with B symptoms, and frequent extra-nodal involvement including skin, lung, bone and liver (5). Breast involvement of ALCL in children has not been previously reported in the English literature. We report a girl presented with a breast mass and diagnosed with systemic ALCL.

CASE

A 14-year-old girl was referred to our hospital with about 2-month history of a growing over time without painless mass in the left breast. She was informed that an excisional biopsy was performed at the center she referred to. During the physical examination, it was seen that the left breast was bigger than the right, an 8x5 cm sized, hard, mobile, and painless mass was found in the region of the left breast covering the lateral and middle region (**Figure 1**).

In addition, the 2x2 cm dimensions of the second mass was palpated which have the same properties as the first mass in the sublateral region. A 2x2 cm, painless, moderately hardened lymphadenopathy was found in the surrounding areas of the left axilla. Hepatosplenomegaly in the case was not detected. She had no specific history including drug or family history. She showed no systemic symptoms such as fever, weight loss or night sweating. Her vital signs were stable and were within the normal range (blood pressure, 100/55 mmHg; heart rate, 96 beats/minute; respiratory rate, 26 breaths/minute; body temperature, 36 C°).

In laboratory tests; Hemoglobin: 14.8 gr/dl, white blood cell count: 6240 / mm³, platelet count: 347000 / mm³, liver and kidney function tests, LDH and uric acid levels were normal. In the imaging and metastasis screenings made to the patient; ultrasound and computed tomography (CT) showed two masses measuring 74x56 and 30x17 mm in the middle and lateral breast region. A large number of lymphadenopathies were detected the largest 25x25 mm size in the left axillary, that surrounded the paraaortic, the paracaval, and the celiac truncus. She was found to have a hypermetabolic two masses in the breast (SUVmax=33.05) and lymphadenopathies (SUVmax=27.04) in the left axillary, paraaortic, the paracaval, and the celiac truncus on Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) scan.

It was learned that the fine needle biopsy was performed at the external center and it was reported as malignant cytology, followed by excisional biopsy. Excisional biopsy of the tumor mass in the breast showed frequent mitoses and pleomorphic atypical cells with vesicular chromatin, prominent nucleoli, and pale cytoplasm (**Fig. 2a**).

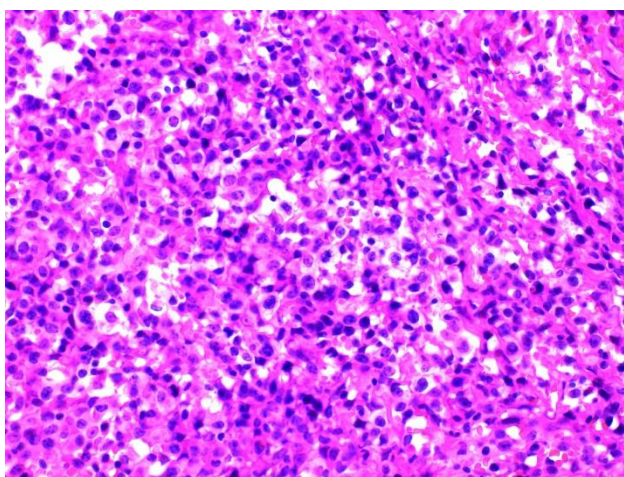


Figure 2a: Neoplastic lymphoid cells, frequent mitoses and pleomorphic atypical cells with vesicular chromatin, prominent nucleoli, and pale cytoplasm. (HE)

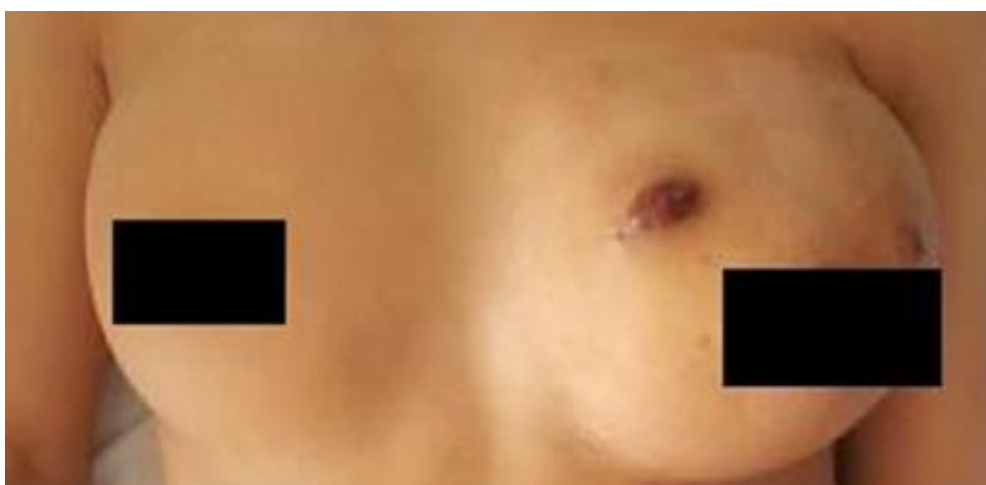


Figure 1: Mass in the region of the left breast covering the lateral and middle region

Immunohistochemical analysis showed the neoplastic cells were positive for CD30 (**Fig. 2b**), anaplastic lymphoma kinase (ALK) (**Fig. 2c**), CD43, CD4 and CD7. Stains were negative for CD20, CD15, CD2, CD3, CD5, CD8, and EBV.

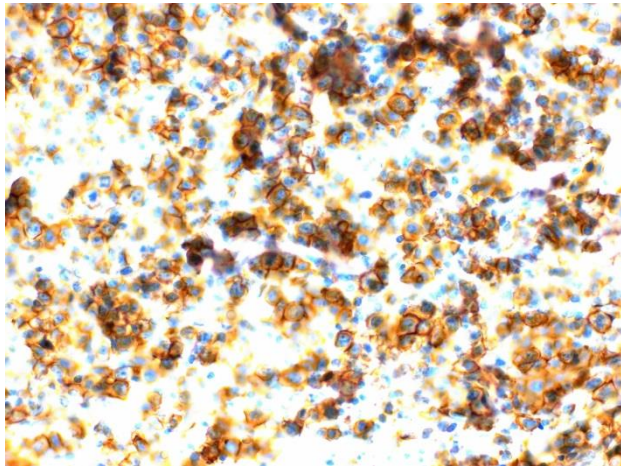


Figure 2b: CD30 positive neoplastic cells

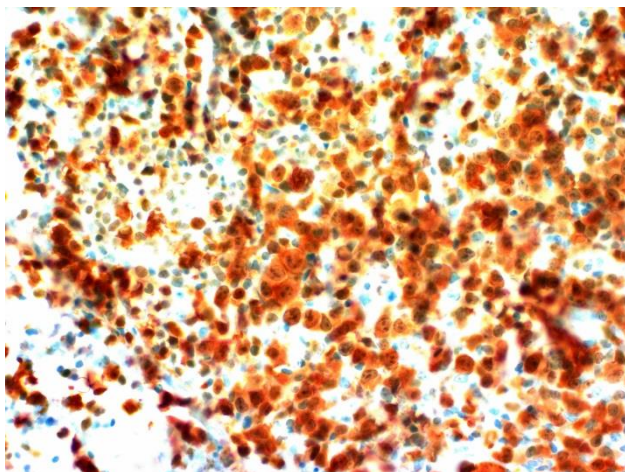


Figure 2c: Anaplastic lymphoma kinase (ALK) –1

These immunohistochemical findings corroborated the diagnosis of ALK positive ALCL. Cytogenetically, karyotype t(2;5) could not be studied due to technical reasons. The patient was diagnosed with stage III anaplastic large cell lymphoma with systemic involvement and she began the induction phase of the chemotherapeutic treatment, according to the NHL BFM 1995 protocol. Bone marrow aspirate was normal, and no malignancy was observed in the cerebrospinal fluid. After V-phase (dexamethasone 5 mg/m²/d on day 1+2, 10 mg/m²/d, on days 3–5; cyclophosphamide 200 mg/m²/d i.v. (intravenous) infusion with cystitis-prophylaxis: MESNA (Uromitexan) 70 mg/m² i.v. each 0, 4, 8 hours after start of cyclophosphamide infusion; methotrexate, cytarabine, prednisolone (MTX/ARA-C/PRED) intrathecal on day 1 in age-adjusted dosing), AM block (dexamethasone 10 mg/m²/d from day 1 to 5; MTX 3 g/m², i.v. infusion on day 1; ifosfamide 800 mg/m²/dose, i.v. infusion with cystitis-prophylaxis: MESNA 70 mg/m² i.v. each 0, 4, 8 hours after start of ifosfamide infusion; cytarabine (ARA-C) 150 mg/m², i.v. infusion on day 4 and 5, 4 doses at 12 hour intervals; etoposide (VP-16) 100 mg/m²/d, i.v. infusion on day 4 and 5, 2 doses at 24 hour interval) and BM block (dexamethasone 10

mg/m²/d from day 1 to 5; MTX 3 g/m², i.v. infusion on day 1; cyclophosphamide 200 mg/m²/dose, i.v. infusion on day 1-5 with cystitis-prophylaxis: MESNA 70 mg/m² i.v. each 0, 4, 8 hours after start of cyclophosphamide infusion; doxorubicin 25 mg/m²/d i.v. infusion, on day 4 and 5) treatments evaluation were performed with ¹⁸F-FDG PET/CT according to protocol. In ¹⁸F-FDG PET/CT, it was seen that the lymph nodes in the abdominal and the small mass in the breast were completely removed, and that the lymph nodes in the left axillary region had an SUVmax value of 2,02 and the large mass had a SUVmax of 2,80. These results showed that the response to the treatment was complete and the patient's chemotherapy was completed by continuing with the protocol. ¹⁸F-FDG PET/CT taken after the completion of chemotherapy revealed no evidence of mass or lymph node. The patient's controls continue smoothly.

DISCUSSION

Lymphoma is the third most common pediatric neoplasm, preceded only by leukemias and brain tumors. Non-Hodgkin lymphoma accounts for about 6% of childhood cancer and nearly half of the lymphoma cases in patients younger than 19 years. Patients typically present with widespread disease. Generally, NHL occurring in children includes Burkitt lymphoma, lymphoblastic lymphoma, diffuse large B-cell lymphoma, and anaplastic large cell lymphoma. Staging and assessment of therapeutic response are based on imaging of the involved sites, bone marrow aspiration and biopsy and examination of cerebrospinal fluid (6). Anaplastic large cell lymphoma is uncommon in children, accounting for approximately 15% of all cases of childhood non-Hodgkin lymphoma. It commonly involves nodal as well as a wide variety of extra nodal sites, as skin, soft tissue, bones, lungs and even esophagus (7, 8). The long-term event-free survival for children with ALCL is approximately 70 %. Novel biological agents, including those that target CD30 or ALK, may hold promise for improving treatment results (9).

Treatment recommendations differ considerably in patients with ALCL. Different chemotherapeutic regimens are used for systemic ALCL, whereas surgical excision and/or radiotherapy are adequate for some patients with extranodal involvement. Han et al (8) evaluated the laboratory findings, involvement sites and treatment outcomes of 28 children with ALCL. They reported that about 80% of patients had lymph node and 64% had extranodal (most commonly mediastinal) involvement at presentation. More than half of the patients were treated with CCG-5941, a T-cell lineage lymphoblastic leukemia-type chemotherapy regimen, and the 88% of five-year overall survival was estimated.

Gajendra et al (5) presented a 14-year-old girl with extensive bone involvement of ALCL. The diagnosis of ALCL was made by examination of the axillary lymph node biopsy samples showing CD30, ALK, epithelial membrane antigen (EMA) and Ki 67 (80%) positivity. She was planned to treat with CHOP protocol (combination of cyclophosphamide, doxorubicin, vincristine, and prednisone) followed by radiotherapy to bulky sites of disease.

In the literature, surgical excision is applied only for single lesions. Oschlies et al (3) reported six children with a single skin lesion of ALK-positive anaplastic large cell lymphoma.

The lesion was completely resected in four of these patients and no further therapy was needed in three. The remaining two patients received additional local radiotherapy and one chemotherapy. Gould JW et al (10) presented a 4-year-old girl with primary cutaneous CD30 positive large cell lymphoma who has been treated by surgical excision and followed for 44 months without the disease.

Tokuyama et al (11) presented a 5-year-old girl with ALK positive ALCL forming a solitary skin tumor on the forearm. She was treated by ALCL-99 trial protocol (combination of dexamethasone, cyclophosphamide, methotrexate, ifosfamide, cytarabine, etoposide and doxorubicin) leading to marked improvement although there was no evidence of systemic dissemination.

On the light of the cases mentioned above, chemotherapy was the only choice for our case with systemic involvement besides of breast mass. She was treated with NHL-BFM 1995 protocol, a chemotherapy regimen designed for mature B-cell lymphomas, and reached complete remission.

CONCLUSION

In conclusion, ALCL should also be considered in the differential diagnosis of children presented with a breast mass. Treatment procedures should be planned according to the involvement site and spread of the disease.

Author contributions: MÖ, ZK, SŞ, ZO, HA; Literature search and study design, Patient examinations and therapy, Pathological evaluations MÖ; Writing article and revisions

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Ethical issues: All authors declare originality of research.

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Geophagia: A cause of distal large bowel obstruction in a Sudanese woman

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ABSTRACT

Objective: Geophagia is defined as the craving and deliberate consumption of dirt, soil, or clay that is practiced sometimes by pregnant ladies, mentally handicapped, or people with iron deficiency anemia. This disorder is seen frequently in people who are native to Africa all around the world. A grave surgical complication can result from the presence of this foreign material inside the intestine notably intestinal perforation, and obstruction

Case: A 34 years old female present with features of distal large bowel obstruction three weeks post-delivery underwent exploratory laparotomy were obstructing piece of clay was found, the patient confirmed after surgery a heavy consumption of river shore clay during the pregnancy.

Conclusions: The patient experienced an uneventful postoperative course, oral intake allowed by the third postoperative day, and the patient was discharged home on the fifth postoperative day. Follow-up at one month after surgery show a clean healed wound with no complaints.

Keywords: Pica, Colon, Sigmoid, Obstruction

INTRODUCTION

Geophagia is defined as the craving and deliberate consumption of dirt, soil, or clay that is practiced sometimes by pregnant ladies, mentally handicapped, or people with iron deficiency anemia (1). This disorder is seen frequently in people who are native to Africa all around the world (2).

The etiology of pica and its subset Geophagia is controversial. There is likely more than one factor involved, including nutritional and psychological factors.

The exact prevalence of Geophagia is difficult to determine because patients often present with complications, which represent a small fraction of the big problem.

A grave surgical complication can result from the presence of this foreign material inside the intestine notably intestinal perforation (3), and obstruction (4, 5).

CASE

A 34 years old Sudanese lady present to the emergency department three weeks following an uneventful vaginal delivery with a complaint of increasing abdominal pain and distension, few episodes of vomiting, and absolute constipation for four days before admission, she denied any fever, with the initial assumption by the patient to be a delivery-related complication.

The patient was hemodynamically stable with a blood pressure of 120/70, the pulse rate: 95/min, respiratory rate: 18/min, temperature: 37.2 °C. Abdominal examination reveals a hugely distended abdomen with striae gravidarum and linea nigra, no previous scar with intact hernia orifices. Soft abdomen on palpation, with resonant percussion note all over the abdomen and exaggerated bowel sounds. Digital rectal examination shows an empty rectum.

Complete blood count, electrolytes, and chemistry were all normal. Erect and supine abdominal x-rays are done and show features of distal large bowel obstruction.

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Plain computed tomography scan of the abdomen confirmed a large bowel obstruction with distal sigmoid colon intraluminal dense mass 10 cm in length and 5 cm in width assumed to be an impacted fecal mass initially (**Figure 1**).

The patient was admitted, started on intravenous fluids therapy, decompression with a nasogastric tube, and rectal wash with cleansing enemas.

Trial of fecal evacuation with proctoscopy done but fail to reach the obstructing lesion due to high-seated position. A Gastroenterologist consulted for possible colonoscopy and trial of extraction but he was reluctant due to severe intestinal distension and fear of perforation. Reassessment done after 24 hours show a failure of conservative measures with expected risk of bowel perforation, so decision taken for operative exploration.

The patient was prepared and the abdomen introduced through a lower midline incision. A previously image noted intraluminal obstructing mass confirmed at the distal sigmoid colon (**Figure 2**).

Firm to hard in consistency and not moldable or amenable for milking distally. Proximal enterotomy was performed and the dense intraluminal mass was extracted in piecemeal and found to be a condensed piece of clay. The proximal bowel looks healthy and no other pathology could be identified. Enterotomy closed in two layers and the abdomen closed in order. The patient experienced an uneventful postoperative course, oral intake allowed by the third postoperative day, and the patient was discharged home on the fifth postoperative day. Follow-up at one month after surgery show a clean healed wound with no complaints.

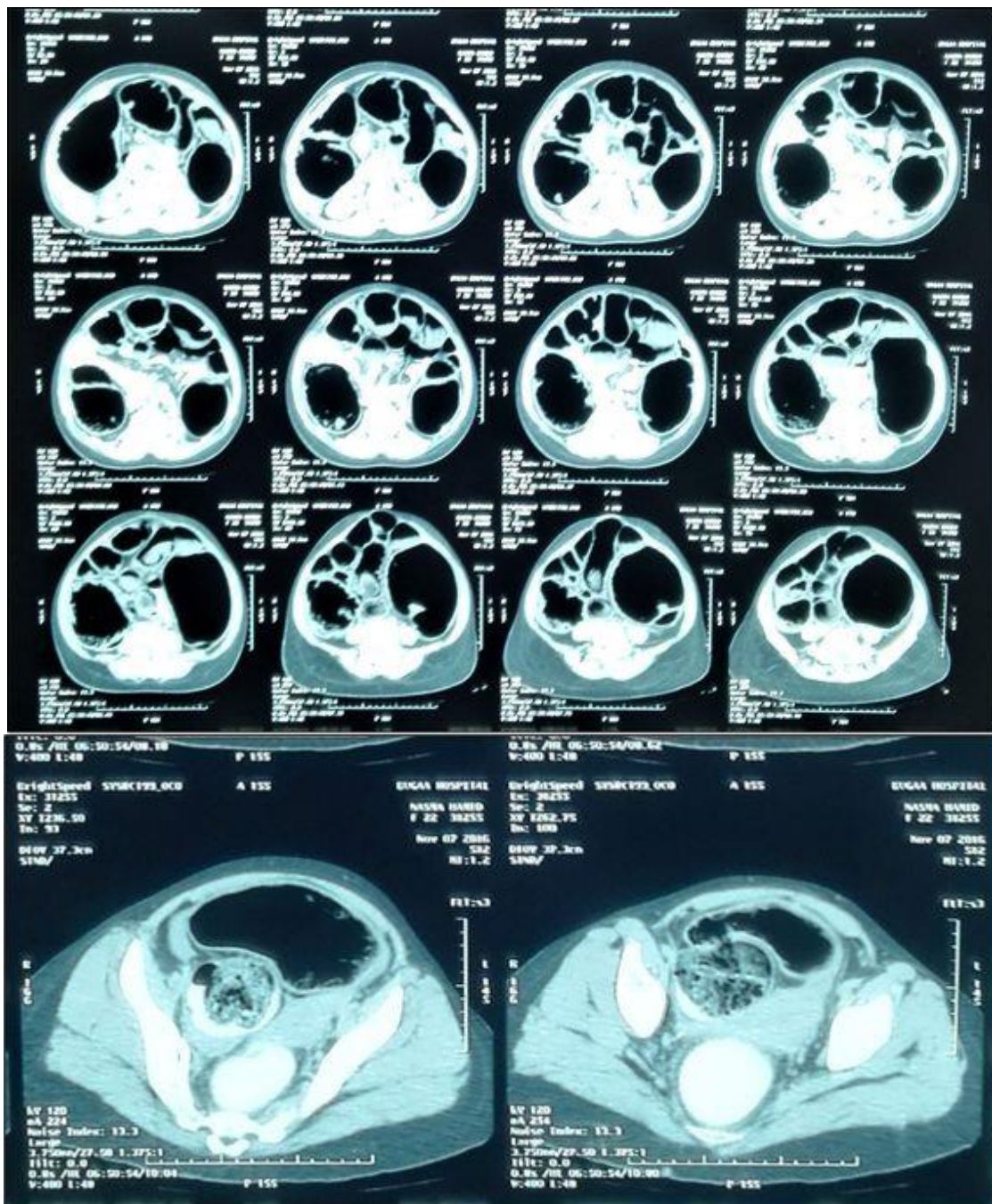


Figure 1: CT scan of the abdomen shows a dilated colon with distal sigmoid intra luminal obstructing lesion.

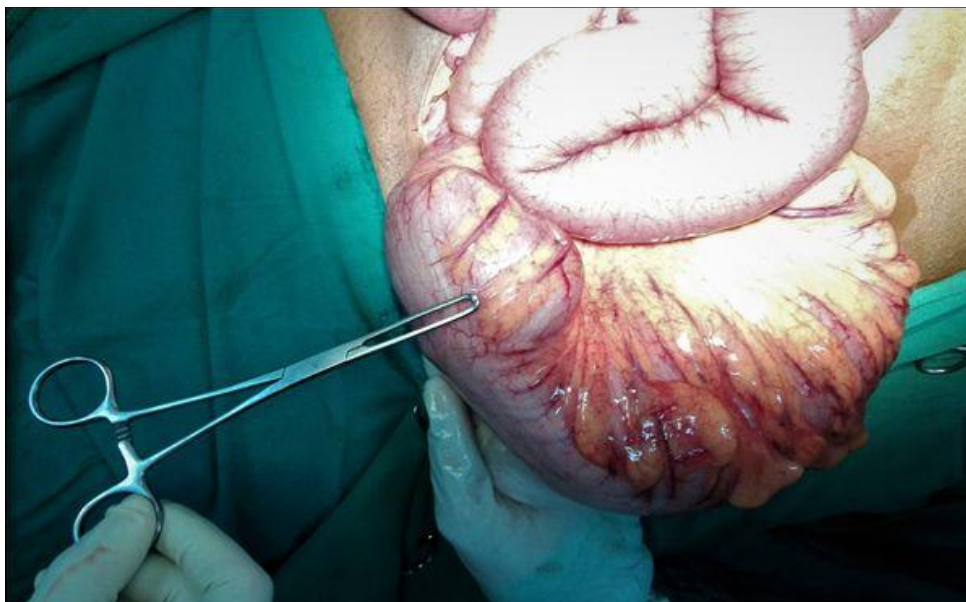


Figure 2: Intraoperative picture showing the obstructing clay mass at the distal sigmoid.

DISCUSSION

A retrograde history taking confirms the consumption of a large amount of river shore clay by the patient, a known habit practiced by pregnant Sudanese ladies and a known form of pica (6, 7).

A spectrum of complications can result from pica habit including electrolyte disturbance like hypokalemia, parasitic infestation, iron deficiency anemia, heavy metal poisoning, intestinal perforation, and obstruction (1).

The exact etiology of surgical complication is not clear but hypothesized to be due to chronic accumulation of hard dry material with subsequent mucosal injury and possible anaerobic bacterial infection (8). Colonic perforation is thought to be the result of the increased luminal pressure and diminished vascular supply of the colonic wall (3).

A diagnostic difficulty may present as the patient is reluctant to inform about their pica habits out of shame or due to underestimation of the seriousness of the condition as in this case where the patient criminate her recent delivery as a cause of her symptoms.

CONCLUSION

A variety of surgical management is available dictated by the level of the obstruction and the general condition of the patient. Enemas, rectal irrigation, or mechanical extraction Trans anal may be valid options for low impactions (rectosigmoid) in minimally symptomatic patients. Surgery with or without resection or diversion may be needed in others (9).

Author contributions: KYAA, OME; Literature search and study design, Patient examinations and therapy, Pathological evaluations KYAA; Writing article and revisions

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Ethical issues: All authors declare originality of research. Informed consent has been obtained from the patient.

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Articulating Os Intermetatarsium with painful ganglion cyst

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ABSTRACT

Objective: Sesamoid and accessory bones are commonly found in the foot and ankle with varying incidence. The Os intermetatarsium, located between the medial cuneiform and the base of the first and second metatarsal, occurs rarely and is frequently asymptomatic. Few symptomatic cases of this condition are reported in the literature. The development of synovial ganglion cyst over an os intermetatarsium is a more occasional finding not clearly reported in the literature.

Case: Here we report the case of a 22 year old female presenting with pain and localized swelling in the dorsum of the midfoot who was found to have a ganglion cyst emerging from an articulating os intermetatarsium.

Conclusion: Although not a common entity, an Os intermetatarsium, with its associated complications, can be one of the causes of dorsal foot pain.

Keywords: Os Intermetatarsium, Lisfranc joint, dorsal foot pain, ganglion cyst.

INTRODUCTION

The accessory ossicles are most commonly found in the foot (1). Many accessory bones have been described with different incidence (1, 2). The os intermetatarsium is a rare ossicle found in the dorsum of the foot between the first and second metatarsal bases and the medial cuneiform (1, 3, 11). Different sizes and shapes have been described in the literature (1, 3). It is usually asymptomatic (1, 3). However, cases of symptomatic os intermetatarsium have been reported, presenting usually as pain in the dorsum of the foot (1, 3, 11). Symptoms could be due to compression of local structures or painful metatarsus primus or less commonly they could be related to a fracture of the os intermetatarsium. (1, 3, 4, 11). We present in our case, a patient presenting with dorsal foot pain who was found to have an articulating os intermetatarsium complicated by a ganglion cyst.

CASE

A 22-year-old healthy female presented to the orthopedic clinic with a complaint of a foot pain. She stated the pain is mainly in the dorsum of the foot and irradiating between the first and second toe. It has been present for two to three months, and is associated with a focal swelling in the dorsum of the foot. The pain was exacerbated by movement. The patient denies any history of trauma. She is otherwise healthy and does not complain of any comorbidities.

On physical exam, a focal swelling was noted in the dorsal aspect of the midfoot over the first intermetatarsal space. There was tenderness on the palpation of the same area. There was no subjective paresthesia.

The opposite foot showed no abnormality. The remaining of the physical exam was unremarkable. With this clinical presentation, the patient was referred to our center to undergo an MRI of the foot.

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A dedicated MRI protocol of the foot was done on our MRI system (3.0 Tesla MRI GE 750 discovery) using a dedicated foot coil. The MRI showed a 2x1.5 cm lobulated, smooth, well-circumscribed, and homogeneous cystic mass compatible with ganglion cyst overlying an articulating type of Os Intermatarsium revealing two articulating surfaces with the medial aspect of the base of the second metatarsal and the medial cuneiform. No bony erosion or subchondral trabecular abnormal signal intensity was noted. No enhancing solid lesions or significant synovial enhancement were seen (**Fig 1**)

No signs of nerve compression were seen. No further diagnostic tests were carried out. After the failure of conservative treatment, the patient underwent surgical excision of the ganglion cyst which resulted in complete resolution of the symptoms.

DISCUSSION

Sesamoid and accessory bones are commonly encountered in the foot and ankle (**1, 6**). Sesamoids help to reduce the friction and properly distribute the impaction forces applied to the plantar aspect of the foot, however, ossicle has no definite known role. Both, sesamoids and accessory bones can be associated with pathological conditions (**3, 6**)

The os intermetatarsium, an accessory ossicle, has a rare occurrence and a frequency of 1-13 % with a slight discrepancy between the prevalence reported on imaging compared to anatomical studies, which is caused mainly by the difficulty of its diagnosis it on standard radiographs. (**Fig 2**) (**1, 2, 3**).

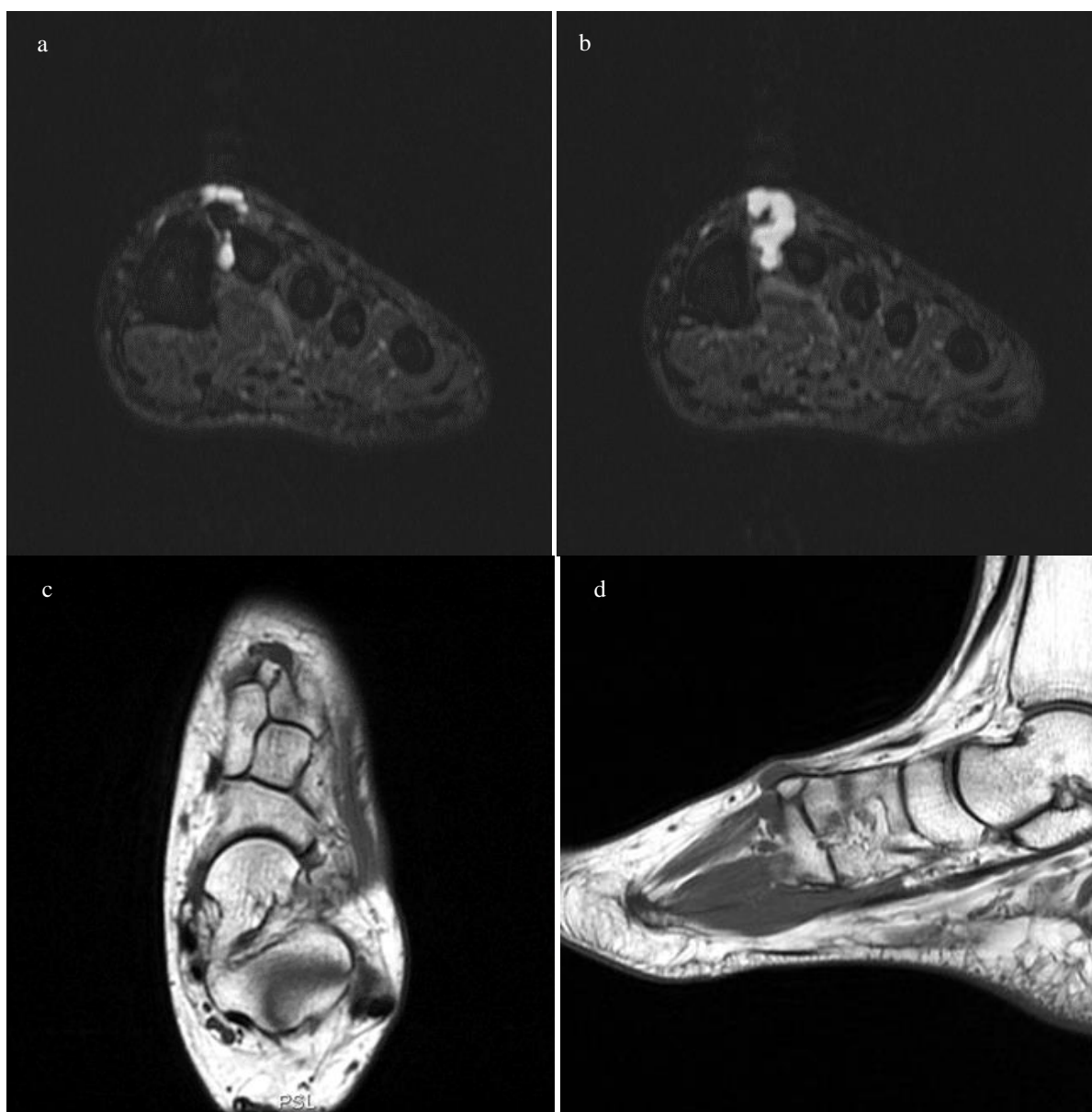


Figure 1: (a) & (b) axial proton density fat sat; (c) & (d) sagittal and coronal T1 sequences of the midfoot reveal lobulated synovial ganglion surrounding an articulating Os Intermatarsium.



Figure 2: (a) & (b) Volume Rendered images and simple radiographic film of a 70y old patient reveals an articulating Os Intermetatarsium not seen on.

It is located at the dorsal aspect of the foot, in the space between the medial cuneiform and the first and second metatarsal bones. (1, 3, 6).

Historically, it was first described by Wenzel Gruber in 1977 and further detailed characterization was done by Pfitzner (1, 12). It might present with different shapes and is usually round, but can be oval, kidney-shaped, linear, spur-like or may even look like a rudimentary ossicle (1, 6).

Three different types are described, the free-standing, the articulating, and the fused. (2, 3). The free-standing type is completely independent without any connection with the adjacent bones.

It is the most common type (11). The articulating type shows cartilage covered synovial articulations with either the first or second metatarsal or cuneiform. The fused variety are considered as bone spurs and is the least common type (1).

Its association with hallux valgus deformity has been described by some authors (1, 5, 11). The accessory ossicle acts as a wedge that spreads apart the first two metatarsals producing deviation between them thus promoting the formation of metatarsus primus varus (11).

Although usually asymptomatic and found incidentally, few cases of painful os intermetatarsium have been reported (3, 4, 6) presenting as painful metatarsus primus (11) or with dorsal foot pain associated with paresthesia between the first and second toe exacerbated by weight-bearing, tight shoes, and activities like ball kicking. (1, 3, 6).

Compression of the deep or superficial peroneal nerve by the ossicle has been reported as a source of the pain (1, 3, 5, 6).

Another described cause of painful os intermetatarsium is caused by fracture of the ossicle. It is important to distinguish this entity from an avulsion fracture of the Lisfranc joint as both cases usually present after a trauma (11).

A Lisfranc injury is defined as an injury of the foot x where one or more metatarsals are displaced from the tarsus (11). The os intermetatarsium can be misinterpreted as small bone fragment between the first and second metatarsal bases (termed the Fleck sign) (11, 12). An accurate diagnosis is essential for the proper management and to prevent complications associated with a Lisfranc fracture such as osteoarthritis and deformity (11).

What seemed interesting in our case, is the appearance of a ganglion cyst arising from an articulating os intermetatarsium which has not been well described in the literature.

A ganglion is a common benign cystic lesion containing mucoid material encapsulated with fibrous tissue (6, 7, 9). The pathophysiology of ganglion cysts remains unclear, but they occur frequently in association with osteoarthritis and less frequently with chronic or acute joint stress, trauma, rheumatoid arthritis or other inflammatory joint diseases. (8, 9)

Other theories of cyst genesis can also be considered. Joint stress, whether acute or chronic, is the common root cause. Joint stress can cause either a small rent in the capsule with subsequent fluid leakage or mucoid degeneration of adjacent extra articular connective tissue with subsequent fluid accumulation or finally it may also stimulate mucin production (9).

Conservative management is preferred as an initial treatment for symptomatic os intermetatarsium as well as ganglion cysts (1, 11). The treatment of painful os intermetatarsium consist of rest and non-steroidal anti-inflammatory, however if there is failure of the conservative treatment or evidence of nerve compression, a surgical exploration is warranted (1, 11). The same applies to the ganglion cyst, for which surgical excision is recommended after failure of the conservative treatment. However, surgical removal showed a significantly lower recurrence rates as compared to non-surgical interventions. (11)

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