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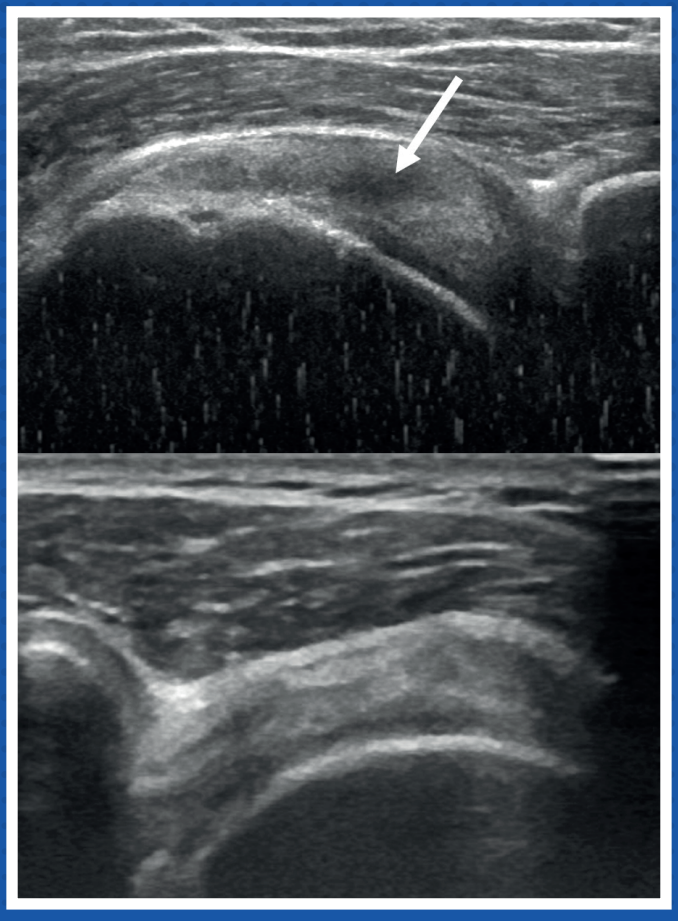

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Editorial

Dear colleagues,

I am glad to announce the publication of Northwestern Medical Journal's last issue in July 2024. We are very proud of uninterrupted releasing of our journal with high quality scientific content since four years.

This issue has nine scientific articles. Bayraktar et al. investigated whether there is a relationship between serum inflammatory indexes and coronary artery disease severity. Emreciksin et al. shed light on effect of perinatal asphyxia on postnatal feeding intolerance. Aydoğmuş et al. investigated the effects of hemodailysis on sepsis in patients who are in intensive care unit. Sevimli et al. evaluated the factors causing congenital nasolacrimal duct obstruction and their effects on probing success. Arıkan et al. tried to get answer the question whether partial rotator cuff tears cause humeral migration. Soydan et al. examined the concordance between dominant eye and hand. Balaban et al. showed a new way for detection rim rent tears of the rotator cuff. Bolu et al. evaluated the clinical and epidemiological characteristics and autoantibody status of children with type 1 diabetes. Frequency and severity of premenstrual syndrome in women diagnosed with brucellosis was detected in a study conducted by Şafak et al.

We wish as previous ones this issue would be beneficial and satisfying for readers. I would like to thank all writers and reviewers of this issue for their great effort.

Best regards,
Prof. Ahmet Ural, M.D.
Editor-in-chief

NORTHWESTERN MEDICAL JOURNAL

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RESEARCH ARTICLE

A new way to detect rim rent tears of the rotator cuff: Real-time sonoelastography

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ABSTRACT

Aim: To evaluate real-time sonoelastography (RTSE) findings of the rotator cuff (RC) in patients with rim-rent tears (RRTs) and compare them with a control group of healthy individuals.

Methods: A total of 101 RC tendons were evaluated in 54 patients with RRTs and 31 healthy individuals. RC tendons were evaluated by routine shoulder dynamic ultrasound (US) and RTSE examination. US and RTSE findings were evaluated in patients with RRTs and healthy individuals for the same tendons of the RC.

Results: A total of 85 individuals (male/female: 34/51) and 101 RC tendons (54 with RRTs and 47 healthy tendons) were included in this study. According to the RTSE evaluation, all of the RRTs had yellow and red areas within green/blue coding, and all of the RC tendons in healthy volunteers had blue and green coding on sonoelastography.

Conclusion: We demonstrated tear areas and softening of the RC tendons in patients with RRTs compared to healthy volunteers. RTSE findings may be associated with RRTs of the RC tendons in this patient population and also can be useful for the evaluation of RRTs.

Keywords: rotator cuff, sonoelastography, supraspinatus, tendon injury

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INTRODUCTION

Codman divided the partial tears of the supraspinatus tendon in the rotator cuff (RC) into 4 subtypes (1). The subtype Partial Articular Surface Tendon Avulsion, also known as PASTA, is also defined as a rim-rent tear (RRT), on the articular surface where the tendon attaches to the greater tuberosity (2). On the B-mode ultrasound (US), RRTs are visualized as a small-sized partial tear area in the anterior segment of the tendon at the articular surface, which leads to intratendinous linear echogenic extension of a small cortical avulsion and a concomitant halo appearance (3). Focal irregularity is also observed in the adjacent cortex due to avulsion. This is a primary and stimulating sonographic finding that leads us to the pathology. Despite the higher incidence among partial tears, it is harder to detect an articular-sided tear in comparison with bursal-sided partial tears (4). The common anisotropy artifact seen on the US may also mistakenly create the appearance of an articular side partial tear. It is necessary to examine whether there is a real tear by giving an angle to the probe and visualizing this section of the tendon in both transverse and longitudinal planes, which requires experience.

With technological developments, the frequency of US examinations of the musculoskeletal system has increased over time, and now US is commonly used in daily practice. Ease of use, low cost, accessibility, repeatability, lack of X-rays, and applicability to all age groups are important advantages of this modality. In addition, compared to magnetic resonance imaging (MRI), US takes less time and is therefore more tolerable for the patients. This makes US to be preferred as the first-line radiological modality for the evaluation of important anatomical structures of the musculoskeletal system, such as tendons. US provides a better assessment of the pathology by offering reliable determination of anatomical localization, real-time dynamic examination, and comparison with the intact side. Recently, sonoelastography has become available for further assessment of tissues, in addition to the standard Bmode imaging. While the findings of RTSE in the musculoskeletal system were limited to a few articles, this number is increasing with the growing commercial use of US devices.

In this study, we aimed to evaluate US and RTSE findings of the RC RRTs in symptomatic patients and compare them with healthy individuals.

MATERIALS AND METHODS

Study population

A total of 101 RC tendons (54 RC tendons of 54 patients with RRTs and 47 RC tendons of 31 healthy individuals) were included in this study. All patients with RRTs had shoulder and deltoid pain, and also a positive Jobe Test. None of the patients had a history of inflammatory arthritis or trauma or operation to the shoulder. The control group had no history of tendon injury or clinical findings that indicate a tendon disorder. This study was approved by our Institutional Review Board (Approval Number: E2-20-76).

Imaging

Patient and control groups underwent US and RTSE evaluation for the RC tendons. Sonographic examinations were performed with GE Logiq E9 (GE Healthcare, Milwaukee, Wisconsin, USA) and Toshiba Aplio 500 (Toshiba Medical Systems Corporation, Tochigi, Japan) with 5 – 11 MHz or 7 – 15 MHz linear array transducers by the two experienced radiologists (M.B. and I.S.I.). When evaluating the supraspinatus tendon, the elbow was flexed the arm was in extension, and the dorsal side of the hand was held posterior to the waist so that optimal tension could be achieved in the fibrils, enabling the best visualization of the fibrillar structures.

RTSE images of the tendons were obtained in the transverse plane while the transducer was perpendicular to the tendon to avoid tissue shifting. The local strain was calculated under slight compression and decompression, applied with a freehand technique. The optimal strain was assessed according to the visual indicator of compression . This indicated the average strain in the region of interest between the two frames. The tissue elasticity distribution was calculated in real-time, and the results were represented on a color map superposed on the B-mode images. The color spectrum ranged from blue (hard) to red (soft) and represented the relative

stiffness of the tissue. Red indicated soft tissue; yellow, intermediate stiffness; and blue and green, hard tissue. At least one real-time sonoelastographic image of each tendon RRT area was assessed and the selection and definition of the elastographic patterns were assessed by two radiologists (M.B. and I.S.I) blinded to patient characteristics.

The tendons were classified according to the sonoelastography findings as normal (a tendon with blue and green coded) and abnormal (a tendon with yellow and red areas representing RRT within a blue and green coded appearance).

RESULTS

A total of 85 individuals (Male/Female: 34/51) and 101 tendons were included in this study. The mean age of the participants was 52.9 years (range, 28-72 years). Fifty-four patients with 54 RC tendons had symptomatic RRTs and thirty-one individuals with no symptoms were included as the healthy controls. The mean age of the RRTs group was 53 years (range, 28-72 years), and the mean age of the healthy group was 52.8 years (range, 34-72 years). A common patient history included severe pain in the deltoid region following a sudden arm movement and inability to lie down on that side at night.

A total of 101 RC tendons were evaluated. Sixty-three of them were on the right shoulder and 38 on the left. Fifty-four of these tendons were RRT cases, 53 of which were in the supraspinatus tendon and one of them was in the subscapularis tendon. No additional US pathology was observed in 19 cases, whereas intense contents of fluid were observed in subdeltoid-subacromial bursitis in 35 cases. There were 41 right and 13 left-sided tendons in the RRT group, and 22 right and 25 left-sided tendons in the healthy group. Supraspinatus tendons were evaluated in the control group, and in the case of a rim-rent tear in the subscapularis tendon, the opposite intact subscapularis tendon was evaluated for comparison.

Only 9 of 54 patients underwent shoulder MRI as an additional radiological imaging. Two cases were reported as minimal tendinosis, three as millimetric intratendinous tear, and four as an articular-sided partial tear. MRI examinations were performed in one case two years after the US examination, in one case after nine months, and in one case after three months, and the other six cases were reported in the same month.

RTSE evaluation demonstrated that all RRTs in the symptomatic patients had an abnormal structure (54 of 54 tendons) (Figure 1), and all RC tendons in the healthy volunteers had a normal structure (47 of 47 tendons) (Figure 2).

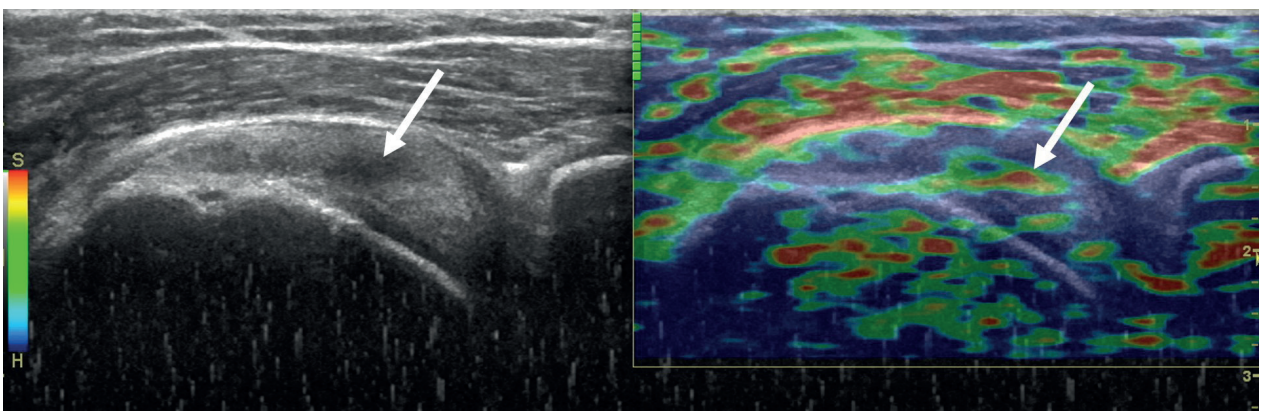

Figure 1. Rim-rent tear of the supraspinatus tendon (arrow). On the grey-scale ultrasound, the rim-rent tear area is hypoechoic relative to the hyperechoic normal tendon. The rim-rent tear is visualized as yellow and red areas within green on the real-time sonoelastography, indicating its intermediate to soft tissue characteristics.

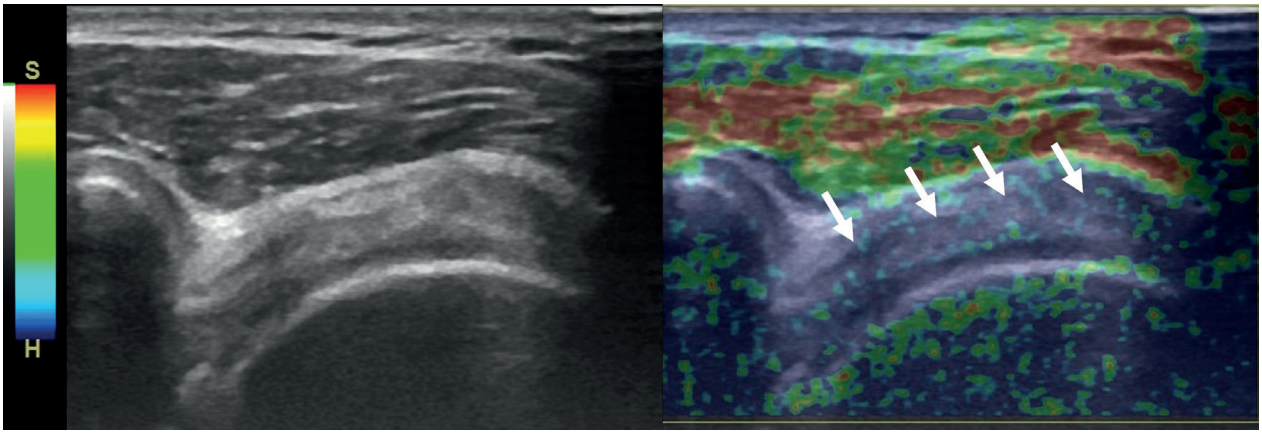

Figure 2. Normal sonographic and sonoelastographic appearance of the supraspinatus tendon (arrows). On the grey-scale ultrasound, the tendon is homogenously hyperintense with smooth contours. The supraspinatus tendon exhibits predominantly blue with some green coloration on the sonoelastography, indicating its hard tissue characteristics.

DISCUSSION

In this study, we evaluated US and RTSE findings of RC supraspinatus and subscapularis tendons in patients with RRTs by comparing them with a healthy control group. In the RTSE evaluation of the RC tendons with RRTs, we observed that all RRTs had an abnormal structure and all RC tendons in healthy individuals had a normal structure according to the main sonoelastography evaluation.

US is a reliable imaging modality in the evaluation of musculoskeletal system (3,4). The RC tendons can be visualized optimally with high-resolution linear probes. The echogenicity of the fibrillar structures of the RC tendons should be iso-hyperechoic compared to subcutaneous soft tissue and hypoechoic compared to subdeltoid-subacromial bursal layers.

Elastography is a sonographic modality used to evaluate the elasticity of different tissues. It was first performed on humans in 1987 by Krouskop et al. (5). The basic principle of RTSE is based on the strain (displacement) due to compression applied to the tissues. This displacement can be calculated with the modified US and reflected on the color scale (6-8). In most tissues and lesions where external compression is applied, different results may be seen due to the different internal molecular structures. A small amount of deformation occurs in the hard tissues, whereas this deformation is significant in soft lesions for the same degree of compression. These deformation results are reflected in the color spectrum on the monitor. The blue color in this color map indicates hard areas, the red color indicates soft areas, and the green color indicates medium-hard areas.

In our study, we observed an abnormal appearance in the RC tendons (mostly supraspinatus, one case subscapularis) with RRTs (green-yellow-red color) and a hard with normal appearance (green-blue color) in the control group of healthy volunteers. This is similar to the previous studies evaluating RTSE findings in tendinopathy cases (9,10).

In a series of 214 patients whose clinical examination suggested tendinopathy or underwent surgical treatment but had no sonographic abnormality on B-mode US, 164 patients had positive findings supporting tendinopathy on RTSE (11). Another study by Prado-Costa et al. evaluated tendon damage in 26 cases of different tendons including the patellar tendon. Compression-based elastography examination showed a decrease in the tendon stiffness as a soft appearance (red coding) in the presence of tendinopathy (12). Porta et al. emphasized that compression-based RTSE examination is a useful and easily applicable method in the evaluation of patellar tendons in healthy

subjects (13). They found that the tendon was coded as hard on RTSE in healthy subjects. However, tendons with pathological changes were coded as soft. Egyptian researchers evaluated the benefits of RTSE in a study of 40 patients with shoulder pain and 40 healthy volunteers. Comparing their results with MRI, they found RTSE to be a sensitive method for RC tears and tendinosis (14).

These findings point to very early changes in tissue elasticity, possibly due to histopathological changes, edema, and inflammation. As a result, it was determined that small changes in the elasticity and mechanical properties of the tissues can be detected by RTSE and RTSE is an additional modality to complement US imaging.

Due to the elasticity of the different tissues depending on their hardness, different color codes are detected on RTSE. It is based on the color scale response of the signals due to acquired displacement with compression of the tissue and/or lesion (15). With this measurement, objective information about the degree of stiffness of a tissue and/or lesion can be obtained (16). The supraspinatus tendon is frequently damaged and affected by tendinosis. Therefore, tendon stiffness and elastic properties should be considered for diagnosis, after treatment and follow-up period.

RTSE examination is successful in showing degeneration that may not be seen on the sonographic image. This provides valuable results when combined with clinical examination and US examination findings. We think that the tendon may not be sufficiently tight, and these small tears may not be clearly visualized, because the arm cannot be in optimal external rotation position on MRI. By evaluating it in this position, it is possible to see the RRTs of the supraspinatus tendon at the tendon adhesion site at the anterior part of the greater tubercle, which is small and could be easily overlooked. In the same position, a torn area is observed in soft, green-red color, coded according to the scale on the color-coding map on synchronous RTSE examination.

Our study has several limitations. One of them is the bias risk in the RTSE examination, because it was possible to determine whether there was a tear in the previous US examination, or it was already known whether the patient was healthy. Another limitation is that a gold standard method such as arthroscopy or MRI is not used for the confirmation of tears.

RRTs should be diagnosed early because they are symptomatic and may progress progression to full-thickness tears. Although MR arthrography is a highly sensitive imaging method to detect RRTs, RTSE is an additional cost-effective sonographic modality that provides early and timely diagnosis. It shows soft-coding in mostly red color in tendons with RRTs and can be performed simultaneously by the same radiologist within a few seconds of routine US examination time. Tendon stiffness and continuity are useful for treatment planning and prognosis.

Ethical approval

This study has been approved by the Ankara City Hospital Institutional Review Board (approval date 16.12.2020, number E2-20-76). Written informed consent was obtained from the participants.

Author contribution

Concept: MB, İSİ; Design: MB, AHÇ; Supervision: İSİ; Materials: MB, AHÇ; Data Collection and/or Processing: MB, AHÇ, SŞİ, İSİ; Analysis and/or Interpretation: MB, AHÇ, SŞİ, İSİ; Literature Search: MB, AHÇ, İSİ; Writing Manuscript: MB, AHÇ, SŞİ, İSİ; Critical Review: MB, AHÇ, SŞİ, İSİ. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

Do partial rotator cuff tears cause humeral migration?

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Cite as: Arıkan E, Ayanoğlu T, Kalaycıoğlu O, et al. Do partial rotator cuff tears cause humeral migration?. Northwestern Med J. 2024;4(3):127-133.

ABSTRACT

Aim: This study aims to analyze the effect of symptomatic partial and full-thickness rotator cuff tears on humeral migration. The hypothesis of the study was that superior humeral migration varies according to the type of rotator cuff tear.

Methods: 80 patients who underwent arthroscopic repair between 2017 and 2021 were retrospectively evaluated. Humerus migration directions and distances of patients in the isolated Bankart lesion (Group 1), bursal-side partial (Group 2), articular-side partial (Group 3), and full-thickness rotator cuff tear (Group 4) groups whose diagnosis was confirmed by shoulder arthroscopic intervention MRI were recorded and evaluated.

Results: There was no significant difference between the groups according to age (p=0.295). Migration distance values of isolated Bankart lesions (Group 1) were significantly lower in men (p<0.005). While superior migration rates were significantly increased in full-thickness tears, they were similar in partial tears (p<0.005). The mean migration distance was similar between groups (p=0.153).

Conclusion: Symptomatic full-thickness rotator cuff tears lead to humeral migration. Superior humeral migration was not found to be significant in partial rotator cuff tears, regardless of bursal or articular.

Keywords: humeral migration, MRI, rotator cuff, shoulder

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INTRODUCTION

There is no consensus among authors who study humeral head migration as to which types of rotator cuff tears cause humeral migration.

There are two types of rotator cuff tears: full-thickness tears and partial tears. Bursal side and articular side tears are two different types of partial tears based on where they are located (1). Rotator cuff tears are more common as people age and are generally brought on by two mechanisms: intrinsic and extrinsic. According to Codman and Matsen, extrinsic factors are caused by subacromial impingement syndrome, while intrinsic factors are caused by degenerative changes (2,3). We also know that non-traumatic tears start as partial tears and then return to full-thickness over time, and then migration develops. However, we know that partial tears occur in different etiologies (4).

Rotator cuff tears impair normal glenohumeral biomechanics and also narrow the acromiohumeral space (5,6). According to Weiner et al., supraspinatus tears were the primary cause of the superior humeral head displacement (7). The humeral head shifts superiorly on the glenoid as a result of rotator cuff damage, changing the biomechanics of the glenohumeral joint (8,9). Subscapularis tendon tears do not cause migration of the superior humerus. Even when the subscapularis tendon is intact, rotator cuff injuries can still result in superior humeral migration and subacromial impingement (10). Rotator cuff injury may result in dynamic anterosuperior instability with loss of the coracoacromial arch and anterior deltoid, abduction, or flexion of the shoulder (11). Acromiohumeral distance is considered an important measure of humeral head elevation (12). Hamada and coworkers diagnosed radiographically significant rotator cuff injuries using this scale and recommended rotator cuff restoration before the acromiohumeral space narrows (13,14).

We sought to understand how the type of rotator cuff tear affects the humeral migration in both direction and distance in this study, as well as whether partial rips contribute to migration. The hypothesis of the study was that superior humeral migration varies according to the type of rotator cuff injury.

PATIENTS AND METHODS

Retrospective analysis was performed on the reported data of patients who underwent shoulder arthroscopy between 2017 and 2021. Ethical approval was obtained from Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (2021/51) for this retrospective study. Patients with compatible MRI and intraoperative findings were selected for the study. In order to support the diagnostic accuracy, there is a period of less than 1 month between the MRI scan times and the time of surgery. Approximately 80 patients, regardless of gender, were included in the study. The isolated Bankart lesion group was included in Group 1, the bursal-side partial supraspinatus injury in Group 2, the articular-side partial supraspinatus injury in Group 3, and the full-thickness supraspinatus injury in Group 4.

After evaluating whether it was normally and homogeneously distributed, humeral migration was found to be suitable for analysis with parametric tests as a continuous variable. The patients included in the study were selected and divided into groups with the help of online software called Research Randomizer Version 4.0 (2015, Geoffrey C. Urbaniak and Scott Plous). The median gender, age, and humeral migration distance and direction of the patients were recorded. Humeral migration distance was measured in the MRI coronal section using RadiAnt application, based on the humeral head center and glenoid center.

Exclusion criteria included patients with a history of surgery, a history of trauma near the shoulders on the same side, and patients diagnosed with osteoarthritis, previous infection, autoimmune joint disease, hemophilic arthritis, and pyrophosphate disease.

The categorization of rotator cuff tears was carried out by a senior surgeon with ten years of experience in shoulder arthroscopy and two junior physicians employed by the same hospital. All surgeries were carried out under general anesthesia. The patients were allowed a 20 degrees of posterior displacement during the procedures since they were performed in the lateral decubitus posture, parallel to the glenoid fossa floor. Under 70 N of longitudinal tension, the arm was stabilized in a posture of 15 degrees of forward flexion

and 45 degrees of abduction. After the necessary cleaning and draping, diagnosis and treatment were performed using a 30-degree angle arthroscope and posterior viewing portal.

MR imaging assessment

MR examinations were performed with a special shoulder coil on the 1.5 T system (Siemens Magnetom Symphony, Erlangen, Germany) in the supine position with the patient's arm lying on the side of the body in neutral rotation. Imaging protocol oblique coronal T1-weighted (TR/TE:600/16) and fat-suppressed intermediate (T2-weighted (TR/TE:3000/56)), oblique coronal T1-weighted [TR/TE:500/ 16] and fat-suppressed intermediate (TR/TE:3000/56) and T2-weighted axial (TR/TE:500/15, rotation angle:30) images, field of view 18 cm in all sequences, matrix 192e384 256 and slice thickness/slice spacing 3e4/ 0e1 mm was.

Statistical analysis

In descriptive statistics, numerical variables were provided as mean, standard deviation, median, and minimum and maximum values, while categorical variables are given as number and percentage values. For statistical analysis, results are presented as mean ± SD. Age distributions were compared using the Student t-test. The Pearson chi-squared test was used to determine whether there was a meaningful correlation between categorical variables. To determine if the means of two or more samples varied from one another, the Kruskal Wallis test was utilized. The statistical significance of the difference between the means of independent groups was examined using the ANOVA test. The threshold for significance was defined as $p<0.05$. SPSS for Windows 24.0 (Chicago, IL, USA) was used for all statistical analyses.

The two authors of this study assessed and measured the MRI scans in collaboration with a professorial radiologist specialized in musculoskeletal imaging. The clinical and arthroscopic information of the patients was hidden from these two observers. Humeral migration measures were modified for MRI based on a previous radiographic description (13-15). In this technique, the center of the humeral head was identified by drawing a circle fitting the humeral head.

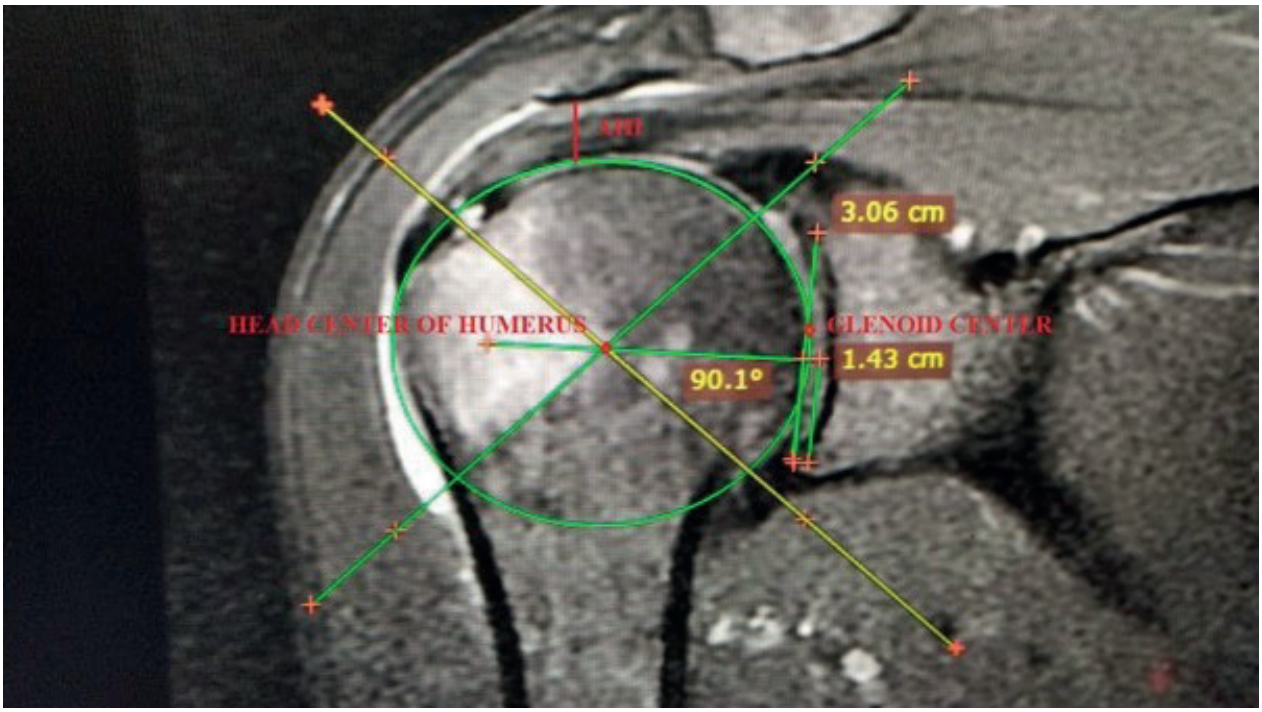

Figure 1. Humerus migration distance values.

The center of the glenoid cavity was identified by drawing two perpendicular reference lines intersecting at the humeral head center (one vertical and one horizontal). Finally, the vertical distance from the humeral head center to a horizontal line through the glenoid center was measured as the superior migration (Figure 1). The humeral migration was measured as a positive or negative number, depending on whether the humeral head was superior to or inferior to the central junction point.

RESULTS

The groups' demographic and clinical traits were comparable (p>0.05 for all) (Table 1). Group 1 had a lower mean age (46.6±6.8) than the other 3 groups. The oldest group of patients (50.2±5.8) had a partial rotator cuff injury on the articular side. Age distribution was similar in all groups (p=0.295). Female gender was most frequent among patients with articular side partial rotator cuff injury (80%). Data from 80 patients were analyzed.

In comparison to the intact group, the migration distance was greater in the groups with bursal, articular, and full-thickness rotator cuff tears (p>0.05, Figure 2). According to gender, the superior migration distance values of the intact male group were lower than the other groups (p<0.005). However, in women, the distance values of patients in the Bankart lesion group were higher. While the rate of superior migration was significantly higher (75%) in full-thickness tears, it was similar in patients with partial tears (35%) (p<0.005) (Figure 3). The mean migration distance was 0.07 (0.02-0.12) cm in Group 1, 0.12 (0.06-0.20) cm in Group 2, 0.11 (0.04-0.19) cm in Group 3, and 0.10 (0.05-0.16) cm in Group 4. There was no discernible distinction between the groups (p=0.153, Table 1).

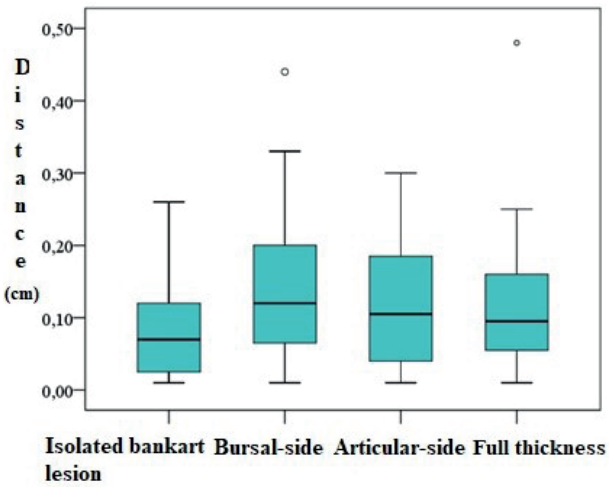

Figure 2. Humerus migration distance measurement.

Table 1. Demographic information and migration measurements (p value)

	Isolated bankart lesion (n=20)	Bursal-side (n=20)	Articular-side (n=20)	Full Thickness (n=20)	p
Age, *year*	46.6±6.8	49.3±5.8	50.2±5.8	48.3±6.5	0.295[a]
Gender					**0.016**[b]
Female	6 (%30)	11 (%55)	16 (%80)	12 (%60)	
Male	14 (%70)	9 (%45)	4 (%20)	8 (%40)	
Superior/Inferior					**0.003**[b]
Superior	4 (%20)	7 (%35)	7 (%35)	15 (%75)	
Inferior	16 (%80)	13 (%65)	13 (%65)	5 (%25)	
Distance, *cm*	0.07 (0.02-0.12)	0.12 (0.06-0.20)	0.11 (0.04-0.19)	0.10 (0.05-0.16)	0.153[c]

Numerical data were summarized as mean±standard deviation or median (1st-3rd quartile), and categorical data were summarized as numbers (percentage). [a]One-way ANOVA, [b]Pearson's chi-square test, [c]Kruskal-Wallis test

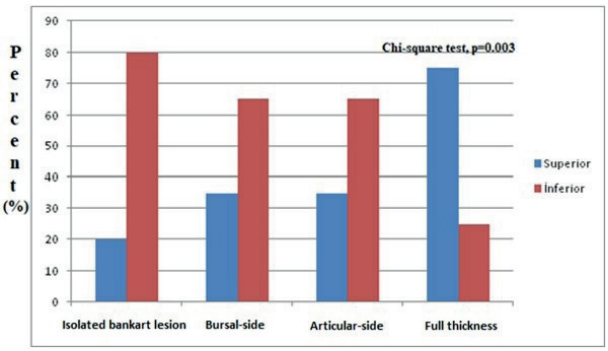

Figure 3. Humerus migration values according to rotator cuff tear types.

DISCUSSION

The study's key conclusion is that superior humeral migration is not brought on by partial rotator cuff injuries. Full-thickness supraspinatus tears are linked to superior humeral migration, which is consistent with the literature. In terms of gender, the migration distance values of the intact group of males were significantly lower than the other groups.

Sharkey and Marder revealed that the stability of the glenohumeral joint is influenced by all of the rotator cuffs parts in a cadaver research (5). There are many studies on superior migration of the proximal humerus, and it is seen with advanced rotator cuff tears (6,16-18). The rotator cuff supplies the deltoids pulling power, which tends to detach the humeral head from the glenoid, and fixes the humeral head in the glenoid to cause elevation (19). If the rotator cuff mechanism is defective, there is no force to resist the deltoid and migration occurs.

Patients with isolated supraspinatus tears and patients with supraspinatus and infraspinatus tears did not significantly differ in their humeral head elevation, according to our research. However, individuals with supraspinatus, infraspinatus, and subscapularis tears had a statistically significant increase in the superior displacement of the humeral head above the glenoid (6).

A limit value for migration was determined according to the tear site in symptomatic shoulders. Tears with an area of 175 mm^2 cause more migration than smaller tears (15). Contrary to prior research, Cetinkaya et al. discovered that isolated supraspinatus tears may allow superior humerus migration even in the presence of an intact subscapularis (10).

Siow et al. suggest that infraspinatus tears are associated with the smallest acromiohumeral distance among all rotator cuff tendons. Massive infraspinatus tears were linked to the biggest reduction in acromiohumeral distance (>3 mm) (20). Additionally, compared to isolated supraspinatus tears or a combination of tears, isolated infraspinatus tears were linked to a smaller mean acromiohumeral distance (20). Superior rotator cuff injuries and therefore an undamaged subscapularis tendon do not prevent superior humeral migration and subacromial impingement produced by a superior rotator cuff tear, but subscapularis tears do not induce superior humeral migration and subacromial compression (10).

On radiography and MRI, individuals treated with partial repair exhibited considerably smaller acromiohumeral spaces and higher upward migration indices than patients with totally repairable tears (21). Our study was compatible with the literature on this subject.

Orthopedic surgeons utilizing non-standard radiographs to assess the acromiohumeral space were shown by Bernhardt et al. to be neither trustworthy nor repeatable (22). Gravity can affect this comparison since MR images are captured in the supine position, but X-ray images are taken in standing and upright position (23). As a result, in our research, we exclusively employed supine MR images of the shoulder. In our practice, these techniques are regularly applied to the preoperative assessment of rotator cuff injuries. For this reason, in our study, both the effect of gravity was eliminated by using MRI and standardization was achieved by using the same position during MRI.

In the Park et al. research, both genders had the same ratio of partial or full-thickness rotator cuff injuries (21). Women are more likely than males to need dominant arm surgery, and their rotator cuff injuries are often smaller (24). According to the study by Lapner et al., when the Upward migration index (UMI) is examined, low UMI is more frequent in males, while high UMI is more frequent in females (25). Decreased UMI is a predictable and reliable sign of rotator cuff tear and degeneration in the clinic (26). In our study, the migration distance values of the healthy group of males were significantly lower than the other groups when grouped by gender ($p<0.005$).

As a result, there are many studies in the literature on total ruptures of the infraspinatus, subscapularis, and supraspinatus muscles, which are among the muscles forming the rotator cuff, and the contribution of these muscles to the migration of the acromiohumeral distance. In our study, we evaluated supraspinatus muscle tears as bursal side partial, articular side partial, and full-thickness supraspinatus tears. We demonstrated that partial rotator cuff tears do not affect migration. We reported that full-thickness supraspinatus tears are linked to superior humeral migration, which is consistent with the literature.

Limitations

This study's primary flaw is the lack of MRI comparisons at different active elevation angles. With vigorous abduction, the degree of humeral migration may change. Another significant restriction is the lack of radiological information on the shoulder on the other side. Additionally, the interval between the onset of symptoms and operation was not tracked. An additional limitation was the low number of patients in the groups. Another limitation is the lack of rotator cable integrity evaluation.

Superior humeral migration is caused by symptoms of full-thickness rotator cuff rupture. However, superior humeral migration distances differ significantly according to gender. In partial rotator cuff tears, superior humeral migration is not observed regardless of the location.

Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 27.04.2021, number 2021/51). Written informed consent was obtained from the participants.

Author contribution

Concept: EA, TA, İÇ, HÇ; Design: EA, OK, İÇ; Data Collection or Processing: EA, ÖFY, MTT; Analysis or Interpretation: EA, OK; Literature Search: EA, ÖFY, TA; Writing: EA, TA, HÇ. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

Evaluation of factors causing congenital nasolacrimal duct obstruction and their effects on probing success

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ABSTRACT

Aim: To determine the etiological and demographic characteristics of congenital nasolacrimal duct obstruction (CNLDO) and to evaluate the effectiveness of probing.

Methods: The study included 33 children who applied to the clinic with epiphora, were diagnosed with CNLDO and underwent probing, and 27 healthy children. Age, gender, probing time, recurrence, accompanying anomalies, and hemogram values were recorded from their records, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR) and systemic immune-inflammation index (SII) were calculated. The term "successful probing" refers to achieving complete resolution of all signs and symptoms of epiphora 1 year after treatment.

Results: The mean age at the time of surgery of 33 patients who underwent probing (16 F, 17 M) was 18.42±7.85 months, while the mean age of the 27 controls (10 F, 17 M) was 22.30± 9.98 months (p=0.108). Platelet levels were significantly lower (p=0.014) and monocyte levels were significantly higher (p=0.012) in the CNLDO group. While there were no significant differences in SII, NLR, and PLR values, the MLR value was significantly higher in the CNLDO group (p=0.026). Recurrence was detected in four patients (12.2%). In the CNLDO group, three patients had undescended testicles, one patient had an inguinal hernia, and one patient had a cleft palate. No significant difference was found between probing time and systemic inflammatory markers and recurrence (for all values p> 0.05).

Conclusion: Platelet, monocyte levels, and MLR ratio were closely associated with CNLDO. Additional anomalies may accompany CNLDO. Successful results can be obtained with probing in the following months.

Keywords: congenital nasolacrimal duct obstruction, epiphora, probing, systemic immune-inflammation index

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INTRODUCTION

Approximately 6%-20% of newborns suffer from congenital nasolacrimal duct obstruction (CNLDO) (1-4). There is a persistent blockage in the nasolacrimal duct (NLD) due to a delay in maturation at the valve of Hasner, where the lacrimal duct opens into the inferior nasal meatus (2,4-7). Typically, infants with CNLDO present within the first month of life with symptoms such as epiphora, mucous discharge, recurrent periocular crusting, or a combination of these (2,5,8,9). CNLDO is typically an isolated condition. However, it may occur more frequently in children with craniofacial anomalies or Down syndrome, and the most common disease pattern in these children is bilateral obstruction (2,10). The condition usually affects one eye, but it can also affect both eyes (2). Confirmation was made through the fluorescein dye disappearance test (FDT) (5).

The majority of cases of CNLDO resolve spontaneously or with conservative methods, such as lacrimal sac massage (Crigler's maneuver) during the first year of life (1,6,10-13). If CNLDO continues to be a problem, the preferred treatment is lacrimal probing (1,4,6,10,13-16). Success rates for resolving obstructions may vary based on factors such as disease severity, cause, patient age, overall health, and history of surgery.

According to the literature, the success rate of lacrimal probing decreases as the child's age increases (1,4,17,18). Cesarean section can increase the likelihood of experiencing CNLDO (19-21).

The precise cause and predisposing factors for CNLDO are currently unknown. It has been reported that chronic inflammation in the nasolacrimal duct (NLD), nasal cavity, and sinuses can cause primary acquired nasolacrimal duct obstruction (PANDO) (22,23). Various markers such as systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), monocytes-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) can be utilized to identify inflammation, predict prognosis, and monitor the disease (18,24,25).

This can help to identify the underlying anatomical and inflammatory factors that contribute to obstruction, guide the selection of the most appropriate surgical technique, and improve surgical outcomes.

The purpose of the study is to identify the inflammatory markers that are associated with CNLDO and to present the factors that affect the success of probing.

MATERIALS AND METHODS

This retrospective study was conducted at the Department of Ophthalmology in Fatih Sultan Mehmet Training and Research Hospital. The study was approved by the Ethics Committee (FSMEAH-KAEK 2023/100). The study was conducted according to the guidelines of the Declaration of Helsinki. Informed consent was obtained from the participants and was archived by the authors.

Clinical data of the patients who underwent probing for CNLDO between January 2015 and December 2022 were analyzed. The exclusion criteria included being older than 5 years, having previous sinus, nose, turbinate or lacrimal surgery, nasopharyngeal malignancy, prior history of maxillofacial fracture and NLD trauma, pathology of the lacrimal canaliculi, reflex hypersecretion, and systemic diseases such as cardiovascular diseases, acute/chronic kidney, diabetes, rheumatic disease.

In the study, 33 children with CNLDO were in the case group (CNLDO), while 27 healthy children were in the control group. Age, gender, probing time, recurrence status, and accompanying anomalies were recorded from the registered electronic files of the patients. The patient's ocular examination involved eliminating the possibility of local reasons for tearing, such as foreign body, conjunctivitis, blepharitis, or buphthalmos. The FDT confirmed the diagnosis of CNLDO. FDT was performed by instilling one drop of 2% fluorescein solution into the conjunctival fornix without anesthesia. After 5 minutes, each eye was examined for proper clearance using the cobalt blue filter light of the slit lamp.

Procedures were performed under general anesthesia. The lower punctum underwent dilation using a punctum dilator of appropriate size. A straight Bowman probe was then inserted vertically in the

lower punctum, progressed into the ampulla, and rotated horizontally into the lower canaliculus while exerting lateral tension on the eyelid. The probe was rotated 90 degrees and advanced downward and slightly backward through the NLD when encountering a hard stop. The valve of Hasner was felt to open.

After the probing procedure, the patient received topical drops containing both an antibiotic and a corticosteroid for several days. FDT was repeated one year after probing. The probing was considered "successful" when there were no symptoms of epiphora and no fluorescence in the conjunctival sac after FDT.

According to the results of blood analysis, serum white blood cell (WBC), neutrophil, lymphocyte, monocytes, and platelet (P) values were recorded; SII, NLR, MLR, and PLR were calculated in both the case and control groups. The SII was calculated from the preoperative counts of peripheral blood P, neutrophils (N), and lymphocytes (L) per liter according to the equation (SII = P x N/L) (26).

Statistical analysis

In the descriptive statistics of the data, mean, median minimum and maximum, standard deviation, and frequency were used. The Kolmogorov-Smirnov test was used to measure the distribution of variables. Independent sample t-test and Mann-Whitney U test were used in the analysis of quantitative independent data. The Chi-square test was used in the analysis of qualitative independent data, and the Fischer test was used when the conditions for the Chi-square test were not met. SPSS 28.0 program was used in the analysis.

RESULTS

Our study consisted of 33 patients (17 male, 16 female) who underwent probing and 27 (17 male, 10 female) healthy controls. The mean age was 18.42±7.85 months in the study group and 22.30±9.98 months in the control group. There was no significant difference in the age and gender ratio between the groups (p=0.108 and p=0.469, respectively). The descriptive characteristics of the patients are presented in Table 1.

Table 1. Descriptive characteristics of the patients in the congenital nasolacrimal duct obstruction and control groups

		Control Group			Case Group			p
		Mean±SD/n-%			Mean±SD/n-%			
Age (months)		22.30	±	9.98	18.42	±	7.85	0.108 [t]
Gender	Female	10		37%	16		48.4%	0.469 [X²]
	Male	17		62.9%	17		51.5%	
WBC 10^9/L		9.8	±	2.2	9.8	±	2.5	0.744 [m]
Platelet 10^9/L		399.0	±	81.9	341.3	±	83.8	**0.014** [t]
Lymphocyte 10^9/L		5.66	±	1.83	5.17	±	1.5	0.552 [t]
Monocyte 10^9/L		0.65	±	0.23	0.83	±	0.28	**0.012** [m]
Neutrophil 10^9/L		3.11	±	1.39	3.45	±	2.02	0.749 [m]
PLR		77.14	±	27.93	73.62	±	36.9	0.369 [m]
MLR		0.12	±	0.06	0.18	±	0.10	**0.026** [m]
NLR		0.61	±	0.37	0.82	±	0.94	0.688 [m]
SII		247.34	±	156.71	283.40	±	363.12	0.508 [m]

[t] Independent sample t-test; [m] Mann-whitney u test / [X²] Chi square test

WBC: White blood cell; PLR: platelet-to-lymphocyte ratio; MLR: monocytes-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; SII: systemic Immune-inflammation index.

Table 2. Descriptive characteristics of the patients according to the presence of recurrence

	Recurrence (-)			Recurrence (+)			p
	Mean±SD/n-%			Mean±SD/n-%			
WBC 10^9/L	7.2	±	1.8	6.6	±	1.9	0.826 [t]
Platelet 10^9/L	342.2	±	15.8	320	±	50.8	0.699 [t]
Lymphocyte 10^9/L	5.24	±	0.28	5.52	±	0.69	0.730 [t]
Monocyte 10^9/L	0.84	±	0.5	0.83	±	0.16	1.000 [m]
Neutrophil 10^9/L	3.35	±	0.35	2.78	±	0.45	0.721 [m]
PLR	70.04	±	4.6	58.5	±	7.47	0.361 [m]
MLR	0.18	±	0.02	0.15	±	0.02	0.934 [m]
NLR	0.70	±	0.1	0.52	±	0.11	0.763 [m]
SII	236.91	±	32.11	223.86	±	24.10	0.640 [m]
PT (months)	17.5	±	1.40	24.86	±	4.31	0.186 [t]

[t] Independent sample t-test; [m] Mann-whitney u test

WBC: White blood cell; PLR: platelet-to-lymphocyte ratio; MLR: monocytes-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; SII: systemic Immune-inflammation index; PT: probing time.

Probing was performed on the right eye of seven patients, the left eye of 15 patients, and both eyes of 11 patients. Platelet values were significantly lower (p=0.014) and monocyte levels were significantly higher (p=0.012) in the CNLDO group. While there was no difference in SII, NLR, and PLR values between the groups, the MLR value was significantly higher in the CNLDO group (p=0.026). Recurrence was detected in four patients (12.2%). No significant difference was found in probing time between recurring and non-recurring CNLDO patients (p=0.186). No significant difference was found in terms of systemic inflammatory markers based on recurrence status (for all values p> 0.05) (Table 2). Undescended testis was found in three patients, an inguinal hernia in one patient, and a cleft palate in one patient in the CNLDO group.

DISCUSSION

We studied the blood samples of patients diagnosed with CNLDO and undergoing probing for CNLDO and compared them with the healthy control group in terms of the nasolacrimal system.

CNLDO is frequently observed in children, which affects their lacrimal system (8). The valve of Hasner membrane opens spontaneously or with Crigler's maneuver in up to 90% of affected children by one year of age. Natarajan et al. reported that CNLDO is more frequently found in male preterm infants with normal birth weight and is typically unilateral (2). It is reported that CNLDO is often related to coexisting ocular or systemic anomalies, such as Down syndrome (2,17). The majority of children in our study had unilateral CNLDO, with a 33% rate of bilaterality. In the CNLDO group, three patients had undescended testis, one inguinal hernia, and one patient had cleft palate, all of which were unilateral.

The timing of probing in children with CNLDO is controversial (4,5). Świerczyńska et al. suggested probing at 7-9 months for children without recurring infections, while early probing may be considered for children with additional signs (10).

Lekskul et al. reported that the effect of Crigler's maneuver decreased in the following months, but the effect persisted with the probing procedure (4). Lee et al. demonstrated that the timing of probing does not impact the success of treatment in patients with bilateral CNLDO (27). Arora et al. found that children probed before age three had higher success rates than those probed after age three (13). We found no significant relationship between probing time and its success.

Al-Faky et al. reported that silicone intubation may be required in complex and bilateral cases while probing is sufficient for children with CNLDO over one-year-old (16,28). In our study, we attempted to probe all patients initially. In cases where probing was unsuccessful, silicone intubation was performed on children.

We used the appropriate straight Bowman probe in all the children we probed. However, Serin et al. found higher success rates with manually curved Bowman probes compared to straight ones (6).

Many factors are indicated for the obstruction of the valve of Hasner, such as fibrosis and inflammation (7). A study suggested a potential link between infection and CNLDO, but findings indicate that there is no significant difference in microbial growth rates between those with and without CNLDO. Moreover, the spontaneous resolution rate appears to be consistent regardless of the presence of pathogenic bacteria (7,29).

Wang et al. found that patients with NLD obstruction had higher levels of pro-inflammatory cytokines in their tears compared to the control group (30).

Matsumura et al. found that IL-6 concentration was significantly higher in eyes with CNLDO compared to control eyes (31).

In many studies, the authors suggested that probing in the following months will reduce the chance of success due to increased inflammation and fibrosis in the NLD (32,33).

We examined the hemogram values of CNLDO patients to determine inflammation markers that cause and affect the prognosis of CNLDO.

We found SII to be a newly suggested predictive inflammatory biomarker in various systemic inflammatory disorders (34). Also, it has been shown that mean platelet volume (MPV) can serve as a new inflammation indicator, with significant decreases observed in conditions such as lung cancer, ankylosing spondylitis, and rheumatoid arthritis (35,36). Atum et al. discovered significantly higher NLR values and significantly lower MPV values in the PANDO group (26).

We observed no significant difference in NLR, PLR, and SII values between the groups. However, monocyte and MLR values, which are indicators of systemic inflammation, were higher in the CNLDO group, while the platelet value was lower. Nevertheless, we could not establish a relationship between systemic inflammatory markers and recurrence.

Monocytes play an essential role in inflammation and can independently predict cardiovascular events (37). We hypothesize that there may be a correlation between monocyte levels and CNLDO.

The study has limitations such as its retrospective nature, small sample size, and lack of biopsy examinations. Future studies with a larger number of recurrent cases and biopsy examinations can better explain the relationship between systemic inflammatory biomarkers and probing recurrence.

This is the first study to assess the relationship between probing in CNLDO patients and inflammatory biomarkers. Monocyte and MLR levels were significantly higher, and platelet values were significantly lower in CNLDO patients compared to healthy controls.

Monocyte and MLR can be used as simple, inexpensive, and reliable indicators to predict the cause and outcome of CNLDO in patients. We have demonstrated that CNLDO patients can achieve successful results with probing in children in later months. Further studies may reveal the link between probing success and systemic inflammation in CNLDO.

Ethical approval

This study has been approved by the Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (approval date 14/09/2023, number 2023/100). Written informed consent was obtained from the participants.

Author contribution

Concept: NS; Design: NS; Data Collection or Processing: MÇ; Analysis or Interpretation: SAK; Literature Search: NS; Writing: NS. All authors reviewed the results and approved the final version of the article.

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RESEARCH ARTICLE

Investigation of perinatal asphyxia in term newborns with postnatal feeding intolerance

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ABSTRACT

Aim: Perinatal asphyxia affects whole body systems and depending on compensation mechanisms, the central nervous system is primarily protected. In this study, we aimed to evaluate brain electrophysiological activity in cases with postnatal feeding intolerance due to perinatal asphyxia and to investigate whether the compensation mechanism is adequate or whether there is a minimal electrophysiological disorder.

Methods: This study was conducted prospectively to compare the amplitude electroencephalography (EEG) recordings of 22 patients who were followed up with the diagnosis of feeding intolerance due to perinatal asphyxia and 10 control groups. Eeg probes were applied by gluing. Conventional EEG was performed in the patient group and the recordings were evaluated with an amplitude integrated electroencephalography (aEEG). It was also compared with feeding time, length of hospital stay, maternal ages, cord blood gas pH and base deficit values, electrolyte values at the 24th hour, appearance pulse grimace activity and respiration (APGAR) and Burdjalov scores.

Results: When aEEG Vmin values, Burdjalov scores, and 1st min APGAR scores were compared, statistically significant difference was found between the patient and control groups. There was an inverse weak correlation between the patients' aEEG Vmin values and their length of hospital stay. A weak correlation was found between the cases' cord blood gas base deficit and aEEG Vmax values. When cases were divided into two groups as less than 7 days of hospitalization and more than 7 days of hospitalization, a statistically significant difference was found between the groups in terms of maternal age.

Conclusion: In our study, it was aimed to show whether there is a minimal effect of perinatal asphyxia on EEG findings in newborns with nutritional deficiency. The difference in the aEEG Vmin values of the case and control groups indicates that brain electrical activity is affected. This is also supported by the fact that those with higher Vmin values had shorter hospital stays.

Keywords: aEEG, cEEG, feeding intolerance, perinatal asphyxia

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INTRODUCTION

Perinatal asphyxia criteria include cord blood gas pH and base deficit values. Neurological examination, amplitude integrated electroencephalography (aEEG), and near infrared spectroscopy (NIRS) are used to monitor whether or not the central nervous system is affected. Conventional EEG (cEEG) is an important diagnostic tool, which is a detailed and complementary examination method in the clinical, neuroradiologic and electrophysiologic evaluation of newborns. cEEG is used to determine the level of brain damage and to determine the possibility of permanent neurologic sequelae. However, its use in the neonatal intensive care units is limited (1).

Continuous monitoring of cerebral activity can contribute to the assessment of the degree of cerebral damage and evaluation of prognosis, monitoring of seizure activity and response to treatment (2-5). In addition, electroencephalographic monitoring helps early identification of neonates suitable for neuroprotective treatment such as hypothermia (5,6).

In the early period following perinatal asphyxia, aEEG tracing is very effective in predicting neurological prognosis in term infants (7). There are many studies in the literature reporting that the background rhythm in aEEG is compatible with the neurological examination (8).

Electrical seizures should be screened with aEEG monitoring in term newborns at risk, and if suspected or when an electrical seizure is detected, this should be confirmed by cEEG or video EEG monitoring before starting antiepileptic treatment (5,9,10).

In this study, it was aimed to investigate perinatal asphyxia in term newborns with postnatal feeding intolerance and its effects on the central nervous system. The CNS impact was evaluated by investigating whether the compensation mechanism was sufficient with aEEG or whether the electrophysiological impaction was minimal.

MATERIAL AND METHODS

In this study, patients with insufficient suction, swallowing coordination or feeding intolerance in the postpartum days were evaluated, between 2020-2022 in the Bolu Abant Izzet Baysal Education and Research Hospital. The cases that are clinical decided or proven early neonatal sepsis were excluded, and only the cases with inadequate feeding were evaluated. Amplitude EEG recordings were compared in 22 patients who were thought to have feeding intolerance as a result of compensation due to perinatal asphyxia and 10 healthy controls, these records were compared for feeding time, hospitalization duration, maternal ages, cord blood gas pH and base deficit values, electrolyte values at the 24th hour, Apgar and Burdjalov scores. At the same time, cEEG recording were obtained to the case group, and it was checked for compatibility with the aEEG recordings. The study was conducted prospectively. aEEG and cEEG probes were applied by gluing.

The study protocol was approved by the Abant Izzet Baysal University Clinical Research Ethics Committee (13.07.2021 / 2021/168).

The data obtained from the study were recorded and analyzed using the standard program "Statistical Package for Social Sciences for Windows 20.0". Microsoft Excel was used for some graphs. The Pearson correlation test was used to measure the relationship between variables. The Mann-Whitney U test was used for nonparametric data. P-value <0.05 was considered significant.

In the study, aEEG scores, cEEG grading results, neurological examination findings, cord blood gas values, aEEG voltage values, feeding initiation times, hospitalization duration and maternal ages were compared.

RESULTS

Twenty-two patients in the neonatal intensive care unit were included in the study. Nine (40%) of the patients were female and 13 (60%) were male. The boy/girl ratio was 1/1.4. The median Vmin value of the patient group was 7.5 (6-8.25) and the median Vmin value of the control group was 9.5 (7.75-13.5). The median Vmax value of the patient group was 53.5(47.25-76.25) and the median Vmax value of the control group was 67.5 (58.75-90) (Table 1).

An inverse correlation was found between the patient's aEEG Vmin values and their length of hospital stay (r=-0.507, p=0.003). A correlation was detected between cord blood gas base values and aEEG Vmax values of the patients (r=0.450, p=0.01) (Table 2).

A statistically significant difference was found between the case and control groups when comparing 1st minute APGAR scores (p<0.05) (Figure 1), aEEG Vmin values (p<0.05) (Figure 2) and Burdjalov scores (p<0.05) (Figure 3).

A statistically significant difference was found in maternal ages between the patients hospitalized for less than 7 days and those hospitalized for more than 7 days (p<0.05) (Figure 4).

DISCUSSION

In our study, we aimed to evaluate brain electrophysiological activity in cases with postnatal feeding intolerance due to perinatal asphyxia and to investigate whether the compensation mechanism is adequate or whether there is a minimal electrophysiological effect on the brain. aEEG Vmin values, APGAR score in first minute and Burdjalov scores were lower in the patient group. There was no difference between the groups in aEEG Vmax, APGAR fifth minute scores, feeding time, cord blood gas pH and base deficit values and electrolyte values at the 24th hour.

In a study of 89 newborns with perinatal asphyxia, a correlation was found between aEEG scores and APGAR 1st and 5th minute scores. In our study, we found no correlation between aEEG scores and 5th minute APGAR scores. However, we found a statistically significant difference between the aEEG and 1st minute APGAR scores of the patient and control groups (p<0.05). We did not include moderate and severe asphyxia cases in the study. There may have been no difference in APGAR scores because the patients did not have significant asphyxia (11).

Table 1. Results of patient and control groups

	Patient Median (IQR 25-75)	Control Median (IQR 25-75)
pH of the cord	7.31 (7.16-7.36)	7.33 (7.3-7.36)
pCO2 of the cord (mmHg)	39.5 (37-61.25)	44.55 (37-51.48)
HCO3 of the cord (mEq/L)	20.35 (17.9-21.77)	22.3 (19-25.53)
Base deficit of the cord (mmol/L)	-6.5 (-11.62- -2.8)	-5.3 (-6.5-3.13)
Lactate of the cord (mmol/L)	3.19 (1.94-5.98)	2.70 (1.5-4.17)
Hospitalization duration (day)	9.5 (7-11)	1 (1-1)
Time to start feeding (day)	1.5 (1-2.25)	1 (1-1)
Voltage minimum (μV)	7.5 (6-8.25)	9.5 (7.8-13.5)
Voltage maximum (μV)	53.5 (47.25-76.25)	67.5 (59-90)
Burdjalov score	12.5 (12-13)	13 (13-13)
APGAR score (1.min)	6.5 (6-7)	7 (7-8)
APGAR score (5.min)	8 (7-9)	8.5 (8-9)
Maternal age	30.5 (25.75-37)	30 (28-34)

Table 2. Correlation values between patients and controls EEG Vmin, Vmax, cord blood base deficits, day to start feeding, and their hospitalization duration values

		pH	V min	V max	Base deficit
V min	r	0.036			
	p	0.843			
V max	r	0.231	0.158		
	p	0.203	0.388		
Base deficit	r	0.768	0.084	**0.450**	
	p	0.000	0.648	**0.010**	
Day to start feeding	r	-0.024	-0.148	-0.267	-0.017
	p	0.895	0.418	0.139	0.926
Hospitalization day	r	-0.175	**-0.507**	-0.309	-0.180
	p	0.339	**0.003**	0.085	0.324

r: Pearson correlation, p: p value

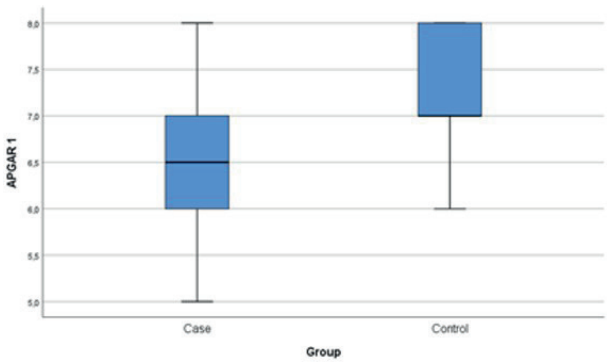

Figure 1. Comparison of the 1st minute APGAR scores between patient and control groups.

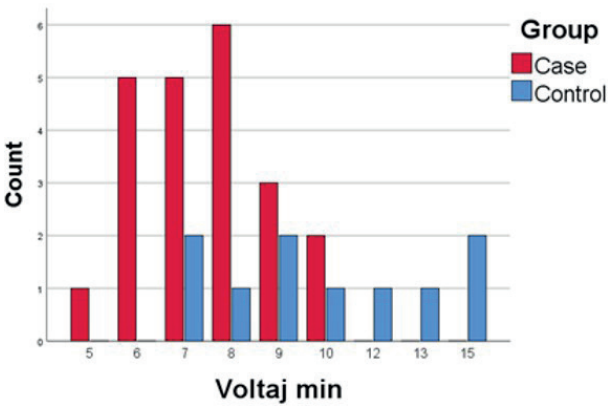

Figure 2. Comparison of aEEG Vmin values between patient and control groups.

In the study conducted by Pichler et al.[12] when the aEEG Vmin and Vmax values of newborns with and without postnatal resuscitation were compared, the Vmin and Vmax values of those without resuscitation were found to be higher. In our study, a statistically significant difference was found between the patient and control groups when the aEEG Vmin values of the cases were compared, ($p<0.05$). At the same time, a weak inverse correlation was found between Vmin values and the length of hospital stay ($r=-0.507$, $p=0.003$). This suggests that there was a decrease in Vmin values due to perinatal asphyxia and that patients needed longer hospitalization. There was no difference in Vmax values between the groups. The reason why we did not detect a difference in Vmax values may be that there was no significant decrease in the Vmax values of the patients because we did not include moderate and severe asphyxia cases. The difference in Vmin values may also be due to insufficient blood supply to the brain and damage from free oxygen radicals. We think that in mild asphyxia, there may be CNS involvement without short-term sequelae.

The two most important parameters in the assessment are the pH and base deficit, which show metabolic acidosis (13). In our study, a weak correlation was detected between cord blood gas base deficit values and aEEG Vmax values ($r = 0.450$, $p = 0.01$). Changes in

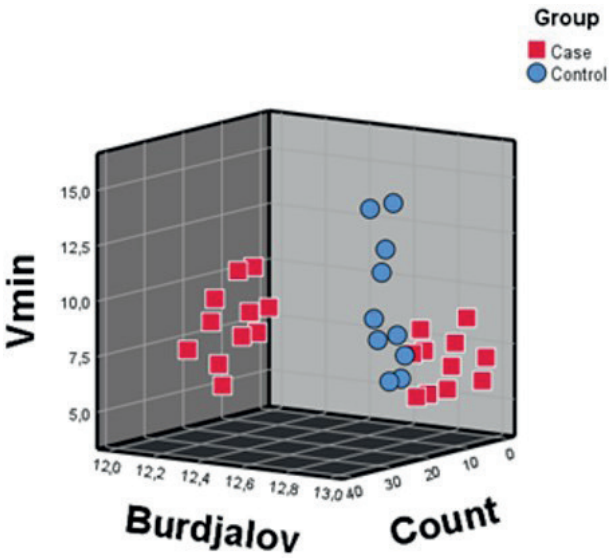

Figure 3. Comparison of Burdjalov scores between patient and control groups.

this base deficit and Vmax values in the cases support the minimal effect of perinatal asphyxia.

Burdjalov et al.[14] developed a different scoring system with 146 aEEG recordings in 30 newborns. Scores were created by rating the continuity, sleep-awake, lower-limit amplitude value and upper-limit value components. In our study, a statistically significant difference was found between the patient and control groups when Burdjalov scores of the patients were compared ($p<0.05$). The significant difference between Vmin, APGAR 1st minute scores and Burdjalov scores supports that the patient group was exposed to minimal asphyxia.

Comparative studies on the effectiveness of aEEG in seizure detection have concluded that electrical seizures in term newborns at risk should be screened with aEEG monitoring and, if suspected or when an electrical seizure is detected, this should be confirmed by cEEG or video EEG monitoring before starting antiepileptic treatment (5,9,10). In our study, no seizure activity was detected on aEEG and cEEG. Normal detection of cEEG was a finding we expected since moderate and severe asphyctic cases were not included in the study.

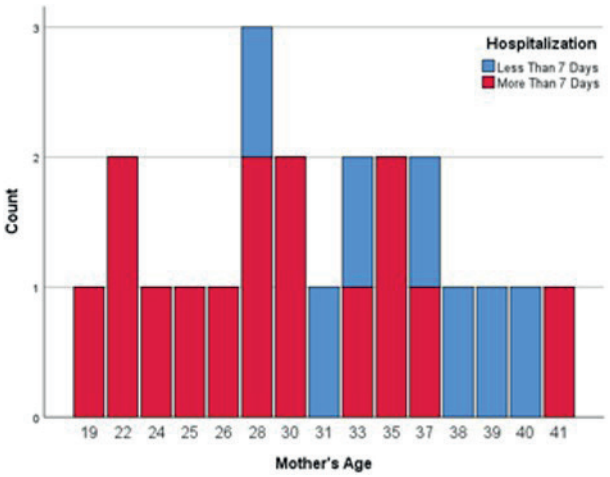

Figure 4. Comparison of mother's ages between patient and control groups.

In a study by Topçuoğlu et al.[15], the use of assisted reproductive techniques, multiple pregnancies, gestational diabetes and pre-eclampsia were found to be higher in older mothers compared to other age groups. In our study, when the cases were divided into two groups with a hospitalization period of less than 7 days and more than 7 days, a statistically significant difference was found between the groups in terms of maternal age ($p<0.05$). Fetuses are exposed to more prenatal stress in the uterus, which disrupted maturation and development, and as risk factors increase with maternal age. Therefore, the length of stay of wewborns in intensive care may be extended.

A study reported that the development and implementation of better evidence-based nutrition support practices in newborns led to improved nutrient intake and decreased growth, length of hospital stay and related costs (16). In our study, the feeding initiation times of the patient groups were found to be similar.

This study shows cerebral involvement as assessed by early aEEG. We included only term infants and excluded moderate and severe asphyctic patients. The relatively small study population is a limitation, and the findings need to be reproduced in larger cohorts. It is known that the brain is severely affected in asphyctic

patients. In our study, we showed that there were changes in brain electrophysiological activity even in mild asphyctic cases.

The limitations of this study are the small number of patients and the selection of term newborns to reduce effect of other risk factors.

Nutritional deficiency is observed in newborns with perinatal asphyxia. In perinatal asphyxia, the central nervous system is protected by compensatory mechanisms. However, although the CNS is preserved, this does not mean that it is not affected. In our study, it was aimed to show whether there is a minimal effect of perinatal asphyxia in newborns with nutritional deficiency. The difference in the aEEG Vmin values between the case and control groups indicates that the electrical activity of the brain is affected. This is also supported by the fact that those with higher Vmin values had shorter hospital stays.

Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 13.07.2021, number 2021/168). Written informed consent was obtained from the participants.

Author contribution

Concept: AE, ST; Design: AE, ST; Data Collection or Processing: AE, ST, AD, FH, MD; Analysis or Interpretation: AE, MD; Literature Search: AE, ST, MD; Writing: AE, ST, AD, FH, MD. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

An evaluation of clinical and epidemiological characteristics and autoantibody status of children with type 1 diabetes mellitus at presentation

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ABSTRACT

Aim: The purpose of this study was to examine clinical and epidemiological characteristics and autoantibody status of children diagnosed with type 1 diabetes mellitus (DM) at presentation.

Methods: The data retrieved from the medical records of 80 patients with type 1 DM, aged under 18 and diagnosed at the Adıyaman Education and Research Hospital, pediatric endocrinology clinic and emergency department between September 2016 and December 2021 were examined retrospectively. Patients' symptoms at presentation and clinical and laboratory findings were recorded.

Results: Thirty-four (42.5%) of the children with type 1 DM were girls and 46 (57.5%) were boys, with a mean age of 10.69±4.75 years. The presentation was most common in the 5-10 (33.8%) and 10-15 (31.3%) age groups. Diabetic ketoacidosis (DKA) was present in 36 (45%) of the children with type 1 DM at presentation, ketosis without acidosis in 30 (38%), and only hyperglycemia in 14. Sixty percent of the patients under five years of age, 48% of those in the 5-10 age group, and 33.3% of the 10-18 age group presented with DKA, and the frequency of presentation with DKA was higher among patients under five years of age than in the other age groups. Severe DKA findings were present in 13 (36%) cases, moderate findings in 10 (27.8%), and mild findings in 13 (36.1%). Anti-glutamic acid decarboxylase positivity was present in 14 cases (53.2%), islet cell antibody positivity in 37 (48%), and anti-insulin antibody positivity in 11 (14.2%).

Conclusion: The incidence rate of DKA in children with newly diagnosed type 1 DM and the rate of severe ketoacidosis among them are quite high in the province of Adıyaman. This shows the need to continue diabetes awareness programs and to reach a larger number of people.

Keywords: children, diabetic ketoacidosis, type 1 diabetes mellitus

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INTRODUCTION

Type 1 diabetes mellitus (DM) is a chronic, progressive disease that progresses with the destruction of pancreatic beta cells, resulting in insufficient insulin secretion, and is mostly seen in the pediatric age group (1). It represents 85% or more of all cases of diabetes in young people under 20 years of age worldwide (2). It exhibits two important peaks in childhood, at 4-6 years and 10-14 years. The first peak is thought to be due to infections, which increase with the start of school, and the second peak is due to increased sex hormones, growth hormone, and psychological stress during puberty (3).

The American Diabetes Association divides the disease into two groups, type A (immune-mediated diabetes [IDM]) and type B (idiopathic diabetes) (4). An autoimmune response to beta cells is observed in 90% of cases of type 1 diabetes, while idiopathic deficiency in beta cells is present in 10% of cases. IDM results from T cell-mediated autoimmune destruction of β-cells (5). Various autoantibodies, such as insulin autoantibodies, islet cell autoantibodies, anti-insulin autoantibodies, glutamic acid decarboxylase antibodies, tyrosine phosphatase antibodies (IA_2), and zinc transporter antibodies (ZnT8A) are implicated in the immune destruction of β-cells (6). This autoimmune destruction of beta cells eventually leads to the clinical findings of diabetes by causing a gradual decrease in insulin secretion. Children with type 1 diabetes are at a greater risk of other autoimmune diseases than healthy children (7). A significant proportion of children and adolescents with type 1 diabetes have detectable organ-specific autoantibodies in addition to pancreatic autoantibodies, and other accompanying autoimmune diseases are present in approximately 25% of patients with type 1 diabetes. The autoimmune diseases most frequently seen in patients with type 1 diabetes is thyroiditis, followed by celiac disease (8).

The purpose of this study was to examine the autoimmune status and clinical and epidemiological characteristics at presentation in children diagnosed with type 1 DM in the Adıyaman Education and Research Hospital pediatric endocrinology clinic or pediatric emergency department, Turkey.

MATERIAL AND METHODS

Data retrieved from the medical records of 80 patients with type 1 diabetes, younger than 18 years of age, diagnosed in the pediatric endocrinology clinic or pediatric emergency department of Adıyaman Education and Research Hospital between September 2016 and December 2021 were analyzed retrospectively. The approval for the study was granted by the Adıyaman University Non-Interventional Research Ethical Committee (decision no. 2021/02-9 dated 16/02/2021).

The diagnosis of type 1 DM was based on the International Society for Pediatric and Adolescent Diabetes criteria (9). Patients' symptoms at presentation, clinical findings, biochemical values, ketone measurements in blood and urine, pancreatic autoantibodies (anti-GAD, islet cell antibody, and anti-insulin autoantibody), C-peptide levels, and venous blood gas results were evaluated. pH <7.3 and/or HCO3 <15 mmol/L in venous blood gas together with hyperglycemia, ketonemia, or ketonuria were defined as diabetic ketoacidosis (DKA). Cases with DKA were divided into three groups, mild, moderate, and severe, based on their pH and HCO3 levels (10). Under that classification, pH 7.2-7.3 or HCO3 10-15 mmol/L were considered mild, pH 7.1-7.2 or HCO3 5-10 mmol/L moderate, and pH<7.1 or HCO3<5 mmol/L severe DKA.

Free T4 and TSH anti-thyroglobulin and anti-thyroid peroxidase antibody levels were investigated in relation to autoimmune thyroid diseases that may accompany type 1 diabetes, anti-tissue transglutaminase (tTG) IgA, and IgG levels were investigated in relation to celiac disease. Free T4 and TSH levels within normal reference ranges were considered euthyroidism, low free T4 and high TSH levels as hypothyroidism, normal sT4 and high TSH as subclinical hypothyroidism, high free T3 and high free T4 were regarded as hyperthyroidism. TSH, fT4, fT3, thyroid peroxidase antibodies, and thyroglobulin antibodies were studied using commercial kits. These tests were performed using electrochemiluminescence assay on a Beckman Coulter DxI800 device with an appropriate kit (Beckman Coulter Access kit, USA). Values above 4.18 IU/mL for Anti-TG and 5.61 IU/mL for anti-TPO

were considered positive. Anti-tTG IgA and IgG levels were analyzed using ELISA REF EIA 31003 and 31004 kits (Euroimmune, Germany). Anti-tTG IgA or anti-tTG IgG ≥15 U/ml reference threshold levels were considered seropositive. The results of the cases with celiac autoantibody levels three or more times higher than the reference threshold value and diagnosed with celiac disease based on upper gastrointestinal endoscopy and biopsy were recorded (11).

Statistical analysis

The research data were analyzed on SPSS Windows 15.0 software. Continuous variables were expressed as mean plus standard deviation, and categorical variables as numbers and percentages.

The chi-square test was applied to compare categorical data. The normality of the data distribution was examined using the Kolmogorov-Smirnov test. In the case of normal distribution, the independent groups t-test was used to compare two independent groups.

RESULTS

Eighty patients, 34 (42.5%) girls and 46 (57.5%) boys, diagnosed with type 1 DM at the Adıyaman Education and Research Hospital between September 2016 and December 2020 were included in the study. Boys outnumbered girls among the newly diagnosed patients with type 1 DM, with a male to female ratio of 1.3:1. The mean age of the patients was 10.69±4.75 years, and there was no significant age difference between the genders (p= 0,365) (Table 1). The presentation was most frequent in the 5-10 age group (33.8%), followed by the 10-15 (31.3%), 0-5 (25%), and 15-18 (10%) age group (Table 2). Thirty-five percent of the patients were diagnosed in winter, 32.5% in the fall, 17.5% in spring, and 13.8% in summer.

Thirty-one patients presented to the clinic with polyuria and polydipsia, 14 with clouded consciousness, 13 with weight loss, 12 with lack of appetite and lethargy, and nine with other non-specific symptoms, while one patient presented for routine screening (Table 2).

DKA was present at the time of the presentation in 36 (45%) of the children with type 1 DM included in the study, ketosis without acidosis in 30 (38%) and hyperglycemia in 14 (17.5%). The patients' laboratory results at the time of the diagnosis are shown in Table 1. Severe DKA was present in 13 (36%) patients, moderate DKA in 10 (27.8%), and mild DKA in 13 (36.1%). No significant difference in the mean HbA1c levels was observed among the cases presenting with DKA and those of patients without DKA at the time of the presentation (p=0,851) (Table 3). Sixteen (44.5%) of the patients presenting with DKA were girls, and 30 (55.5%) were boys. No significant difference was determined in terms of gender (chi-square p: 0.101). In terms of age groups, 60% of patients under five years of age, 48% of those aged between 5-10, and 44% of those aged between 10-15 presented with DKA. None of the patients in the 15-18 age group presented with DKA, and the highest incidence rate of DKA was observed in the children group under five years of age (p=0.017) (Table 4). There was a family history of type 1 DM in seven (9%) cases, type 2 DM in 35 (43.8%),

Table 1. Patients' age distribution and laboratory findings at presentation

Gender	Mean	SD	Minimum	Maximum
Age of female patients' (year)*	9,1	4,4	1,5	15,4
Age of male patients' (year)*	11,8	4,7	2,4	17
Serum Glucose (mg/dL)	487,18	191,65	145	811
HbA1c	12,43	2,61	7,3	18
Serum C-peptide (ng/mL)	0,45	0,42	0,10	2,44
Venous blood pH	7,23	0,15	6,78	7,41
Venous blood HCO3 (mmol/L)	14,21	6,93	2,4	25,2
Venous blood pCO2 (mmHg)	27,34	10,47	8	46

*İndependent samples t-test (p=0,365)

Table 2. Distribution of some characteristics of the patients

	n	%
Application age		
0-5 age	20	25
5-10 age	27	33,8
10-15 age	25	31,2
15-18 age	8	10
Application complaint		
Polyuria-polydipsia	31	38,75
Clouding of consciousness	14	17,5
Weight loss	13	16,25
Lack of appetite and fatigue	12	15
Nausea and vomiting	4	5
Dry mouth	2	2,5
Abdominal pain	2	2,5
Tiredness	1	1,25
Routine examination	1	1,25
Autoantibody Positivity in Female		
Anti GAD	22	66,7
Anti insulin antibody	7	21,7
Islet cell antibody	17	51,5
Autoantibody Positivity in Male		
Anti GAD	19	44,2
Anti insulin antibody	4	9,3
Islet cell antibody	20	46,5

Anti GAD: anti-glutamic acid decarboxylase

Table 3. Comparison of patients' initial HbA1c levels according to presentation with DKA

Initial Application Table	n	HbA1c Mean±SD	p value*
DKA	14	12,65±2,61	0,851
Non-DKA	66	12,25±2,62	

DKA: Diabetic ketoacidosis *İndependent samples t-test

and both type 1 and type 2 DM in seven (9%) cases. Thirty-six cases had no family history of diabetes. The incidence of presentation with DKA was significantly lower among children with a family history of diabetes compared to those with no such family history (p=0,005) (Table 4).

Autoantibody status

Analysis of pancreatic autoantibodies revealed anti-GAD positivity in 41 (53.2%) cases, islet cell antibody positivity in 37 (48%), and anti-insulin antibody positivity in 11 (14.2%). No autoantibody positivity was observed in 18 (22.5%) cases. Three patients' autoantibody values were unavailable. While no statistically significant difference was observed for all pancreatic autoantibodies, the autoantibody positivity rate was higher in girls than in boys (Table 2). Anti-GAD positivity was 66.6% in girls and 44.2% in boys (p=0.05), anti-insulin antibody positivity was 21.2% in girls and 9.3% in boys (p=0.144), and islet antibody positivity was 51.5% in girls and 46.55 in boys (p=0.665). No association was found between autoantibody positivity, age at diagnosis, or C-peptide levels and presentation with DKA (p=0.473, p=0.580, and p=0.827, respectively).

Patients with type 1 DM were also screened for other potential accompanying autoimmune diseases at the time of the diagnosis. When the patients were evaluated for chronic autoimmune thyroiditis, anti-TPO positivity was detected in seven (8.8%), and anti-thyroglobulin positivity in four (5%). Hypothyroidism was present in only one case with autoantibody positivity. A screening for celiac , which is another autoimmune disease, was also carried out. Anti-tTG IGA positivity was present in 21 (26.3%) cases and anti-tTG IgG positivity in 15 (18.8%). Celiac disease was diagnosed in eight (10%) of the cases with celiac antibody positivity. Two patients with negative celiac autoantibodies at presentation became positive in the subsequent months, and celiac disease was diagnosed after biopsy. Three patients with initial mildly positive autoantibodies were found to be celiac antibody negative during the investigation after six months.

Table 4. Relationships between presence of DKA at initial presentation and age and familial history of diabetes mellitus

	DKA (+)		DKA (-)		p value
Age group	**n**	**%**	**n**	**%**	
0-5 age	12	60	78	40	**0,017**
5-10 age	13	48,1	14	51,9	
10-15 age	11	44	14	56	
15-18 age	0	0	8	100	
DM in the family					
Tip 1 DM	4	28,6	10	71,4	**0,005**
Tip 2 DM	11	31,4	24	68,6	
No diabetes	10	67,7	21	32,3	

DM: Diabetes Mellitus, DKA: Diabetic ketoacidosis

DISCUSSION

This study was conducted in the province of Adıyaman in the southeast of Türkiye and is important in terms of examining the immediate clinical and epidemiological characteristics and autoantibody status of children with type 1 diabetes in the region.

The mean age at diagnosis of the children with type 1 DM in this study was 10.69±4.75 years. Presentation was most common in the 5-10 year age group, followed by the 10-15 year age group. Differences between age groups have also been observed in other studies. Studies from Sweden and Finland, where type 1 diabetes is frequently seen, have reported a peak in the 5-9 age group (12,13). Studies from Türkiye have also identified the ages at which type 1 diabetes is frequently seen. In another study of 1079 children with type 1 DM in the Turkish province of Izmir, the mean age at diagnosis was 7.78 years, and presentation was most frequent in the 4-12 age group (14). A study from Northwest Türkiye investigating the incidence of type 1 DM reported that presentation was most common in the 5-14 year age group, followed by the 15-17 year age group (15).

Type 1 DM exhibits gender differences. Male dominance has been reported in countries with a greater incidence of type 1 diabetes, and female dominance in those with a lower incidence (16-18). A study from Sweden reported no gender difference in the incidence of type 1 diabetes between the ages of 0 and 14, but that male dominance emerged at 15-40 years of age (19). This gender difference has been attributed to greater peripheral insulin resistance in males and to hormonal effects. Poyrazoğlu et al. reported male dominance in children under 18 years of age with type 1 DM, except in the 5-9 age group, in which female gender was dominant (15). Similarly, Svensen et al. found male dominance in children with type 1 DM in the 0-14 age group in Denmark (16). Although autoimmune diseases are more common in girls, studies have shown that type 1 diabetes has a greater effect on boys. Consistent with the previous literature, male gender dominance was also observed in newly diagnosed children with type 1 DM in the present study.

Several studies have shown a seasonal association with the time of diagnosis of type 1 DM. A study from Greece involving 105 children with type 1 DM, aged between one and 16 years, found that the diagnosis was made in cold, rainy months such as March and October (20). Another study from the city of Medina in Saudi Arabia, where the average temperature in spring and summer is 40 degrees Celsius, also reported that more patients were diagnosed in the fall and winter, which are relatively cooler than the summer (21). This seasonal correlation has also been supported by extensive studies. Research by the SWEET study group involving 203,603 patients with type 1 DM documented that rates of diagnosis were higher in the fall and winter and lower in the spring and summer,

while no variation was observed in terms of gender or geographical latitude (22). Attempts have been made to explain the relationship between diagnosis of diabetes and seasonal variations in terms of such factors such as exposure to viral infections, changes in physical activity, school stress, and changes in vitamin D synthesis. Consistent with the previous literature, in the province of Adıyaman, with its warm and rainy winters and hot and dry summers, this study showed that presentations with type 1 DM were also more frequent in the fall and winter in this study.

The most common symptoms at time of diagnosis in children with type 1 DM are polyuria, polydipsia, weight loss, and fatigue (23). The most common complaints at presentation in the present study were polyuria-polydipsia (39%), blurred consciousness (18%), and weight loss (16%). Clinical symptoms in type 1 diabetes generally commence 2-3 weeks before diagnosis. Some studies have shown that the time to onset of symptoms is even shorter in very young children (24,25). Diagnosis may be delayed since these symptoms are non-specific, and DKA, a fatal complication, may be the first reason for presentation (26). The incidence of DKA at the time of diagnosis in studies from Türkiye ranges between 41% and 65% (12,27). Germany and Sweden, countries with higher socio-economic levels, reported rates of 20% and 19.5% respectively (26,28). Despite the awareness campaigns aimed at preventing DKA, data from 13 developed countries showed that the incidence of DKA at the time of diagnosis in children with type 1 DM increased slightly between 2006 and 2016 (26). Another international study reported that incidence of ketoacidosis in children with type 1 diabetes was 30% in 2002-2010 and increased to 38.5% in 2010-2016 (29). Similarly, a study from the Aegean region of Turkey reported that the incidence of DKA at the time of diagnosis was 36.4% in 1999-2014 and subsequently increased to 46.5% (30). In the present study, the incidence of DKA at the time of the diagnosis was 45%. The incidence rate of presentations with DKA in our province reflects the data from Türkiye. However, it exceeds the figures reported for developed countries. Cases of severe DKA accounted for 36% of all patients presenting with DKA at the time of diagnosis. A study of 41,189 newly diagnosed cases of type 1 DM in Germany reported that only 6.1% of them involved severe DKA (28), which is much lower than the figure in our region. Various studies have shown that living in countries with a high incidence rate of type 1 diabetes and having a family history of type 1 diabetes reduce the rate of presentation with DKA, whereas being younger than five years of age and having a low socioeconomic level increase the risk of presentation with DKA (31,32). Segerer et al. determined a higher incidence of ketoacidosis at the time of diagnosis in young children compared to older children and adolescents and attributed the difference to the difficulty in interpreting clinical symptoms and findings in young children (28). In the present study, the rate of presentation at time of diagnosis in children under five with type 1 DM was approximately 60%, higher than in the other age groups. Awareness of the symptoms of diabetes may reduce the rate of presentation with DKA by allowing early recognition of the disease. The rate of presentation with DKA at the time of diagnosis and the incidence of severe DKA, both of which were being high in the present study, may be related to low socioeconomic status and difficulties accessing health services in these families.

Studies have found pancreatic autoantibody positivity in approximately 80-90% of children newly diagnosed with type 1 DM (33,34). In a study of 757 patients under the age of 15 newly diagnosed with type 1 DM, Sabbah et al. reported anti-GAD positivity in 73.2% of cases, IA-AA positivity in 85.7%, IAA positivity in 54.2%, and multiple autoantibody positivity in 72.6% (35). Children with multiple autoantibody positivity in that study were younger than the others, had lower serum C-peptide levels at the time of diagnosis, and had higher daily insulin needs at 12-, 18-, and 24-months of follow-up. Based on their findings, Sabbah et al. hypothesized that diabetes-associated multiple autoantibody positivity accelerates pancreatic b-cell destruction and is also associated with increased exogenous insulin requirements in the second year of the disease (35). Pancreatic autoantibody positivity was present in 78% of the cases in the present study. The most common was anti-GAD antibody positivity (51.2%), followed by islet cell antibody positivity (46.3%) and anti-insulin antibody (13.8%) positivity. Single autoantibody positivity was present in 49% of cases, double autoantibody positivity in 40%, and triple autoantibody positivity in 5%. No relationship was

determined between autoantibody positivity and age at diagnosis, C-peptide levels, or presentation with a manifestation of DKA.

Type 1 DM may be comorbid with other autoimmune diseases. Autoimmune thyroiditis is one of the most common immunological disorders in patients with type 1 DM, with rates of thyroid autoantibodies ranging between 3% and 50% (36). Jung et al. reported a rate of 26% in their study of children newly diagnosed with type 1 DM (37). Analysis of our patients for chronic immune thyroiditis at presentation revealed anti-TPO positivity in seven (8.8%) cases and anti-thyroglobulin positivity in four (5%). Hypothyroidism was diagnosed in only one of these cases, and thyroid hormone therapy was initiated. Accompanying celiac antibody positivity may also be seen in children with type 1 DM at the time of diagnosis. In their study of 425 newly diagnosed children with type 1 DM, Rinawi et al. determined anti-tTG antibody elevation in 34 children (8%), of whom 14 were diagnosed with celiac disease after biopsy (38). In the present study, anti-tTG IGA positivity was observed in 21 (26.3%) and anti-tTG IgG positivity in 15 (18.8%) cases at presentation, which are higher than those reported by Rinawi et al. Eight of these cases were diagnosed with celiac disease after biopsy (38). In two patients with negative autoantibodies at presentation, autoantibodies became positive in the following months and celiac disease was diagnosed after biopsy. In addition, Rinawi et al. reported an initial mild anti-tTG positivity in 13 patients, which normalized over time (38). Similarly, in the present study, antibody levels investigated after six months were found to have normalized in three patients with an initial mild autoantibody elevation. This finding shows that patients with mild anti-tTG antibody elevation at baseline should not be rushed into a gluten-free diet.

The main limitations of this study are its single-center nature and the small number of cases. However, this study is particularly valuable in presenting four years of type 1 DM data for our region.

In conclusion, the average rate of presentation with DKA in children newly diagnosed with type 1 DM in the province of Adıyaman is 45%, but is as high as 60% in children under the age of five. In addition, the rate of severe ketoacidosis among cases presenting with DKA is quite high. Continuing of diabetes awareness programs and raising awareness of families and society about diabetes symptoms can reduce the incidence of this important complication of type 1 diabetes. Screening newly diagnosed children with Type 1 DM for other autoimmune diseases such as Hashimoto's thyroiditis and celiac disease is important for early diagnosis and treatment.

Ethical approval

This study has been approved by the Adıyaman University Non-Interventional Clinical Research Ethics Committee (approval date 16.02.2021, number 2021/02-9). Written informed consent was obtained from the participants.

Author contribution

Concept: SB, AA; Data Collection or Processing: SB, AA; Analysis or Interpretation: İHB, AA; Literature Search: SB, AA, İHB; Writing: SB, AA, İHB. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

Can the systemic immune inflammation index (SII) and the systemic inflammation response index (SIRI) predict the severity of coronary artery disease?

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ABSTRACT

Aim: To examine the relationship between complete blood count metrics and the severity of coronary artery disease (CAD) in patients undergoing coronary angiography.

Methods: Patients diagnosed with stable angina pectoris or acute coronary syndrome by coronary angiography between October 2018 and February 2019 were included in the study. Based on their angiography results, patients were divided into two groups: one with severe CAD (n=258) and one with non-severe CAD (n=219). The initial clinical characteristics, along with data from laboratory tests and complete blood counts, were recorded and compared between the two groups.

Results: The Wight Blood Cell (WBC) count, Neutrophil (NEU) count, Monocyte/Lymphocyte Ratio (MLR), Neutrophil/Lymphocyte Ratio (NLR), Monocyte/High-Density Lipoprotein Cholesterol Ratio (MHR), systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) were each significantly higher in the group with severe CAD than in the group without severe CAD. The analysis utilized logistic regression, factoring in recognized CAD risk factors such as age, gender, diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), and smoking, identified NLR, MHR, MLR, SII, and SIRI as notable and independent indicators of severe CAD.

Conclusion: Our study showed that since it was an independent predictor of CAD, SII and SIRI could be utilized as a novel indicator for assessing the severity of CAD.

Keywords: complete blood count, coronary artery disease, inflammation, systemic immune inflammation index, systemic inflammation response index

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INTRODUCTION

Coronary artery disease (CAD), characterized by a prolonged progression over time and primarily attributed to atherosclerosis, stands as the primary cause of mortality globally, accounting for more than 30% of deaths beyond the third decade of life (1). Known for its latent development over an extended duration, atherosclerosis eventually manifests clinically and contributes notably to CAD. The recognized risk factors for atherosclerosis such as diabetes mellitus (DM), hypertension (HT), dyslipidemia, and smoking, are at least one risk factor in most individuals with CAD, and the presence of more than one of these risk factors creates a synergistic effect (2). When atherosclerotic plaques are examined, they have lipid deposits and foam cells in the center, a cap of smooth muscle cells, and a core region surrounded by a collagen-rich matrix. T cells, macrophages, and mast cells infiltrate the atherosclerotic lesion play a role in its growth, and produce inflammatory cytokines with signs of activation. These inflammatory cytokines and acute phase reactants produced and released into the circulation pose a risk for CAD (3,4). Recent studies have highlighted cost-effective. Hemogram (CBC) parameters that provide critical diagnostic and prognostic insights for diseases related to chronic inflammation, including CAD (5,6). In addition, recent studies have demonstrated the potential of inflammatory hematologic ratios including the NLR, platelet/lymphocyte ratio (PLR), and monocyte/lymphocyte ratio, which are both cost-effective and readily accessible, as well as reflecting the degree of systemic inflammation, and have shown a correlation between the severity, prognosis, and presence of CAD (7). The newly established SII and SIRI are also shown to improve risk prediction in CAD (8,9). In our study, we aimed to compare systemic inflammation indices in patients with and without severe CAD by coronary angiography (CAG).

METHODS

Study design and patient selection

This analysis, performed as a retrospective cohort study, was carried out in the cardiology department of a tertiary referral hospital in Türkiye, with the approval of the local ethics committee. Patients diagnosed with stable angina pectoris or acute coronary syndrome by coronary angiography between October 2018 and February 2019 were included in the study. Exclusion criteria were a recent history of acute coronary syndrome (ACS) before CAG or coronary artery bypass graft (CABG), major valvular heart condition, unstable heart failure, stroke, kidney and liver disease, acute and ongoing infection and inflammatory conditions, oncologic disease, poor nutritional status, hematologic conditions, low platelet count, symptomatic peripheral artery disorder, immune system diseases, pregnancy, and chronic lung disease.

All patients undergoing CAG were tested and categorized into two groups based on the findings of the CAG examination. Group 1 includes the severe CAD group, and Group 2 consists of the non-severe CAD group. All demographic information and laboratory parameters of all patients were obtained from their files by screening. The following laboratory parameters were analyzed: basic biochemical tests; CBC parameters of white blood cell (WBC), neutrophil (NEU), lymphocytes (LYM), platelet count (PLT), mean platelet volume (MPV), NLR, PLR, MLR, and monocyte/high-density lipoprotein cholesterol ratio (MHR). SII is calculated by the formula: (P×N)/L where P, N, and L stand for peripheral platelet, neutrophil, and lymphocyte counts, respectively. SIRI was calculated by the formula (N×M)/L, where N is the peripheral count of neutrophils, and M is the peripheral count of monocytes. A comparison of these recorded data was conducted between the groups. We further analyzed the role of SII and SIRI in predicting the severity of CAD after adjustment for age, sex, DM, HT, and smoking status.

Statistical analysis

SPSS version 15.0 was used to analyze the data. The Kolmogorov-Smirnov method was used for normality tests of the variables. The Student t-test was used to compare normally distributed variables, and these data are shown as mean ± SD. The comparison of non-normally distributed variables was performed using the Mann-Whitney test, and these data are shown as median (IQR). The comparison of categorical variables was done using the chi-square test. Univariate analyses were complemented by multivariate logistic regression analysis to determine the independent variables associated with severe CAD, adjusting for

Table 1. Baseline characteristics of the groups

	Severe CAD (+) n=258	Severe CAD (-) n=219	p value
Age (years)	65±11	61±12	p<0.001
Gender (F/M), n	65/193	94/125	p<0.001
HT, n	159	111	p=0.02
DM, n	131	72	p<0.001
HL, n	78	48	p=0.05
Family History, n	107	70	p=0.04
Smoking, n	112	65	p=0.02
BMI, kg/m^2	29.06±4.9	29.80±5.3	p=0.14
Waist Circumference, cm	106.1±13.8	105.12±15.1	p=0.60

HT: Hypertension, DM: Diabetes Mellitus, HL: Hyperlipidemia, BMI: Body Mass Index, CAD: Coronary artery disease.

Table 2. Laboratory findings of the groups

	Severity CAD (+) n=258	Severity CAD (-) n=219	P Value
HbA1c	7.02±1.7	6.50±1.3	<0.001
Urea	37.69±17.22	33.00±10.6	0.001
Creatinine	0.97±0.50	0.84±0.15	<0.001
GFR	81.03±18.93	87.6±14.9	0.002
Glucose	146.3±69	115.8±51.3	<0.001
TSH	1.17±1.02	2.46±7.17	0.013
HDL, mg/dl	42.33±9.69	46.41±11.16	<0.001
LDL, mg/dl	116.47±39.18	112.93±37.10	0.355
TC, mg/dl	186.88±44.76	187.22±45.42	0.973
TG	152.15±107.10	143.29±94.44	0.461
WBC	8.95±3.11	7.58±2.05	<0.001
NEU	6.0±2.97	4.69±1.68	<0.001
MONO	0.56±0.25	0.49±0.20	<0.001
NLR	3.50±3.10	2.58±1.97	0.001
PLR	138.72±80.38	133.84±68.94	0.794
RPR	0.066±0.018	0.065±0.018	0.678
MPR	0.034±0.011	0.034±0.011	0.363
MLR	0.29±0.17	0.25±0.15	0.004
MHR	0.014±0.007	0.011±0.006	<0.001
SII plt × neu/lym	883.41±829.70	639.32±467.67	0.03
SIRI neu × mono/lym	1.95±1.97	1.27±1.22	<0.001

CAD: Coronary artery disease, HbA1c: hemoglobin A1c, GFR: glomerular filtration rate, TSH: thyroid-stimulating Hormone, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TC: total cholesterol, TG: trigliceride, WBC: wight blood cell, NEU: Neutrophil, MONO: Monocyte, LYM: lymphocyte, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, RPR: red blood cell distribution width/platelet ratio, MPR: mean platelet volume/platelet ratio, MLR: monocyte/lymphocyte ratio, MHR: monocyte/high-density lipoprotein cholesterol ratio, SII: systemic immune inflammation index, SIRI: systemic inflammation response index.

other variables. Statistical significance was defined as a P value of less than 0.05.

RESULTS

A total of 477 patients were enrolled in the study. Group 1 consisted of 258 patients, while Group 2 consisted of 219 patients. A significant difference in gender distribution was observed between the two groups (p<0.001). Group 1 consisted of 75% male and 25% female patients, while Group 2 comprised 57% male and 43% female patients (p<0.001). The mean age of patients in Group 1 was higher than in Group 2. (p<0.001). The general characteristics of the study groups are summarized in Table 1. The groups did not differ significantly in other study data, including height (p=0.03), weight (p=0.95), body mass index (BMI) (p=0.11), and waist circumference (p=0.60), LDL-cholesterol (p=0.36), total cholesterol (p=0.97), LYM (p=0.85), mean corpuscular volume (MCV) (p=0.44), PLT (p=0.96), mean platelet volume (MPV) (p=0.11), and platelet-to-lymphocyte ratio (PLR) (p=0.79).

Compared to Group 2, Group 1 had significantly elevated levels of height, glucose, hemoglobin A1c (HbA1c), urea, creatinine, serum aspartate transferase (AST), potassium (K), WBC, NEU, NLR, MLR, MHR, SII, and SIRI (all p<0.05). Conversely, Group 1 had significantly lower levels of glomerular filtration rate (GFR), thyroid-stimulating hormone (TSH), and high-density lipoprotein (HDL) compared to Group 2 (all values p<0.05) (Table 2). The analysis utilized logistic regression, factoring in recognized CAD risk factors such as age, gender, DM, HT, HL, and smoking, identified NLR, MHR, MLR, SII, and SIRI as notable and independent indicators of severe CAD (Table 3).

Table 3. Independent predictors of coronary artery disease by logistic regression analysis

Variables	p value*	Odds ratio (95% CI)
Age (years)	<0.001	1.036 (1.018, 1.053)
Gender (F/M)	<0.001	2.233 (1.515, 3.292)
HT	0.016	1.563 (1.085, 2.251)
DM	<0.001	2.106 (1.450, 3.058)
HL	0.041	1.544 (1.018, 2.340)
Smoking	0.002	1.817 (1.242, 2.659)
NLR	<0.001	1.169 (1.072, 1.275)
MHR	<0.001	2.225 (7.490, 6.608)
MLR	0.010	5.040 (1.473, 17.246)
SII	<0.001	1.001 (1.000, 1.001)
SIRI	<0.001	1.334 (1.160, 1.535)
PLR	0.482	1.001 (0.998, 1.003)

CI: confidence interval, DM: diabetes mellitus, HL: hyperlipidemia, HT: Hypertension, MHR: monocyte count/HDL cholesterol ratio, MLR: monocyte/lymphocyte ratio, NLR: neutrophil/lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: (Platelet x neutrophil)/ lymphocytes, SIRI: (Neutrophil x monocyte)/ lymphocytes.

*Results of multivariate logistic regression analysis of significant coronary artery disease as the dependent variable.

Bold values indicate p<0.05.

DISCUSSION

Our study revealed that recognized CAD risk factors, including HT, DM, and dyslipidemia, were more prevalent, and certain CBC parameters, including WBC, Neu, Monocyte (MONO), NLR, and MLR, were significantly elevated in patients with severe CAD compared to those without severe CAD. Logistic regression analysis of these parameters, including well-known risk factors for CAD, showed that NLR, MHR, MLR, SII, and SIRI were all significant and independent predictors of substantial CAD, which would label these parameters and indices as an independent predictor of the severity of CAD.

Asymptomatic inflammation is now recognized as pivotal in CAD pathogenesis and progression, involving costly and limited availability of agents like growth factors, cytokines, and adhesion molecules (10). In contrast, CBC parameters, being simple, inexpensive, and easily accessible, have gained traction in recent research for their diagnostic potential.

In various studies, NLR emerged as a determinant of severe CAD, predicting cardiac risk in patients (11). Elevated NLR values correlated with advanced CAD and poorer prognosis (12). Meta-analyses further confirmed the predictive value of NLR for cardiovascular events and all-cause mortality, particularly in groups with progressive atherosclerosis (13). Consistent with the existing literature, our study also found significantly higher NLR levels in Group 1.

Recently, MLR has garnered attention as a notable CBC parameter. Previous studies have shown that MLR levels can help identify fragile plaques in patients with stable angina pectoris and have been proven to independently predict the presence and severity of CAD. Similarly, our study found that MLR was higher in Group 1.

Another inflammation parameter, MHR, has been defined as a new and dramatic marker of cardiovascular diseases in recent years and associated with SYNergy between PCI with TAXUS and Cardiac Surgery' (SYNTAX) and Gensini scores, and is thought to be related to the burden of coronary atherosclerosis. MHR was significantly higher in Group 1 in our study as well.

The recently described SII and SIRI are new inflammatory biomarkers. In a study of 85,154 patients, Jin et al.[8] investigated the associations between SII and SIRI with cardio vasculer diseases (CVD) and all-cause mortality risks, and both indices showed positive associations with stroke risk and all-cause mortality risk. In addition, higher SIRI was associated with a higher risk of MI, whereas SII was not.

Yildiz et al.[9] examined coronary CT angiography data from 1456 patients and observed higher SIRI and SII values in mixed plaque types. They identified SII and SIRI as independent predictors of one-year major adverse cardiac events (MACE), with SIRI enhancing risk prediction in CAD.

Based on the hypothesis that chronic low-grade inflammation is associated with a variety of diseases, Xia et al.[14] recently made an effort to assess the SII, SIRI, and the risk of all-cause mortality and cardiovascular mortality in 42,875 adults during a follow-up of 20 years. They showed higher levels of SII and SIRI associated with higher all-cause and cardiovascular mortality compared to lower levels of SII and SIRI. In a recent study, Wei et al.[15] studied the correlation of SII and SIRI to clinical risk factors that included Global Registry of Acute Coronary Events (GRACE), Gensini, and QTc in 310 patients with AMI. They found that major adverse cardiac events were higher in those with higher levels of SII and SIRI. Moreover, SII was associated with SIRI and potential post-infarction risk factors. Dziedzic et al.[16] aimed to analyze the relationship of inflammation intensity by SII and SIRI with CAG-measured CAD burden and the ACS or stable CAD diagnosis in 699 patients. Stable CAD and ACS patients showed significant differences in SII. The ACS population had significantly higher values, while there was no significant difference among ST elevation myocard infarction (STEMI), non ST elevation myocard infarction (NSTEMI), unstable angina pectoris (USAP) patients. Besides, no such significant relationship was found for SII and SIRI with the severity of CAD.

In a cohort of 669 individuals with stable CAD, Candemir et al.[17] demonstrated a positive correlation between SII and CAD severity as measured by the SYNTAX scale. Similarly, in a study involving 400 patients who underwent coronary angiography, Liu et al.[18] identified a correlation between SII and the Gensini scale of CAD severity. They characterized SII as an independent variable for diagnosing and gauging the severity of CAD.

In our study, both SII and SIRI levels were higher in the group with severe CAD compared to the group without severe CAD.

Finally, logistic regression analysis showed that biomarkers such as NLR, MHR, MLR, SII, and SIRI were significant and independent predictors of CAD. This emphasizes the importance of evaluating markers of inflammation as predictors of disease beyond traditional CAD risk factors.

These findings not only contribute to the understanding of CAD pathophysiology and risk factors but may also help to improve risk prediction and treatment strategies in future clinical practice. However, more prospective studies and further research are needed to integrate these biomarkers into clinical practice.

The retrospective design and the relatively small number of patients are limitations of this study. Nonetheless, it aligns with other studies in the literature. Gensini or Syntax scores were not applied to the study population, which could be the other limitation.

Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 04/07/2023, number 2023/232). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: MFB; Concept: MFB, MC; Design: MFB, MC; Data Collection or Processing: MC; Analysis or Interpretation: MC; Literature Search: MFB; Writing: MFB, MC. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

Evaluation of acute kidney injury patients in intensive care unit and determining effects of hemodialysis on sepsis

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ABSTRACT

Aim: Sepsis-associated acute kidney injury (AKI) is a frequent complication of critically ill patients, and results need for renal replacement therapy (RRT). We aimed to investigate the difference in vital signs, hemodynamic parameters, and laboratory values after receiving RRT in the AKI patients with/without sepsis. Also, we examined the different renal injury grading systems relationships used in intensive care units (ICU).

Methods: RRT-treated patients due to AKI were enrolled. Patients were divided into two groups by using Sepsis-2 criteria (2012); whether there is sepsis or not. Acute physiology and chronic health evaluation II (APACHE II) scores, 28th and 90th day mortality recorded. RIFLE classes, renal sequential organ failure assessment (SOFA) scores, and kidney disease: improving global outcomes (KDIGO), stages were also calculated. Patients' Glasgow Coma Scale (GCS), vital parameters, laboratory values, Horowitz rates, vasopressor/inotropic agent requirements at RRT start, 12th and 24th hours were recorded.

Results: 153 patients were included in the study, and 93 were septic. APACHE II score and 28th day mortality were significantly higher in Group Sepsis. Advanced age was found to be associated with 90th day mortality. Both in two groups many parameters such as acidosis, Horowitz ratio, and GCS improved after RRT initiation. When renal scoring systems were compared with each other KDIGO was associated with the RIFLE classification and renal SOFA.

Conclusion: Many improvements were observed in all AKI patients after RRT but in septic patients, oxygenation and GCS showed better improvement. The mortality rate increased when AKI got complicated with sepsis.

Keywords: acute kidney injury, intensive care medicine, renal replacement therapy, sepsis

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INTRODUCTION

Deterioration in renal functions has been named in different ways. Acute kidney injury (AKI) is characterized by decline in the glomerular filtration rate (GFR), elevation of serum blood urea nitrogen (BUN), creatinine, and other metabolic waste products. The term AKI rather than acute renal failure (ARF), is highly used because of not every case results with organ failure (1).

Sepsis-associated acute kidney injury (S-AKI) is a frequent complication of the critically ill patient and is associated with high morbidity and mortality. Nearly 1 in 3 patients with sepsis develop AKI so the global incidence of S-AKI might be approximately 6 million cases or nearly 1 per 1000 population (1,2).

There has been made a variety of definitions to standardize the diagnosis of AKI. In 2004 Acute Dialysis Quality Initiative (ADQI) Group made the RIFLE classification to be used in the diagnosis and treatment of AKI. In 2007, the RIFLE criteria have been revised and corrections were made by the Acute Kidney Injury Network (AKIN) Group (3). In March 2012 KDIGO (Using the Kidney Disease: Improving Global Outcomes), the new staging system is developed for the diagnosis of AKI based on RIFLE and AKIN criteria (4). In KDIGO, AKI severity is divided into three phases shown in Figure 1.

The first treatment choice in AKI patients is supportive, in serious renal injury cases this means RRT. In a study the incidence of patients diagnosed AKI requiring RRT is 11 of 100,000 people per year (5).

There are many studies in the literature examining the relationship between AKI and sepsis in intensive care units (ICUs) (3,4,6). However, there are not enough studies evaluating the AKI patients receiving RRT comparing groups with and without sepsis and the effectiveness of RRT in septic patients. In our study, we aimed to investigate the difference in hemodynamic parameters and laboratory values after receiving RRT in the AKI patients with or without sepsis. Also, we wanted to display the differences in mortality rates and examine the different renal injury grading systems relationships used in intensive care patients.

MATERIALS AND METHODS

After obtaining ethical approval from Uludağ University Faculty of Medicine, Health Application and Research Center on 9 December 2014 (2014-23/13), CVVHD (Continuous veno-venous hemodialysis)

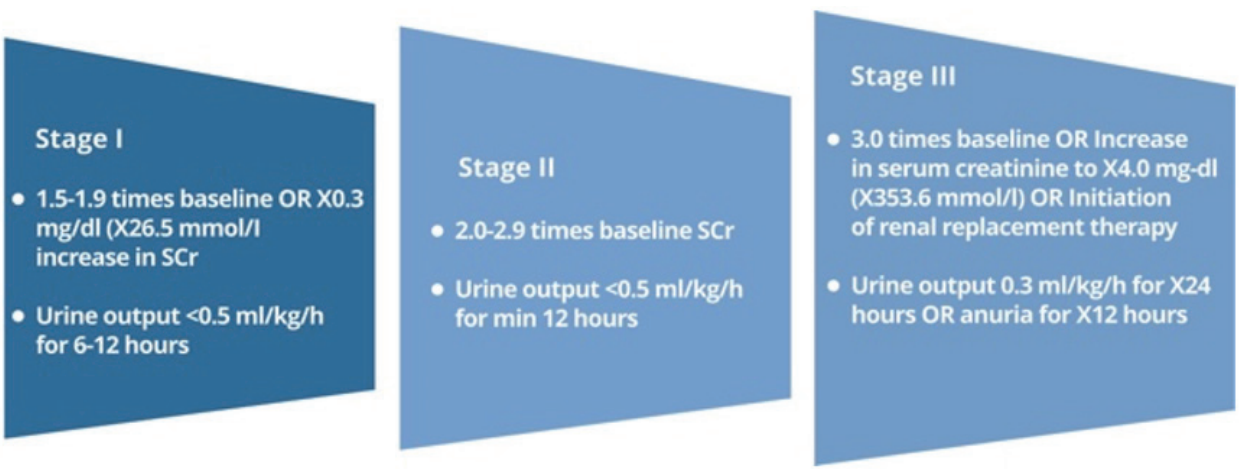

Figure 1. KDIGO stages.

SCr: Serum creatinine value.

treated patients due to the ARF who were accepted to the Reanimation Unit between 01.01.2010–30.06.2014 were enrolled. Patients' demographic datas, concomitant systemic diseases and laboratory values were analyzed retrospectively on the electronic archive of Uludağ University School of Medicine.

A total of 294 patients data were analyzed. 141 patients were excluded; 90 patients were already diagnosed chronic renal failure (CRF), 1 case was 23 weeks pregnant, 26 cases died within 24 hours of CVVHD, 3 patients were under 18 years old, 20 cases had lack of data, 1 case transferred to another clinic within 24 hours CVVHD. A total of 153 patients were enrolled in the study.

Patient demographics, APACHE II (Acute Physiology and Chronic Health Evaluation II) scores, ICU admission indication, 30th day and 90th day mortality were recorded. RIFLE classes, renal SOFA scores, and KDIGO stages were calculated at the beginning of CVVHD. Patients Glasgow coma score (GCS), systolic and diastolic arterial pressure, heart rate, body temperature, central venous pressure, mechanical ventilation and oxygenation parameters, laboratory values, analysis of arterial blood gases, Horowitz rates, vasopressor or inotropic agents requirements in CVVHD start, the next 12 and 24 hours were recorded. GFR (glomerular filtration rate) was calculated by the 'Modification of Diet in Renal Disease' (MDRD) formula. After the decision to start dialysis, it was performed using a Fresenius Medical Care Multifiltrat device with ULTRAFLUX AV600S 1,4m² membrane.

Statistical analysis of the data was held by Uludağ University School of Medicine Department of Biostatistics, at the IBM SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) statistical software. Data show normal distribution were analyzed with the Shapiro-Wilk test. The comparison of the two independent groups, the Mann-Whitney U test for continuous data, and the comparison of the two groups dependent Wilcoxon signed rank tests were used. The level of significance was set at p=0.05.

RESULTS

A total of 153 patients were included in the study. There were 93 patients with septic shock (Group S) and 60 patients without septic shock (Group C). Demographic data of the patients, admission APACHE II scores and concomitant systemic diseases were reported in Table 1. APACHE II score was significantly higher in Group S (p <0.001).

Table 1. Demographic data and accompanying systemic disease of patients (mean ± SD)

	Group C (n=60)	Group S (n=93)	p value
Age	54.3 (18.3)	57.7 (16.3)	0.239
Gender (F/M)	25/35	32/61	0.365
APACHE II score	18.8 (±6.8)	24.5 (±7.4)	<0.001
Concomitant disease			
Hypertension	22 (36.7)	35 (37.6)	0.904
Diabetes mellitus	11 (18.3)	27 (29)	0.192
Malignancy	8 (13.3)	20 (21.5)	0.288
Cardiac failure	13 (21.7)	33 (35.5)	0.101

F: Female, M: Male, APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 2. Laboratory values and vital parameters for Group C [median (min-max)]

	Initiation	12th hour	24th hour	p-value Initiation-12th hour	p-value Initiation-24th hour
GCS	7 (3-11)	7 (3-11)	7 (3-11)	0.401	0.004
MAP (mmHg)	76 (52-134)	76 (50-128)	77 (39-118)	0.717	0.843
Urea (mg/dL)	175 (31-382)	141 (24-340)	117 (30-294)	0.001	<0.001
Creatinine (mg/dL)	3.3 (1-10)	2.55 (0.5-8)	2.05 (0.5-5.7)	0.001	<0.001
GFR (mL/min/1.73 m²)	88 (24-348)	118 (32-751)	148 (50-957)	<0.001	<0.001
pH	7.31 (7.11-7.5)	7.35 (7.12-7.5)	7.36 (7.07-7.5)	0.012	0.002
Bicarbonate (mmol/L)	20 (11-42)	21 (14-31)	22 (11-40)	0.289	0.069
Lactate (mg/dL)	17.5 (5-166)	18 (5-140)	17 (6-141)	0.147	0.118
SpO_2 (%)	98 (81-100)	98 (87-100)	98 (84-100)	0.336	0.855
FiO_2 (%)	0.8 (0.3-1)	0.8 (0.3-1)	0.5 (0.3-1)	<0.001	<0.001
PEEP (cm H_2O)	7 (5-15)	7 (4-15)	6 (4-13)	0.119	<0.001
Body temperature (°C)	36.9 (35-39)	36.5 (36-35)	36.9 (35.7-39.2)	0.051	0.601

GCS: Glasgow Coma Score, MAP: Mean arterial pressure, GFR: Glomerular filtration rate, SpO_2: Pulse oximeter, FiO_2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure.

Table 3. Laboratory values and vital parameters for Group S [median (min-max)]

	Initiation	12th hour	24th hour	p-value Initiation-12th hour	p-value Initiation-24th hour
GCS	6 (3-11)	7 (3-11)	7 (3-11)	0.005	0.001
MAP (mmHg)	71 (42-108)	73 (40-106)	70 (32-107)	0.472	0.422
Urea (mg/dL)	155 (22-314)	124 (22-298)	97 (14-273)	<0.001	<0.001
Creatinine (mg/dL)	3 (0.3-8.4)	2.7 (0.5-7)	2.2 (0.5-7)	<0.001	<0.001
GFR (mL/min/1.73 m²)	103 (33-1319)	129 (38-680)	161 (30-1002)	<0.001	<0.001
pH	7.32 (6.9-7.6)	7.35 (7-7.53)	7.37 (7-7.54)	0.003	<0.001
Bicarbonate (mmol/L)	20 (10-32)	21 (14-35)	21 (13-53)	0.004	0.002
Lactat (mg/dL)	18 (3-164)	18 (7-143)	17 (6-152)	0.701	0.121
SpO_2 (%)	97 (75-100)	98 (68-100)	97 (70-100)	<0.001	0.031
FiO_2 (%)	0.65 (0.3-1)	0.55 (0.25-1)	0.5 (0.25-1)	<0.001	<0.001
PEEP (cm H_2O)	7 (4-15)	7 (4-15)	7 (4-14)	0.002	<0.001
Body temperature (°C)	37.3 (35.5-39.5)	36.8 (34.8-39.4)	36.9 (35.7-39.2)	<0.001	0.003

GCS: Glasgow Coma Score, MAP: Mean arterial pressure, GFR: Glomerular filtration rate, SpO_2: Pulse oximeter, FiO_2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure.

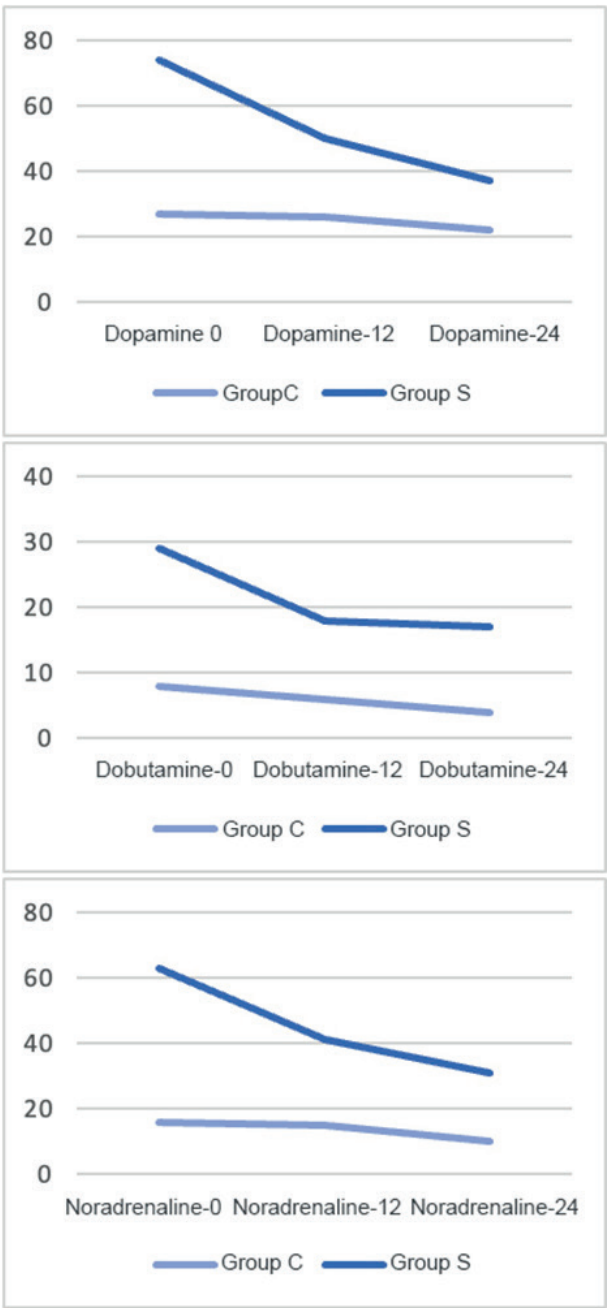

Figure 2. Inotropic and vasopressor drug use.

There were no significant differences between the two groups' KDIGO stages, RIFLE classification and renal SOFA scores in CVVHD start. When renal scoring systems were compared with each other, KDIGO was associated with the RIFLE classification and renal SOFA. Significance values were p<0.001 r=0.354; r=0.248 p=0.02.

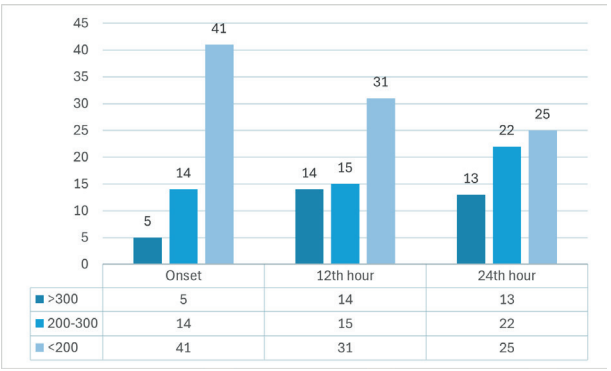

Figure 3. Horowitz ratio of Group C (n).

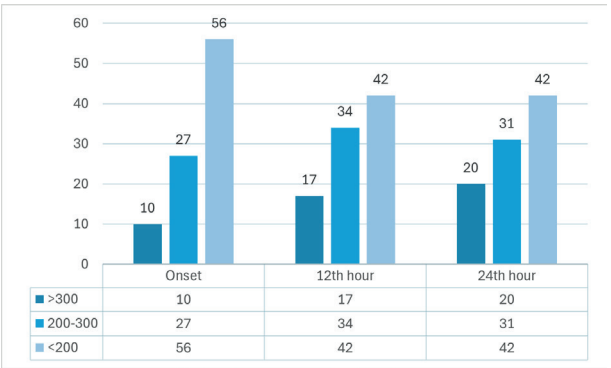

Figure 4. Horowitz ratio of Group S (n).

When age of the patients and 28-90th day mortality relationship are compared; advanced age increases the incidence of mortality at day 90 (p=0.002).

The comparison of laboratory values and vital parameters between CVVHD start the day, 12 and 24 hours after the treatment of Group C and Group S are shown in Table 2 and Table 3.

The comparison of inotropic and vasopressor agent use is shown in Figure 2. In both groups, the use of inotropic and vasopressor agents decreased significantly at 12 and 24 hours after CVVHD (p<0.001).

Horowitz ratio significantly increased after CVVHD in both groups. The significance value is p<0.001 in both groups in 12th hour, while 24th hour for Groups C's significance is p=0.04 and Groups S's significance is p=0.05. Changes are shown in Figure 3 and Figure 4.

DISCUSSION

Acute kidney injury is a clinical syndrome that accompanied by usually reversible reduction in GFR, accumulation of nitrogen metabolites such as urea and creatinine, fluid and electrolyte imbalances, and acid-base metabolism disorders which is closely associated with high mortality.

The incidence of AKI is increased in elderly patients. In our study, although there was no difference in mean age between Group C and Group S, advanced age was associated with 90th day mortality.

Different factors may play a role in the etiology of AKI. One of the most common causes of AKI in the ICU is sepsis. In Poston and Koyner's (2019) study; sepsis is associated with up to 50% of AKI, and up to 60% of patients with sepsis have AKI (7). In Parmar et al.'s (2009) study, more than 50% of AKI patients were in sepsis or septic shock (8). In our study, 60% of patients with AKI were in septic shock.

The presence of systemic diseases increase the risk of developing AKI. In our study, 2% of patients had diabetes mellitus, 37% had hypertension, and 18% had different malignancies.

The presence of AKI significantly increases mortality in intensive care, mortality rate rises to 90% in cases requiring RRT (7). In Parmar et al's retrospective study (2009) including 211 septic patients; 28th day mortality was found to be significantly higher in the AKI group (8). In another study performed in sepsis patients, AKI has been shown to increase the 28th day mortality (9). Our study supports previous studies; 28th day mortality rate is 66% in Group S which is significantly higher than Group C, while the 90th day mortality rate is 56%.

Many different scoring systems have been developed to detect the severity of the clinical condition of patients in the ICU. These scoring systems are important because they show a direct relationship with mortality rates. Using a combination of different scores allow better prediction about patients. One of the previous studies showed that AKI patients had a higher APACHE II score. In the same study, the relationship with the AKIN classification and KDIGO was investigated, and they were found to be highly correlated (9). We also found a significantly higher APACHE II value in Group S than in Group C. In our study, KDIGO staging was associated with RIFLE classification and renal SOFA score.

Poukkanen et al. (2013) conducted a multicenter FINNAKI study; patients' KDIGO stages were calculated during their stay in the ICU and worst values were included in the study (10). Only KDIGO stage 3 was found to be associated with 90th day mortality. In another study, patients' RIFLE classification and KDIGO stages were calculated on admission to ICU, and no relationship was observed (11). In our study, patients' KDIGO stages, RIFLE classifications, and renal SOFA scores were calculated only on the day CVVHD started, and were not associated with either 28th day or 90th day mortality. We believe that this is because the staging of patients in our study and the calculation of scores were only made on the day CVVHD started, and recorded values are inadequate to determine the relationship between mortality.

In shock status, the use of inotropic and vasopressor agents to provide appropriate mean arterial pressure becomes necessary. Legrand et al. (2013) examined the use of inotropic and vasopressor agents between septic patients with or without AKI and found no significant difference (12). Abdo et al. (2012) published an 18-case series with MODS, after CVVHD was compared to non-septics needs of noradrenaline in the septic group had an overall reduction 12th hour (13). In our study, the use of a vasopressor and inotropic agent at the initiation of RRT was 47% in Group C and 87% in Group S. In both groups, the use of these agents decreased in 12th and 24th hour. When a comparison was made between the groups at 24th hour, decrease was more significant in Group S. In septic patients' plasma levels of many inflammatory cytokines are elevated and also when local inflammation in kidney is added too; risk of developing AKI gets higher. Another result of inflammatory cytokines is cardiac depression and decreased systemic vascular resistance. In a study performed in neonates with septic shock, normal blood pressure values could be maintained after 12-hour CVVHD (14). This also can be the explanation for our findings.

One of the changes reported in the MODS case series was the improvement in serum bicarbonate values of the septic group (13). Another study targeted further improvement with dialysis in septic patients; however, there were no significant changes in pH and lactate values. In our study, the pH increased in both groups. There were no significant changes in lactate levels in both groups, it was only a significant increase in the bicarbonate value of Group S at12th and 24th hours.

Many different methods can be used to monitor the level of consciousness. One of the most commonly used methods in clinical practice is GCS. Bagshaw's study showed no difference in GCS after CVVHD (9). In our study, there was no difference in the initial GCS scores between the groups. While there was a significant change in Group C only at 24th hour, in Group S recovery started at 12th and continued at 24th hour.

As a result of the CVVHD expected, nitrogen plasma metabolites reduced. A significant reduction in nitrogen plasma metabolites was detected in all patients. In addition, both groups also showed significant decrease in oxygen demand and increase in Horowitz ratio, in addition to Group S, 12th and 24th hour pulse oximetry values increased. The reduction in renal uremia improved respiratory system, seems to confirm the relationship between the lung and the kidney. Also, more inflammation injury characterized in Group S showed more improvement in respiratory parameters after CVVHD, supporting that the injury in the lungs dose not only depend on the volume overload also are as a result of inflammation.

Acknowledgements

This study had several limitations. First, it wasn't built as a multicenter study, it was performed in our hospital. Also, sepsis related biomarkers were not measured from blood samples, and changes in their levels after RRT couldn't show numerical. The follow-up period in this study was short, and the association between sepsis and long-term acute kidney failure did not followed up on. In conclusion, improvement observed in many parameters in all AKI patients after CVVHD application; however, in septic patients, oxygenation and GCS showed better improvement. The mortality rate increased when AKI got complicated by sepsis. KDIGO, another renal injury grading system, was found to correlate with RIFLE criteria and renal SOFA scores.

Ethical approval

This study has been approved by the Faculty of Medicine, Uludağ University Ethics Committee (approval date 09/12/2014, number 2014-23/13). Written informed consent was obtained from the participants.

Author contribution

Concept: İA; Design: İA, FŞK; Data Collection or Processing: İA, EIS; Analysis or Interpretation: İA; Literature Search: İA; Writing: İA. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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NORTHWESTERN MEDICAL JOURNAL

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RESEARCH ARTICLE

Frequency and severity of premenstrual syndrome in women diagnosed with brucellosis

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ABSTRACT

Aim: Brucellosis is a zoonotic infectious disease caused by Brucella with 4 different subtypes, transmitted to humans mainly through undercooked meat, milk, and dairy products, leading to the involvement of many organs in the body. The purpose of this study is to investigate the frequency and severity of premenstrual syndrome in patients with brucellosis.

Methods: The research was conducted at İdil State Hospital in Şırnak between 15.02.2024 and 15.03.2024. The premenstrual syndrome scale and sociodemographic data form were applied to female patients aged 18-50 years who presented to Idil State Hospital between 01.01.2022 and 01.01.2024 and were diagnosed with brucellosis.

Results: The mean premenstrual syndrome score of women with brucellosis was 164.87 with a standard deviation of 31.58. In the control group of women who had not been exposed to brucellosis, the mean premenstrual syndrome score was 98.39 with a standard deviation of 40.31. The comparison between the two groups was significant at $p<0.05$, indicating a significantly higher frequency and severity of premenstrual syndrome in women who had experienced Brucellosis compared to those who had not.

Conclusion: Our study investigated the relationship between the frequency and severity of premenstrual syndrome and brucella infection and found that Brucella infection significantly increased the frequency and severity of premenstrual syndrome.

Keywords: brucellosis, pain, premenstrual syndrome, zoonoses

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INTRODUCTION

Brucellosis is an infectious disease caused by the Brucella pathogen. In humans, brucellosis is a zoonotic disease that can be caused by four different Brucella species: B.suis, B.melitensis, B.abortus, and B.canis, and as few as 10 to 100 organisms can cause the disease in humans (1).

Brucella pathogens are facultative intracellular gram-negative coccobacilli, with sheep and goats being the most common animal reservoirs for species causing disease in humans. The bacteria often pass into the milk of infected animals and can infect humans through the consumption of contaminated milk or occupational exposure. Brucella bacteria can survive in dairy products for days or even weeks, but they can be killed by boiling, pasteurization, or lactic acid fermentation (2,3).

Brucellosis is more common in the young population, with 60% of cases occurring in individuals aged 13-40 years, 16% in those aged 40-60 years, and 2.5% in those aged 60 years and over. Brucellosis is more common in men than in women, and occupational exposure to animals is thought to be the presumed cause of this difference (1,4).

Premenstrual syndrome (PMS) is a clinical condition characterized by somatic and psychological symptoms that occur during the luteal phase of the menstrual cycle and disappear a few days after menstruation begins, causing significant distress and functional impairment. PMS symptoms include changes in appetite, weight gain, abdominal pain, back pain, lower back pain, headache, breast swelling and tenderness, nausea, constipation, anxiety, irritability, anger, fatigue, restlessness, mood swings, and crying (5,6).

Brucellosis can present with various symptoms; one study observed that patients diagnosed with recurrent high fever during menstruation. Brucellosis is known to disrupt the menstrual cycle in women and lead to conditions such as amenorrhea and metrorrhagia. It should also be noted that Brucella pathogens often affect the genitourinary system and can cause symptoms similar to dysmenorrhea (7-9).

In this study, we aimed to investigate the frequency and severity of expected PMS symptoms in female patients diagnosed with brucellosis.

MATERIAL AND METHOD

The research was conducted at İdil State Hospital in Şırnak between 15.02.2024 and 15.03.2024. The contact information of female patients aged 18-50 who presented to İdil State Hospital between 01.01.2022 and 01.01.2024 and were diagnosed with brucellosis was accessed through the system. Patients willing to participate in the study and signing the informed consent form were included in the study. Individuals in the same age group with no known diseases or history of brucellosis who agreed to participate formed the control group.

Data collection tools

A sociodemographic data form and the premenstrual syndrome scale were applied to eligible patients.

Sociodemographic data scale

The sociodemographic data scale included questions about patients' name, surname, age, additional diseases, additional medication use, and psychiatric diagnosis and treatments.

Premenstrual syndrome scale

This is a scale developed by Gençdoğan in 2006 aiming to measure the severity of premenstrual symptoms according to DSM III and DSM IV-R. The scale, widely used in Türkiye, includes 44 items that individuals mark considering their "state in the week before menstruation." The Premenstrual Syndrome Scale, in five-point Likert type, consists of 9 sub-dimensions (depressive mood, anxiety, fatigue, irritability, depressive thoughts, pain, appetite changes, sleep changes, bloating). The lowest score that can be obtained from the scale is 44, and the highest score is 220. The sub-dimension scores are obtained by summing up the items in these dimensions, and the total Premenstrual Syndrome Scale score is also obtained by summing up the sub-dimension scores. Those with a Premenstrual Syndrome Scale total score

of more than 50% are classified as PMS positive. A high Premenstrual Syndrome Scale score indicates more severe premenstrual symptoms. The Cronbach's Alpha (α) of the original scale is .75, and it was calculated as α = .95 for this study (10).

Statistical analysis

SPSS version 22.0 was used for the statistical analysis of the data. Arithmetic mean +- standard deviation was calculated for numerical data. Independent samples t-test was used as the statistical method, and p<0.05 was considered significant.

RESULTS

The premenstrual syndrome scale survey was applied to 38 female patients diagnosed with brucellosis in our study and 38 female patients were selected as the control group who had not experienced brucellosis. The results obtained are shown in Table 1.

Table 1. Comparison of Premenstrual Syndrome Scale data between women with brucellosis and the control group

Groups	N	X	SS	t	sd	p
Brucellosis Case (n=38)	38	164.87	31.58	8.002	69.988	0.000
Brucellosis Control (n=38)	38	98.39	40.31			

N: Number of participants, X: mean, SD: Standard deviation, sd: Degrees of freedom, Confidence interval 95%

Examination of the data revealed that the mean Premenstrual Syndrome Scale score of women who had brucellosis was 164.87 with a standard deviation of 31.58. In the control group of women who had brucellosis, the mean Premenstrual Syndrome Scale score was 98.39 with a standard deviation of 40.31, and the comparison between the two groups was significant at p<0.05, indicating a significantly higher frequency and severity of premenstrual syndrome in women who had brucellosis compared to those who had not.

Table 2. Comparison of women with brucellosis and women without brucellosis according to demographic data

	Brucellosis Case (n=38)	Brucellosis Control (n=38)	P
Age			
18/26	15	16	0.215
27/35	15	14	0.211
36/49	8	8	0.246
BMI			
18/24	25	26	0.226
25/29	10	8	0.238
29>	3	4	0.211
Marital Status			
Married	35	3	0.166
Single	3	8	0.094

When the data in Table 2 are examined, it is observed that the age range, Body Mass Index (BMI), and marital status of women who have had brucellosis are compared with those who have not had brucellosis based on age range, BMI, and marital status, and no significant difference was found between the two groups. (p>0.05).

DISCUSSION

Brucellosis is a zoonotic disease affecting approximately 50,000 people annually. It is frequently observed in our country, especially in the Eastern Anatolia and Southeastern Anatolia regions, due to undercooked meat, milk, and dairy products (11). It has been shown that brucellosis affects many systems in humans. Upon reviewing the literature, it was found that there are numerous studies related to brucellosis, but no study examining the relationship between brucellosis and the frequency and severity of premenstrual syndrome. There are studies in the literature aiming to show the relationships of various infectious agents with PMS. In a study by Alvarado-Esquivel et al., the relationship between Toxoplasma gondii infection and PMS was investigated, but no significant result was obtained (12).

In a study by Doyle et al., the relationship between sexually transmitted diseases and premenstrual syndrome was investigated. Among sexually transmitted diseases, Human Papillomavirus, Chlamydia trachomatis, Neisseria gonorrhoeae, Gardnerella vaginalis, Candida albicans, and Trichomonas vaginalis infections were examined for their relationship with premenstrual syndrome. In the study, it was found that Chlamydia trachomatis was significantly associated with premenstrual syndrome. No relationship was found between premenstrual syndrome and other sexually transmitted diseases examined in the study (13).

A study by Testa et al. showed that psychiatric manifestations such as psychosis, depression, anxiety, manic episodes, behavioral and vegetative symptoms, cognitive deficits, and consciousness impairment can occur in brucellosis (14).

In a study by Sheata et al., brucellosis emerged as an infectious agent that primarily produces acute psychic symptoms and mimics psychiatric disorders. Additionally, in a rare form of brucellosis known as neurobrucellosis, various psychiatric manifestations have been observed to accompany the disease (15).

In our study, the frequency and severity of premenstrual syndrome were found to be significantly higher in patients with brucellosis.

In our study, the relationship between the frequency and severity of premenstrual syndrome and Brucella infection was investigated, and it was found that Brucella infection significantly increased the frequency and severity of premenstrual syndrome. Our study was conducted with a limited number of patients. More comprehensive studies are needed to elucidate the relationship between brucella infection and premenstrual syndrome.

Ethical approval

This study has been approved by the Ethics Committee of Mardin Artuklu University Non-Interventional Clinical Research Unit (approval date 13/02/2024, number 2024/2-41). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: İŞ; Concept: İŞ; Design: İŞ; Data Collection or Processing: İŞ; Analysis or Interpretation: İŞ; Literature Search: İŞ, BGA; Writing: İŞ, BGA. All authors reviewed the results and approved the final version of the article..

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Conflict of interest

The authors declare that there is no conflict of interest.

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RESEARCH ARTICLE

Examining the concordance between dominant eye and hand preference in healthy adults

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ABSTRACT

Aim: This study was designed to reveal the relationship between dominant hand and dominant eye and to present the dominance rates of the population.

Methods: 160 healthy subjects (80 females, 80 males) between the ages of 18-60 were included in the study. While the determination of the dominant hand was based on the answers of the participants, the Dolman test was used to determine the dominant eye. The chi-squared test was used to determine the relationship between the variables.

Results: Of the sample, 91.3% (146 subjects) predominantly used their right hand and 68.8% (110 subjects) used their right eye. The right eye and hand were dominant in 106 subjects, and the left eye and hand were dominant in 10 subjects. As a result of the chi-square test, there was a statistically significant difference between the dominant hand and the eye.

Conclusion: Since the right hand and right eye were highly dominant in the study, it is thought that the left hemisphere of the participants was dominant in terms of functional lateralization. Additionally, it is thought that the repetition of the study in patients with presbyopic cases and in patients before cataract surgery will be clinically beneficial.

Keywords: cerebral lateralization, Dolman method, dominance, eye, hand

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INTRODUCTION

Anatomical and functional asymmetry of the right and left cerebral hemispheres is defined as the cerebral lateralization. Anatomically, symmetrical hemispheres work counter laterally on controlling the body (1). Organs such as the hands, feet, eyes, and jaw, which are anatomically symmetrical but functionally side-dominant in the body, can be used to determine the dominant hemisphere (1,2). Likewise, several studies have documented that the connection between the dominant hand and the hemisphere attracts attention (1-4). Yet, other researches have indicated that the usage of dominant hand varies according to family, education, and other environmental factors (3,4), suggesting that the dominant hand alone may be insufficient to determine the natural lateralization of the hemispheres.

The brain receives images from both eyes, but the eye that is used primarily is known as the dominant eye, which is most often used while looking through a keyhole or aiming. Since the dominant eye is not affected by the external environment, it reflects more accurately the functional asymmetry between the hemispheres. When calculating the intraocular lens adjustment for cataract surgery or when applying contact lenses in presbyopia patients, the adjustment of the dominant eye to see distance and the other eye to see near is called monovision. This implementation is used in the treatment process in the clinic (1,5).

Literature extensively documents hand and eye dominances in determining interhemisphere lateralization across various populations, but the concordance relationship and linkage between the two organs in this context have not been fully clarified yet (5,6). Therefore, this study, conducted in healthy adults of different age groups has focused on determining the dominant hand-eye ratio of the population and revealing the possible correlation between them. It was designed with the hypothesis that the dominant hand and the eye would be statistically highly correlated.

MATERIALS AND METHODS

The study began after receiving approval number 2023/49 from the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University, Türkiye. The study was cross-sectional and was conducted on participants attending the Department of Ophthalmology, Bolu Abant İzzet Baysal University Training and Research Hospital. A total of 160 participants aged between 18 and 60 years were included in the study. They were informed about the study and voluntarily signed the consent form. Those with a history of diseases related to the upper extremities and eyes were excluded from the study.

The Edinburgh Dexterity Questionnaire was used to determine the dominant hand. It is a valid and reliable questionnaire that allows us to determine the most frequently used hand activities in daily life, as underlined in the literature (7). Participants were asked which hand they used most often for writing, brushing teeth, using a spoon, and throwing something. A scale ranging from one (always right) to five (always left) was used for each activity. The left hand was recorded as dominant for those scoring higher than three, and the right hand was recorded as dominant for those scoring lower than three, as pointed out in the literature (8).

The Dolman method was applied to determine the dominant eye. In this test, participants were asked to sit with their arms stretched and parallel to the body. They were then asked to hold a 25x15 cm card with a 3 cm diameter hole in the middle with both hands and look at a target 6 meters away with both eyes. After closing the right and left eyes, respectively, and looking at the target, whichever eye was closed, the eye on that side was recorded as dominant when the target was not visible, just as explained in the literature (9).

Statistical analysis

Statistical analyses were performed using the Minitab® 21.2 (64-bit) package program. After the descriptive statistics of the variables were calculated, the chi-squared test was applied to analyze the correlation between the dominant hand and the eye. $P<0.05$ was considered statistically significant.

Table 1. Descriptive statistical results of the variables

		Dominant Eye		
		Right	**Left**	**All**
Dominant hand	Right	106 (96.4%)	40 (80%)	146 (%91,3)
	Left	4 (3.6%)	10 (20%)	14 (%8,7)
	All	110 (68.8%)	50 (31.2%)	160 (%100)

RESULTS

The study was conducted on 160 participants, 80 women and 80 men. The mean age of the women was 37.7 years and that of the men was 37.5 years. The statistical analysis revealed that the right eye was dominant in 106 right-handed individuals, the left eye was dominant in 40 right-handed individuals, the right eye was dominant in 4 left-handed individuals, and the left eye was dominant in 10 left-handed individuals. While the number of right-handed individuals constituted 91.3% of the participants, the number of left-handed individuals was determined to be 14 (8.7%). The number of individuals with dominant right eye was 110 (68.8%) and the number of individuals with dominant left eye was 50 (31.2%) (Table 1).

The majority of right-handed individuals have a right dominant eye (106 out of 146), suggesting a strong preference or coordination between the dominant hand and eye on the same side. Among left-handed individuals, more have a left dominant eye (10 out of 14), indicating a similar coordination but with fewer individuals (Tables 1 and 2).

DISCUSSION

This study has revealed the dominant hand to eye ratio of the healthy adult participants and has explained the correlation between them, since the concordance relationship and link between the two organs have not been fully documented as indicated in the literature (5,6). As a result of the current study, 91.3% of the participants were right hand dominant and 68.8% were right eye dominant. The chi-squared test indicated a statistically significant difference between dominant hand and dominant eye.

Table 2. The result of the Chi-Square test

	Chi-Square	**DF**	**P-Value**
Pearson	11.528	1	P<0.001
Likelihood Ratio	10.542	1	P<0.001

p<0.05 was considered statistically significant

Research has extensively documented hand, foot, and eye dominance in various communities. A study investigating the relationship between hand, eye, and foot dominance and motor learning ability in 107 healthy young people (91 females, 16 males) with an average age of 21.81 years, found that 84.1% of the sample group used their right hand and 72% used their right eye dominantly (1). The study found no relationship between hand, eye and foot dominance and motor learning skills. Additionally, no statistical relationship was found between dominant hand and dominant eye. A similar result was found in another study that investigated the dominant hand, eye, and foot of 160 patients who presented to the clinic for refraction (2). This study found that 88.8% of the sample group used the right hand and 81.5% used the right eye predominantly but emphasized that there was no statistical relationship between the dominant hand and the dominant eye. Likewise, another research investigating the dominant eye rate and related factors in a sample group of 300 men in Türkiye, revealed that right-hand dominance was 95% and right-eye dominance was 80%, again showing no statistical relationship between the dominant eye and the hand (5). However, another study examining the relationship between dominant hand and eye preferences and certain systemic pathologies including respiratory and urogenital diseases in 95 university students found that 67.5% of the right hand and 49.5% of the right eye were dominant, while there was no statistically significant relationship between the dominant hand and the eye (6). In a study comparing visual reaction

times in 30 swimmers with and without the dominant eye and the dominant hand, the dominant hand and eye were determined using the same methods as in the current study. As a result of the study, it was emphasized that the dominant eye on the same side and the dominant hand did not affect the visual reaction time (7). In the present study, the dominance rates were consistent with the literature, and the dominant hand and eye rates were determined to be 91.3% and 68.8%, respectively. In addition, unlike the data in the literature, a statistically compatible result was obtained between the dominant hand and the eye. It is possible that the wide age range and equal number of genders in the current study sample may have influenced the results.

One study investigating eye dominance in adults has concluded that the dominant hand and the dominant eye are not always compatible (8). However, several other researches with different materials and methods have reported that the dominant hand and eye are consistent, as is the case with the data from the current study (9-11). Another study, reporting similar results to the literature, has compared methods and found the hand preference and dominant eye to be consistent (3).

Another research focusing on the relationship between ocular dominance and macular structure has included 144 patients without ophthalmic anomaly. The results of this study have found the dominant eye rate to be 68.75%, and no relationship was observed between the macular vascular asymmetry and ocular dominance (12). In another study investigating the relationship between the macular thickness and dominant eye in 89 healthy children, 64.7% of the right eye was dominant, but no significant correlation was found (13). Considering that the determination of the dominant eye is essential in cataract or presbyopia cases, it is thought that paying attention to the dominant eye is also necessary in the design of clinical studies, as indicated in the literature (14).

Reviewing the literature, we think that the limitations of the current study include the exclusion of the dominant lower extremity, the small number of left-handed participants, and the lack of a relationship between the dominant eye and the clinical cases.

The study results are expected to provide a database on the dominant hand and eye within the current population. Furthermore, for patients scheduled to undergo presbyopic and cataract surgery, identifying the dominant eye may provide more visual acuity and comfort to the patient after surgery.

Ethical approval

This study has been approved by the Clinical Research Ethics Committee of Bolu Abant İzzet Baysal University (approval date 14/03/2023, number 2023/49). Written informed consent was obtained from the participants.

Author contribution

Concept: AS, GR; Design: GR, AR; Data Collection or Processing: GR, AR; Analysis or Interpretation: GR, AR; Literature Search: AS, İK, GR, AR; Writing: AS, İK, GR, AR. All authors reviewed the results and approved the final version of the article.

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