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Efficacy of therapeutic plasma exchange in HELLP syndrome: A single-center experience

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MAIN POINTS

- A statistically significant reduction in hemolysis findings was achieved with therapeutic plasma exchange.
- In patients with renal failure, a poor prognostic factor in HELLP syndrome, improvement in renal function was observed with therapeutic plasma exchange.
- Therapeutic plasma exchange is an effective treatment modality for both clinical improvement and reduce mortality in patients with persistent postpartum hemolysis.

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ABSTRACT

Aim: The objective of this study is to investigate the clinical efficacy of therapeutic plasma exchange in HELLP (Hemolysis, Elevated Liver Enzyme, Low Platelet) syndrome and its contribution to renal failure, which is an independent risk factor for maternal mortality.

Materials and Methods: From 2019 to 2024, 20 patients diagnosed with HELLP syndrome who underwent therapeutic plasma exchange (TPE) were included. We evaluated the patients' pre- and post-procedure values to determine the efficacy of the procedure.

Results: The median age of patients was 30 (19-38) years, and the median number of days of TPE was 6 days (3-14). There was a statistically significant increase in hemoglobin and platelet values and a statistically significant decrease in lactate dehydrogenase, total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase, urea, and creatinine values. The number of TPE sessions, length of stay in hospital, and the length of intensive care unit stay were significantly higher in hemodialysis patients.

Conclusion: TPE is an effective treatment modality for both clinical improvement and prevention of permanent renal failure in patients with persistent postpartum hemolysis who are followed for HELLP syndrome.

Keywords: HELLP syndrome, Therapeutic plasma exchange, Renal failure

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INTRODUCTION

HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelet count) syndrome is a serious pregnancy complication with a high risk of fetal and maternal morbidity. Although HELLP syndrome occurs in about 0.5% to 0.9% of all pregnancies, its incidence is higher in women with severe preeclampsia [1]. While it typically develops between 28 and 37 weeks of gestation, it can also occur in the postpartum period, accounting for approximately 30% of cases [2].

Clinical findings of HELLP syndrome vary. Patients may present with nonspecific symptoms such as weakness, fatigue, headache, nausea, vomiting, and pain in the epigastric and right upper quadrant [3]. The exact cause and development process are not fully understood. Vasospasm, endothelial dysfunction, and impaired microcirculation caused by fibrin deposition may lead to clinical signs in affected organs. Complications include disseminated intravascular coagulopathy (DIC), hepatic rupture or hematoma, fulminant liver failure, pulmonary and brain edema, ascites, pleural effusion, retinal detachment, and acute kidney injury (AKI) [4]. Studies have shown that renal failure, one of the complications of HELLP syndrome, is an independent risk factor for maternal mortality [5].

Two classification systems, Tennessee and Mississippi, are used in the diagnosis of HELLP syndrome. Patients are divided into complete or partial according to the Tennessee classification. Patients who meet all the specified criteria are considered complete, while those meeting one or two are considered partial. The criteria are as follows:

1. Having at least two findings related to hemolysis (presence of schistocytes in peripheral smear, serum bilirubin $\geq$1.2 mg/dl, lactate dehydrogenase (LDH) $\geq$2 times the upper limit of normal, or serum haptoglobin $\leq$25 mg/dl, hemoglobin (Hb) value <8-10 g/dl not associated with bleeding)

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2. Elevated liver enzymes (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper limit of normal)

3. Presence of thrombocytopenia [platelet (PLT) <100.000 /μL] [3].

In the Mississippi classification, the severity of thrombocytopenia is assessed. In the presence of LDH > 600 IU/L and AST or ALT > 70 IU/L, PLT≤50.000/μL is considered class-1, PLT 50.000 to 100.000/μL is considered class-2, and PLT 100.000 to 150.000/μL is considered class-3 [6].

The only effective treatment for HELLP syndrome is delivery. In cases < 34 weeks of gestation without serious complications, delivery can be delayed up to 48 hours after corticosteroid treatment to induce fetal lung development. Patients older than 34 weeks or with serious complications such as hepatic bleeding, DIC, AKI, or pulmonary edema should be delivered immediately [7]. Although therapeutic plasma exchange (TPE) is generally not considered a primary treatment for the disease, studies indicate it can be applied effectively and safely in clinically selected patients [8,9].

Thrombotic microangiopathy is preventable with therapeutic plasma exchange (TPE). TPE can be indicated for patients exhibiting progressive increases in serum bilirubin and creatinine levels and severe thrombocytopenia, even after obstetric management and supportive care. The objective of this study is to share the clinical characteristics and treatment outcomes of patients with HELLP syndrome who received TPE after demonstrating unresponsiveness to labor, corticosteroids, and supportive care, and to contextualize these findings within the current literature.

MATERIALS AND METHODS

This retrospective study included 20 patients who were diagnosed with HELLP syndrome and underwent TPE between September 2019 and April 2024. The institutional review board approved the study (approval number: 2025/04-16) regarding ethical and scientific conduct. This study was conducted by the principles of the Helsinki Declaration.

Patients and data

All patient data were retrospectively collected from hospital registries and individual clinical notes. For each patient, the following information was recorded: age, gestational age, gestational week at delivery, survival status, presence of renal failure, hemodialysis status, number of therapeutic plasma exchange (TPE) sessions, total hospitalization days, intensive care unit (ICU) stay, and laboratory values before and after the TPE procedure. These laboratory values included hemoglobin (Hb), platelet count (PLT), lactate dehydrogenase (LDH), total bilirubin (TB), direct bilirubin (DB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine (Cr), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen. Patients were classified according to both the Mississippi and Tennessee criteria for HELLP syndrome.

Patients with HELLP syndrome who did not respond to initial management including labor induction/delivery, corticosteroids, and supportive treatment (blood products, antibiotics, and antihypertensives) were identified. For these patients, central venous catheters were inserted, and TPE treatment was initiated within 24 hours postpartum. TPE was performed daily using a Braun device (Melsungen, Germany) with a 1.5 plasma volume exchange per session. TPE continued until the patient's LDH level normalized and platelet count remained above 100,000/μL for two consecutive days.

Statistical analysis

We didn't determine the sample size beforehand. Instead, we calculated the post-hoc power based on our results; if the power was above 80%, we proceeded with the relevant analysis. G*Power version 3.1 was used for all power calculations. For our statistical analyses, we used IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as n (%) for categorical variables and median (min-max) for continuous variables. We assessed the normality of continuous data using the Shapiro-Wilk test, with a p-value of less than 0.05 indicating non-normal distribution. Consequently, we used the nonparametric Wilcoxon test for pre- and post-procedure comparisons, and the Mann-Whitney U test for independent group comparisons. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The median age of the patients was 30 years (range: 19-38). Renal failure occurred in 12 (60%) patients, with 6 (30%) requiring hemodialysis. Of those requiring hemodialysis, three died, while the remaining three (15%) showed no permanent renal failure during follow-up. HELLP syndrome developed after miscarriage in 1 (5%) patient, after delivery in 10 (50%) patients, and during the third trimester in 9 (45%) patients.

The median number of TPE sessions was 6 (range: 3-14). Fresh frozen plasma (FFP) served as the replacement fluid for 19 patients, with albumin used for only 1 patient. According to the Mississippi classification, 50% of patients were Class 1 and 50% were Class 2. Based on the Tennessee classification, 65% were classified as complete and 35% as partial.

Baseline coagulation parameters showed a median aPTT of 24 seconds (range: 21-44), PT of 12 seconds (range: 10-24), INR of 0.9 (range: 0.8-2.1), and a fibrinogen level of 244 mg/dL (range: 100-597). Fifteen patients required intensive care unit (ICU) admission, while five did not. The median length of hospitalization was 12 days (range: 7-45), and the

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Table 1. Demographic and clinical characteristics of patients.

Variables	N:20	%
Age		
Median (min-max)	30 (19-38)	
Surival		
Alive	17	85.0
Exitus	3	15.0
Renal Failure		
Yes	12	60.0
No	8	40.0
Hemodialysis		
Yes	6	30.0
No	14	70.0
Pregnancy week		
After miscarriage	1	5.0
Postpartum	10	50.0
3th trimester	9	45.0
Number of TPE sessions		
Median (min-max)	6.0 (3-14)	
Replacement		
FFP	19	95.0
Albumin	1	5.0
Mississippi		
Class-1	10	50.0
Class-2	10	50.0
Tennessee		
Complete	13	65.0
Partial	7	35.0
aPTT		
Median (min-max)	24 (21-44)	
PT		
Median (min-max)	12 (10-24)	
INR		
Median (min-max)	0.9 (0.8-2.1)	
Fibrinogen		
Median (min-max)	244 (100-597)	
Duration of hospitilization (days)		
Median (min-max)	12 (7-45)	
Duration of intensive care unit (days)		
Median (min-max)	3 (0-33)	
Intensive care		
Yes	15	60
No	5	40

aPTT; activated partial thromboplastin time, FFP; fresh frozen plasma, INR; international normalized ratio, PT; prothrombin time, TPE; therapeutic plasma exchange.

median ICU stay was 3 days (range: 0-33). During the follow-up period, 85% of patients survived, while 15% died.

Treatment response and outcomes

Following TPE, hemoglobin (Hb) and platelet (PLT) values significantly increased (p<0.001 for both). Conversely, LDH (p<0.001), total bilirubin (Tb, p=0.001), direct bilirubin (Db, p=0.003), AST (p<0.001), ALT (p<0.001), urea (p=0.002), and creatinine (Cr, p<0.001) values significantly decreased (Table 2).

Table 2. Comparison of laboratory parameters before and after TPE.

Variables	Before Process N=20 Median (min-max)	After Process N=20 Median (min-max)	p
Hb (g/dl)	7.4 (6.3-11.4)	10.4 (7.5-12.3)	**<0.001**
PLT (µL)	50000 (10000-75000)	155000 (71000-395000)	**<0.001**
LDH (U/L)	1412.5 (438-5897)	306.5 (134-864)	**<0.001**
Tb (mg/dl)	2.2 (0.6-9.4)	0.7 (0.3-14.8)	**0.001**
Db (mg/dl)	0.7 (0.1-7.3)	0.2 (0.1-9.5)	**0.003**
AST (U/L)	158 (16-2496)	28.5 (14-624)	**<0.001**
ALT (U/L)	122.5 (6-1046)	23.5 (9-140)	**<0.001**
Urea (mg/dl)	58 (19-174)	40 (19-101)	**0.002**
Cr (mg/dl)	1.67 (0.5-47)	0.9 (0.4-2.7)	**<0.001**

Hb: Hemoglobin PLT: Platelet LDH: Lactate dehydrogenase Tb: Total bilirubin Db: Direct bilirubin AST: Aspartate aminotransferase ALT: Alanine aminotransferase Cr: Creatinine.

Subgroup comparisons

Patients who required hemodialysis had a significantly higher number of TPE sessions (p=0.015), longer hospitalization days (p=0.046), and longer ICU stays (p=0.024) compared to those who did not (Table 3). There were no significant differences in the number of TPE sessions, length of hospitalization, or ICU stay when comparing patients by Mississippi classes (p>0.05) (Table 4) or Tennessee types (p>0.05) (Table 5).

DISCUSSION

Ongoing debates regarding the diagnosis, treatment, and prognosis of HELLP syndrome stem from several challenges: the lack of standardized diagnostic criteria, the failure of clinical and laboratory improvement post-delivery in some cases (despite it being the main treatment), and no consensus on which multi-system organ involvement carries a worse prognosis. Our study aims to contribute to the literature by demonstrating that renal failure may be a poor prognostic indicator and that therapeutic plasma exchange (TPE) is an effective treatment option for patients who do not clinically improve after delivery.

HELLP Syndrome is a clinical condition associated with microangiopathic hemolytic anemia, thrombocytopenia, and elevated liver enzymes. Two definitions are used in the diagnosis of the disease: the Tennessee and Mississippi classifications. In our study, we used both classification systems and classified all patients according to both classification systems. According to the Mississippi classification, there were equal numbers of patients in class 1 and class 2, and we did not observe a significant difference among the groups in terms of the number of days of procedure, length of hospitalization, and intensive care unit length of stay. According to the Tennessee classification, although our patients did not show a homogeneous distribution, we again did not observe a significant difference in terms of the number of days of procedure, length of hospitalization, and intensive care unit length of stay. Although

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Table 3. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to hemodialysis groups.

Variables	HD		p
	Yes N=6 Median (min-max)	No N=14 Median (min-max)	
TPE session	9.5 (5-14)	6 (3-9)	0.015
Length of hospitalization (days)	15.5 (9-34)	11 (7-45)	0.046
Length of intensive care stay (days)	9.5 (3-33)	2.5 (0-30)	0.024

Table 4. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to Mississippi classes.

Variables	Mississippi		p
	Class-1 N=10 Median (min-max)	Class-2 N=10 Median (min-max)	
TPE session	7 (4-11)	5.5 (3-14)	0.436
Length of hospitalization (days)	11 (7-20)	14 (8-45)	0.631
Length of intensive care stay (days)	4 (0-11)	3 (0-33)	0.990

Table 5. Comparison of the number of TPE session, length of hospitalization and intensive care unit stay according to hemodialysis groups according to Tennessee types.

Variables	Tennessee		p
	Complete N=13 Median (min-max)	Partial N=7 Median (min-max)	
TPE session	6 (4-14)	5 (3-9)	0.376
Length of hospitalization (days)	11 (7-34)	15 (8-45)	0.551
Length of intensive care stay (days)	3 (0-33)	6 (0-30)	0.992

these classification systems aid in diagnosis, we found no statistically significant differences regarding patient follow-up or prognosis. This lack of difference is likely attributable to the limited number of patients in our study.

HELLP syndrome, a severe pregnancy complication, carries a significant risk of maternal mortality, with reported rates in the literature ranging from 1% to 60%. For instance, Martin et al. reported a mortality rate of 3.2%, Sibia et al. found 1.1%, and Isler et al. observed 60%. In our study, the mortality rate was 15%, aligning with this broad range [10-12]. This variability likely stems from differences in patient clinical characteristics, the timing of TPE initiation, and variations in study sample sizes.

Studies consistently highlight renal failure as an independent risk factor for increased mortality in HELLP syndrome [5], often presenting as the most severe form of acute renal failure in pregnancy [13]. While appropriate management of Acute Kidney Injury (AKI) can prevent irreversible renal damage in HELLP syndrome, delays in diagnosis and treatment can lead to permanent renal failure [14]. In our cohort, 12 patients (60%) experienced renal failure, with 6 (30%) requiring hemodialysis. Of those on hemodialysis, three (15%) died, but importantly, the remaining three (15%) showed no permanent renal failure during follow-up. Comparing patients who underwent hemodialysis to those who did not, we found a statistically significant increase in TPE sessions, length of hospitalization, and intensive care unit stay in the hemodialysis group. This underscores that renal insufficiency is indeed a poor prognostic factor in HELLP syndrome, consistent with existing literature.

Childbirth remains the primary treatment for HELLP syndrome, with spontaneous resolution of thrombotic microangiopathy expected in most cases postpartum. However, in some instances, clinical and laboratory parameters may not improve despite delivery, corticosteroid administration, and supportive treatment. In these refractory cases, therapeutic plasma exchange (TPE) is performed to reduce pathogenic antibodies, minimize organ damage, and improve clinical and laboratory outcomes. Our study demonstrated that in patients unresponsive to initial management, TPE led to a statistically significant increase in platelet counts and a decrease in LDH levels.

Limitations

Our study has several limitations, including the inability to evaluate ADAMTS-13 levels due to technical inadequacy, the absence of a control group, and a small sample size.

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CONCLUSION

Given the high mortality rate associated with HELLP syndrome, timely diagnosis and early intervention are of vital importance. For patients who do not adequately respond to delivery and corticosteroid treatment, and who continue to exhibit signs of hemolysis, low platelet counts, and elevated LDH, TPE can be initiated within 24 hours postpartum. This intervention can potentially prevent persistent renal failure with its poor prognosis and reduce mortality by improving overall clinical outcomes.

Ethics Committee Approval: This study received approval from the Institutional Review Board of Fırat University (Date: 27.02.2025, Approval Number: 2025/04-16).

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

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no competing interests.

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First-trimester screening markers in pregnancies complicated by cervical insufficiency: A comparative retrospective study

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MAIN POINTS

- Cervical insufficiency was associated with a significantly earlier gestational age at delivery compared to the control group.
- The study identified a distinct pattern in pregnancy outcomes among women with spontaneous preterm birth versus cervical insufficiency.
- A multi-group comparison revealed statistically significant differences in neonatal outcomes across all study groups.
- This research highlights the importance of early detection and classification of risk groups to prevent adverse perinatal outcomes.

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ABSTRACT

Aim: This retrospective study aimed to evaluate the relationship between first-trimester screening markers and cervical insufficiency, comparing biochemical parameters and pregnancy outcomes among women with cervical insufficiency, spontaneous preterm birth, and term pregnancies.

Materials and Methods: A total of 248 singleton pregnancies were included and divided into three groups: control (term deliveries, n=121), cervical insufficiency with cerclage (n=60), and spontaneous preterm birth (n=67). First-trimester serum markers including pregnancy-associated plasma protein A (PAPP-A), free beta-human chorionic gonadotropin (β-hCG), nuchal translucency (NT), and alpha-fetoprotein (AFP) were analyzed. Obstetric and neonatal outcomes such as gestational age at delivery, birth weight, Apgar scores, and adverse neonatal outcomes were recorded.

Results: No significant differences were observed in first-trimester PAPP-A, β-hCG, NT, and AFP levels between the cervical insufficiency and control groups. However, the spontaneous preterm birth group exhibited significantly lower PAPP-A and higher β-hCG levels compared to both other groups ($p<0.001$). Gestational age at delivery, birth weight, Apgar scores, and adverse neonatal outcomes were significantly worse in both cervical insufficiency and spontaneous preterm birth groups compared to controls ($p<0.05$).

Conclusion: First-trimester biochemical markers have limited predictive value for cervical insufficiency but show significant alterations in spontaneous preterm birth. Cervical insufficiency appears to be a localized structural pathology not reflected by early systemic biochemical changes. Clinical management should prioritize second-trimester cervical length assessment and appropriate interventions over reliance on first-trimester serum markers. Further research is needed to identify specific biomarkers for early detection of cervical insufficiency.

Keywords: Cervical insufficiency, First-trimester screening, Beta-human chorionic gonadotropin(β-hCG), Pregnancy-associated plasma protein A

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INTRODUCTION

Preterm birth is a major global obstetric problem, accounting for approximately 35% of all neonatal deaths worldwide [1]. Cervical insufficiency (CI) is of particular concern due to its impact on second-trimester pregnancy loss and preterm birth. CI is defined as painless cervical shortening and dilation occurring before 24–28 weeks of gestation without uterine contractions [2]. It affects approximately 1% of pregnant women but is the most common cause of recurrent second-trimester losses and extremely preterm births [2]. Given its serious effects on fetal health and neonatal morbidity, early diagnosis of women at risk of cervical incompetence is of great importance. Clinically, it is quite difficult to detect cervical incompetence before cervical changes become apparent.There is no reliable first-trimester diagnostic test for CI, and the condition is often recognised only after significant cervical shortening or dilation occurs in the second trimester [3]. The diagnosis is usually based on a characteristic obstetric history, such as two or more painless miscarriages or births during the second trimester, or on objective findings of cervical changes in the

middle of pregnancy [4,5]. In the second trimester, a cervical length of less than approximately 25 mm is one of the best clinical predictors of spontaneous preterm birth and may require prophylactic cerclage or vaginal progesterone to prevent preterm birth.

In routine prenatal care, the first trimester combined screening test is performed at 11–13 weeks of gestation to assess the risk of fetal aneuploidy [6]. This test measures fetal nuchal translucency (NT) on ultrasound, along with maternal serum pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (β-hCG) [7,8]. Specifically, abnormalities in these first trimester screening markers have been linked to numerous poor obstetric outcomes, indicating that they may offer early insights into placental function or developmental anomalies beyond chromosomal defects. Decreased PAPP-A levels in early gestation, together with elevated or diminished MoM (multiple of median) values of free β-hCG, have been correlated with a heightened risk of placental insufficiency syndromes, including preeclampsia, fetal growth restriction (FGR), and spontaneous premature birth [9,10,11]. However, it remains unclear whether first-trimester screening markers have any predictive value, particularly for cervical insufficiency.

This study aims to address this gap by evaluating whether first-trimester screening markers differ from other pregnancy outcomes in pregnancies complicated by cervical insufficiency. In conclusion, clarifying the relationship between first-trimester markers and cervical insufficiency may provide information for future strategies aimed at early diagnosis of high-risk pregnancies and the development of targeted preventive interventions.

MATERIALS AND METHODS

Study design

This study was designed as a retrospective cohort analysis to investigate the prognostic value of first-trimester screening markers in pregnancies complicated by cervical insufficiency, compared to spontaneous preterm birth and uncomplicated term deliveries. Data were collected from patients who applied to the Perinatology Department of Ankara Etlik City Hospital Hospital between January 1, 2023, and January 1, 2025. Ethical approval was obtained for the study from Ankara Etlik City Hospital Ethics Committee (approval number: AESH-BADEK-2025-028).

Selection of case and Selection of control

A total of 248 pregnancies were included in the study. The pregnant women were divided into three groups for comparison: those diagnosed with cervical insufficiency and who underwent cerclage, those who presented with spontaneous preterm labour, and a control group whose pregnancies ended without complications at term. The study included only patients who presented for ultrasound examination between 16+0 and 23+6 weeks of gestation due to an indication for cervical length measurement and who had a cervical length of <25 mm measured by transvaginal ultrasound during this period, followed by cerclage. Progesterone therapy was initiated in patients with a cervical length of <25 mm, and transvaginal cervical length monitoring was performed every 1–2 weeks until the 24th week of pregnancy. Cervical cerclage was performed in patients whose cervical length continued to shorten to <10 mm under progesterone therapy [3]. Patients with a history of second-trimester losses in previous pregnancies or a previous history of cerclage were excluded from the study. The spontaneous preterm birth group included cases with spontaneous labour onset before the 37th week of pregnancy and no diagnosis of cervical insufficiency. The control group included patients who had not experienced preterm birth threat throughout their pregnancy, had no cervical insufficiency or other complications, had a singleton and healthy pregnancy, and delivered at term. All patients were evaluated at our clinic and delivered their babies. All pregnant women were evaluated for first trimester screening tests (PAPP-A MoM, β-hCG MoM, NT MoM) between the 11th and 14th weeks of pregnancy as part of routine pregnancy follow-up. These values were obtained retrospectively from patient files. Additionally, second-trimester AFP MoM results and delivery information were obtained from hospital records. Cases with a history of cervical insufficiency who received prophylactic cerclage, multiple pregnancies, cases with fetal structural or chromosomal anomalies, cases with maternal chronic systemic diseases, and cases that did not complete the follow-up process or had insufficient medical records were excluded from the study.

Data collection and laboratory procedures

Patient data were obtained from medical records and the hospital's information management system. Maternal age, number of pregnancies, number of births, pre-pregnancy BMI (kg/m^2), in vitro fertilisation (IVF) pregnancy rates, history of previous preterm birth, PAPP-A MoM, β-hCG MoM, NT MoM, and Alpha-fetoprotein (AFP) MoM values,gestational age at birth (weeks), birth weight (g), 1-minute and 5-minute Apgar scores, and mode of delivery were obtained from the patients' medical records and compared between subgroups. Adverse neonatal outcomes included the presence of at least one of the following adverse outcomes: admission to the neonatal intensive care unit (NICU), neonatal hypoglycaemia, need for phototherapy, Apgar scores <7 at 1 and 5 minutes, caesarean section due to fetal distress, mechanical ventilation, sepsis, RDS, or IVH.

Statistical analysis

Statistical analysis was performed utilising IBM SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was employed to assess adherence to normal distribution. Since this was a retrospective study, no a priori sample size calculation was performed. However,

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a post-hoc power analysis based on the differences in PAPP-A and β-hCG MoM levels revealed an achieved power above 80% at a 0.95 confidence level with a medium effect size (Cohen's d ≈ 0.5). Descriptive statistics for continuous variables were reported as "mean ± standard deviation" for normally distributed data and "median (interquartile range)" for non-normally distributed data. Categorical variables were analysed using the chi-square test or Fisher's exact test. Continuous variables were analysed using the independent sample t-test or the Mann-Whitney U test, contingent upon their normal distribution status.The statistical analysis performed in this study involved the utilization of One-Way ANOVA, followed by post hoc tests to assess intergroup comparisons in cases where significant differences were observed. Pairwise comparisons were performed using Bonferroni-adjusted independent samples t-tests following one-way ANOVA and Bonferroni-corrected Mann–Whitney U tests following Kruskal–Wallis tests, as appropriate. Statistical significance for all tests was defined as a p value less than 0.05.

RESULTS

The study population consisted of 121 women in the control group, 60 women in the cervical insufficiency group, and 67 women in the spontaneous preterm birth group (Figure 1). There were no statistically significant differences between the groups in terms of maternal age, gravida, parity, or body mass index (p>0.05). In vitro fertilisation was more common in the control group and the preterm birth group, while none of the women in the cervical insufficiency group became pregnant through IVF (p = 0.037). A history of preterm birth was most common in the preterm birth group and significantly less common in the cervical insufficiency group and the control group (p<0.001). Gestational age at delivery was significantly lower in both the cervical insufficiency group and the preterm birth group compared to the control group (p<0.001). The caesarean section rate was also significantly higher in the cervical insufficiency group and the preterm birth group compared to the control group (p = 0.017). The birth weight of newborns was significantly lower in the preterm birth group and the cervical insufficiency group compared to the control group (p<0.001). Similarly, Apgar scores were significantly lower in both the cervical insufficiency and preterm birth groups at both the first and fifth minutes (p<0.001). The incidence of adverse neonatal complications, including admission to the neonatal intensive care unit, neonatal hypoglycaemia, need for phototherapy, low Apgar scores, and respiratory or infection complications, was significantly higher in the preterm birth group and the cervical insufficiency group compared to the control group (p<0.001). These results are summarised in Table 1. As shown in Table 2, there was no significant difference in gestational age among the three groups during the first-trimester screening (p = 0.719). There were also no significant differences in nuchal translucency (p = 0.255) or AFP MoM values (p = 0.197). However, beta-hCG MoM levels were significantly higher in the preterm birth group compared to the cervical insufficiency group and the control group (p<0.001). Conversely, PAPP-A MoM values were significantly lower in the preterm birth group compared to the other two groups (p<0.001). No significant differences were found between the cervical insufficiency group and the control group in these markers. The cervical insufficiency group was divided into two subgroups based on gestational age at delivery: those who delivered before 34 weeks (n = 22) and those who delivered at or after 34 weeks (n = 38). The results are presented in Table 3. There were no significant differences between the subgroups in terms of maternal age, BMI, PAPP-A MoM, NT MoM, or AFP MoM values. However, beta-hCG-MoM values were significantly higher in women who gave birth before 34 weeks compared to those who gave birth at or after 34 weeks (p<0.001). The birth weight of newborns in the group with gestational age less than 34 weeks was significantly lower than that of newborns in the group with gestational age 34 weeks or more (p = 0.003). The incidence of adverse neonatal outcomes was also higher in the <34-week group (35% vs. 10.5%; p = 0.024), although caesarean section rates and Apgar scores were similar in both subgroups.

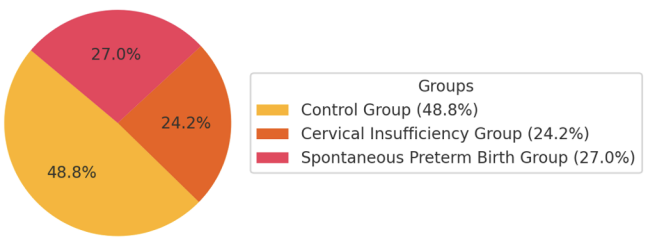

Figure 1. Distribution of study participants across groups.

DISCUSSION

First trimester screening markers, including PAPP-A and β-hCG, do not significantly differ in pregnancies with cervical insufficiency, highlighting the limited predictive value of these biomarkers for this condition. In this retrospective study, we investigated the relationship between first trimester screening tests and the development of cervical insufficiency. Our findings revealed that the first trimester biochemical parameters PAPP-A MoM, β-hCG MoM, and NT MoM in pregnant women diagnosed with cervical insufficiency did not differ significantly from those in the control group and the spontaneous preterm labour group. These results suggest that cervical insufficiency may not be predictable using first-trimester biomarkers, unlike preterm labour. Additionally, it was found that the cervical insufficiency and spontaneous preterm birth groups had significantly lower values compared to the control group in terms of gestational age and birth weight. These findings indicate that cervical insufficiency leads to preterm birth, resulting in newborns being born at a lower gestational age and having lower birth weights.

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Table 1. Demographic and clinical characteristics of the groups.

	Control Group n = 121	Cervical insufficiency Group n = 60	Preterm Birth Group n = 67	p value
Maternal age (year) (mean ± SD)	27.45± 4.59	29.13 ± 5.67	28.7 ± 5.12	0.308
Gravida (median, IQR)	2 (2)	2 (2)	2 (1)	0.181
Parity (median, IQR)	2 (1)	1 (1)	1 (2)	0.063
BMI (kg/m^2) (mean ± SD)	30.12 ± 4.84	30.46 ± 6	29.81 ± 5.4	0.860
In vitro fertilization (n,%)	12 (9.9%)	0 (0%)	7 (10.4%)	**0.037**[a,b]
History of Preterm Birth (n,%)	10 (8.3%)	14 (4.1%)	42 (62.7%)	**<0.001**[b,c]
GA at delivery (weeks) (mean ± SD)	39.12 ± 1.4	36.38 ± 1.71	35.4 ± 2.39	**<0.001**[a,c]
Gender				0.264
Male prevalance (n,%)	55 (45.5%)	35 (58.3%)	33 (49.3%)	
Female prevalance (n,%)	66 (54.5%)	25 (41.7%)	34 (50.7%)	
Cesarean section rate (n,%)	52 (43%)	33 (55%)	43 (64.2%)	0.017
Newborn birth weight (gram) (mean ± SD)	3230 ± 420	3005 ± 545	2700 ±710	**<0.001**[b,c]
Apgar score at 1st minute (mean ± SD)	8.76 ± 0.65	8.62 ± 0.61	8.12 ± 1.16	**<0.001**[b,c]
Apgar score at 5th minute (mean ± SD)	9.67 ± 1	9.63 ± 0.52	9 ± 1.16	**<0.001**[b,c]
Adverse CNO (n,%)	13 (10.8%)	11 (19%)	32 (47.8%)	**<0.001**[b,c]

Note: [a] The difference between Group 1 and Group 2 is significant; [b] The difference between Group 2 and Group 3 is significant; [c] The difference between Group 1 and Group 3 is significant. A p value of <0.05 indicates a significant difference and statistically significant p-values are in bold. Abbreviations: BMI, body mass index; GA, gestational age; CNO: composite neonatal outcome; SD: Standard deviation; IQR: İnterquartile range.

Table 2. Comparative analysis of first- and second-trimester maternal serum biomarkers and screening parameters across study groups.

	Control Group n = 121	Cervical insufficiency Group n = 60	Preterm Birth Group n = 67	p value
GA at Screening (weeks) (mean ± SD)	12.41 ± 0.75	12.31 ± 0.84	12.52 ±0.89	0.719
NT MoM (median, IQR)	0.71 (0.21)	0.75 (0.38)	0.88 (0.33)	0.255
B-hcg MoM (median, IQR)	0.75 (0.69)	0.64 (0.42)	2.12 (1.43)	**<0.001**[b,c]
PAPP-A MoM (median, IQR)	0.95 (0.6)	0.83 (0.73)	0.67 (0.9)	**<0.001**[b,c]
AFP MoM (median, IQR)	0.89 (0.3)	0.8 (0.66)	0.94 (0.59)	0.197

Note: [a] The difference between Group 1 and Group 2 is significant; [b] The difference between Group 2 and Group 3 is significant; [c] The difference between Group 1 and Group 3 is significant. A p value of <0.05 indicates a significant difference and statistically significant p-values are in bold. Abbreviations: GA: Gestational age; NT MoM: Nuchal translucency multiples of the median; B-hCG MoM: Beta-human chorionic gonadotropin multiples of the median; PAPP-A MoM: Pregnancy-associated plasma protein A multiples of the median; AFP MoM: Alpha-fetoprotein multiples of the median.

Table 3. Subgroup comparison of cervical insufficiency cases by gestational age at delivery (<34 vs ≥34 weeks).

	<34 weeks n= 22	≥34 weeks n=38	p value
Maternal age (years), mean ± SD	31 ± 5.74	28 ± 5.41	0.988
BMI (kg/m²), mean ± SD	29.76 ± 5.88	30.86 ± 6.17	0.516
GA at delivery (weeks) (mean ± SD)	34.27 ± 1.65	38.62 ± 1.99	**<0.001**
PAPP-A MoM, median (IQR)	0.84 (0.64)	0.78 (0.69)	0.434
β-hCG MoM, median (IQR)	1.91 (0.86)	0.46 (0.51)	**<0.001**
NT MoM (median, IQR)	0.72 (0.28)	0.73 (0.28)	0.690
AFP MoM (median, IQR)	0.81 (0.55)	0.82 (0.64)	0.380
Cesarean section rate (n,%)	12 (54.5%)	21 (55.3%)	0.957
Newborn birth weight (gram) (mean ± SD)	2755 ± 414	3225 ± 430	**0.003**
Apgar score at 1st minute (mean ± SD)	8.68 ± 0.66	8.63 ± 0.63	0.664
Apgar score at 5th minute (mean ± SD)	9.75 ± 0.53	9.68 ± 0.47	0.073
Adverse CNO (n,%)	7 (35%)	4 (10.5%)	**0.024**

Note: A p value of <0.05 indicates a significant difference and statistically significant p-values are in bold. Abbreviations: BMI, body mass index, GA: Gestational age; NT MoM: Nuchal translucency multiples of the median; B-hCG MoM: Beta-human chorionic gonadotropin multiples of the median; PAPP-A MoM: Pregnancy-associated plasma protein A multiples of the median; AFP MoM: Alpha-fetoprotein multiples of the median.

In the literature, cervical insufficiency and preterm birth are frequently highlighted as important risk factors for neonatal morbidity and mortality [12].

PAPP-A is a protease secreted by trophoblasts that increases insulin-like growth factor (IGF) bioavailability by breaking down IGF binding proteins [13,14]. With this feature, it plays an important role in placental growth, trophoblast invasion, and the regulation of uteroplacental circulation. Previous studies have investigated whether biochemical parameters measured in first-trimester screening tests can provide clues about the course of pregnancy [15]. It has been suggested

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that PAPP-A and free β-hCG levels may be associated with pregnancy complications because they reflect placental function. In the literature, diminished PAPP-A levels have been consistently associated with an elevated risk of preeclampsia and an increased probability of FGR in subsequent weeks. A study by Papamichail et al. indicated that the probability of developing preeclampsia or pregnancy-induced hypertension was markedly elevated when PAPP-A levels were 0.4 MoM in the first trimester; correspondingly, the incidence of FGR was also dramatically increased in these conditions [16]. In a similar manner, β-hCG promotes progesterone synthesis by sustaining the corpus luteum during early gestation and contributes to the proliferation and differentiation of trophoblastic cells. Pregnant women exhibiting markedly elevated β-hCG levels during the first trimester have an up to fivefold increased chance of subsequently developing preeclampsia [17]. In a study conducted by Younesi et al., statistical correlations were found between excessive β-hCG MoM values and various adverse outcomes such as low birth weight, premature birth, and gestational diabetes [7]. In our study, consistent with the literature, elevated β-hCG levels were noted in cases of preterm labour. Despite all this, many studies point to the limited value of first-trimester markers in predicting preterm birth. In a large cohort study by Swiercz et al., although low PAPP-A and abnormal β-hCG levels were found to statistically increase the risk of spontaneous preterm birth, it was noted that the diagnostic success of these markers alone remained moderate [18].

In our study, the lack of significant differences in the levels of these biomarkers in the cervical insufficiency group supports the notion that the pathophysiology of these cases is due to local structural cervical weakness rather than systemic or placental dysfunction. Cervical insufficiency primarily stems from weakness in the collagen structure of the cervical stroma, abnormal remodeling, or congenital connective tissue disorders [19]. This condition may not be directly linked to varying levels of PAPP-A or β-hCG associated with trophoblastic activity during the first trimester. However, the low PAPP-A and high β-hCG levels detected in the spontaneous preterm birth group suggest that some of the births in this group developed through placental dysfunction-based mechanisms. In addition, inflammation is also a possible mechanism in the pathophysiology of cervical insufficiency [20]. It is known that subclinical infection or inflammatory processes accelerate the early softening of cervical tissue by increasing collagen degradation enzymes such as MMP-9 and cytokines such as IL-6 and IL-8 in the cervix [21]. However, since the pathophysiology of cervical insufficiency is primarily associated with later-stage mechanisms such as accelerated local tissue remodelling and collagen matrix dissolution that occur in the second trimester, no significant changes in systemic biomarkers have been observed during weeks 11–14 of pregnancy. In this context, it is expected that first-trimester screening tests would fail to detect this late-onset process and, consequently, no significant differences would emerge in the cervical insufficiency group.

This study is significant as it is an original retrospective analysis examining the relationship between first trimester screening tests and obstetric outcomes in pregnancies with cervical insufficiency. The use of multiple group comparisons enhances the generalizability of the results. The detailed evaluation of both biochemical markers and neonatal outcomes demonstrates a multidisciplinary and comprehensive approach. In these aspects, the study provides important data contributing to the literature. However, the retrospective design of the study increases the risk of uncertainty in data collection and analysis processes. Furthermore, the limitation of first-trimester screening tests to specific biomarkers (PAPP-A, β-hCG, AFP, NT) and the failure to evaluate other potential biomarkers that could fully reflect the pathophysiology of cervical insufficiency can be considered a limitation. The fact that the sample was collected from a single center, along with the possibility that results may vary across different geographic and ethnic populations, may limit the universal validity of the study's findings. For these reasons, further prospective studies to validate the findings are important.

In conclusion, our study also demonstrates that first-trimester PAPP-A and β-hCG levels do not provide meaningful predictive value in cases of cervical insufficiency, thereby supporting the current guidelines' approach of focusing on clinical and ultrasonographic screening rather than biochemical markers [3]. These markers are more meaningful in preterm births associated with placental dysfunction but may not induce biochemical changes in the early stages of localized anatomical abnormalities such as cervical insufficiency.

CONCLUSION

First trimester screening markers did not show significant changes in cervical insufficiency cases, indicating their limited value for early prediction. However, altered biochemical profiles were observed in spontaneous preterm births. These findings support prioritizing second trimester ultrasound evaluation over reliance on early biochemical markers.

Ethics Committee Approval: The study was conducted in accordance with the principles stated in the Declaration of Helsinki and ethical approval was obtained from Ankara Etlik City Hospital Hospital Ethics Committee (approval number: AESH-BADEK-2025-028).

Informed Consent: Not applicable due to the retrospective design.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declared that there are no conflicts of interest.

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Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization: D.D.B.

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Evaluation of patient-related factors and index treatment in recurrent ingrown toenail cases

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MAIN POINTS

- This study evaluates patient-related factors underlying high recurrence rates in patients with ingrown toenails.
- The research highlights the impact of patient hygiene, appropriate footwear, and nail trimming habits on recurrence.
- Orthonyxia was found to be the most commonly applied initial treatment method.
- Comorbidities, particularly obesity and diabetes, were identified as risk factors for ingrown toenail recurrence.
- Appropriate treatment methods and patient education are critical in reducing recurrence rates.

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ABSTRACT

Aim: This study aims to evaluate patient-related factors and previous treatments in patients with ingrown toenails that subsequently recurred. In this context, recommendations for clinical practice are proposed to contribute to the development of both effective treatment methods and preventive strategies.

Materials and Methods: This retrospective study included 42 patients previously treated for ingrown toenails who developed recurrences due to various reasons. Patients with post-treatment complications (e.g., infection and bleeding), pain associated with the treatment, or dissatisfaction with the treatment were not considered as a recurrence and were excluded from the study. All patients gave informed consent for participation in the study. The demographic characteristics such as age and gender, patient-related factors that might affect recurrence (foot hygiene, footwear usage, nail trimming, additional deformities, trauma history, comorbidities), the clinics where the initial treatment was performed, and the initial treatment methods were recorded.

Results: The mean age of the patients was 26.8±10.1 years, with the youngest being 12.0 years and the oldest 49.0 years. Of the patients, 33.3% (n=14) were female, and 66.7% (n=28) were male. Comorbidities included diabetes mellitus in 21.4% (n=9), obesity in 31.0% (n=13), peripheral arterial disease in 7.1% (n=3), and hyperhidrosis in 16.7% (n=7). No predisposing factors were identified in 11.9% (n=5) of the 42 patients. An evaluation of initial treatment methods revealed that 40.5% (n=17) of the patients underwent Orthonyxia, 21.4% (n=9) underwent Chemical Partial Matricectomy, 21.4% (n=9) underwent Spicule Excision, and 16.7% (n=7) underwent Partial Matricectomy.

Conclusion: Ingrown toenails are common in the general population and can significantly impair quality of life. When left untreated or improperly treated, they may result in unexpected and troublesome outcomes. Reducing risk factors and receiving appropriate treatment from an experienced clinician will help lower recurrence rates.

Keywords: Ingrown toenail, Recurrence, Index treatment, Partial matricectomy, Nail trimming

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INTRODUCTION

Ingrown toenail, also known as 'Onychocryptosis' or 'Unguis Incarnates' is a common nail condition caused by the nail plate embedding into the lateral nail folds, resulting in swelling, erythema, edema, pain, and, as the condition progresses, purulent discharge, ulceration, and granulation tissue. It accounts for approximately 20% of foot problems and is most commonly observed in the great toe [1]. It primarily affects young adults [2], leading to significant morbidity and loss of productivity. Patient-related factors such as improper nail trimming, inappropriate footwear and sock usage, poor foot hygiene, hyperhidrosis, trauma, obesity, diabetes, peripheral arterial disease, and intense physical activity increase the risk.

Patients presenting with ingrown toenails may seek care in dermatology, general surgery, orthopedics, or plastic surgery clinics. Various treatment methods are available. Conservative approaches are employed in early stages, whereas surgical interventions are preferred in advanced cases. Conservative treatments include techniques such as cotton-wick inser-

tion under the nail corner, dental floss technique, the gutter splint or sleeve technique, taping procedure, nail wiring, slit tape-strap procedure, acrylic nails, and nail braces. Surgical treatments include spicule excision and partial matricectomy, chemical partial matricectomy, wedge resection of the toenail and nail fold, excision of the affected nail and total matricectomy, soft-tissue nail fold excision technique, electrocautery, radiofrequency ablation, and carbon dioxide laser ablation [3]. Patient-specific treatment plans not only address the current condition but also effectively prevent recurrences in the long term. Inadequate or improper treatment may lead to recurrence. Current literature compares all available treatment methods, and recurrence has been reported across all studies and treatment methods [4]. However, the definition of recurrence varies between studies. Surgical interventions are generally more effective in preventing recurrences of ingrown toenails compared to non-surgical methods [5].

This study aims to evaluate patient-related factors and previous treatments of patients with ingrown toenails that subsequently recurred. In this context, clinical practice recommendations are proposed to contribute to the development of both effective treatment methods and preventive strategies.

MATERIALS AND METHODS

The study was conducted between 2021 and 2024 in the Orthopedics and Traumatology Clinic of a tertiary hospital and was designed as a descriptive study. The study included 42 patients previously treated for ingrown toenails who developed recurrences due to various reasons. Post-treatment symptomatic regrowth of the nail (nail spicules/nail spikes) was considered a recurrence. Patients with post-treatment complications (e.g., infection and bleeding), pain associated with the treatment, or dissatisfaction with the treatment were not considered recurrences and were excluded from the study [4]. Approval for the study was obtained from the Clinical Research Ethics Committee of Kafkas University Faculty of Medicine with decision number 19 on 30.04.2024. Both verbal and written (informed consent) approval was obtained from the participants. The study was conducted in accordance with the Declaration of Helsinki. After obtaining informed consent, demographic characteristics such as age and gender, patient-related factors that might affect recurrence (foot hygiene, footwear usage, nail trimming, additional deformities, trauma history, comorbidities), the clinics where the initial treatment was performed, and the initial treatment methods were recorded.

Statistical analysis

For the study, frequency (n) and percentage (%) were provided for nominal data, while mean and standard deviation, median, first and third quartiles, and minimum and maximum values were presented for numerical data. In the study, the age variable was taken as quantitative data. Gender, patient characteristics (foot hygiene, nail cutting, shoe use, additional deformity or trauma history, presence of additional disease), treatment of the index clinic, first treatment method are nominal data. For age, which is numerical data, the Shapiro-Wilk test was used to assess normality. The age data were found to follow a normal distribution. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 21 (IBM SPSS Corp.; Armonk, NY, USA).

RESULTS

A total of 42 patients with recurrent ingrown toenails were included in the study. Of the patients, 33.3% (n=14) were female, and 66.7% (n=28) were male. the test of normality of the distribution of the ages of the patients using the Shapiro-Wilk test, and the ages were found to follow a normal distribution (p=0.126).The mean age of the patients was 26.8 ± 10.1 years, with the youngest being 12.0 years and the oldest 49.0 years (Table 1).

Among the patients, 81.0% (n=34) had good foot hygiene, while 19.0% (n=8) had poor hygiene. Correct nail trimming was observed in 35.7% (n=15) of the patients, whereas 64.3% (n=27) had incorrect nail trimming practices. Proper footwear usage was noted in 57.1% (n=24) of the patients, while 42.9% (n=18) used improper footwear. A history of additional foot deformities or trauma was present in 26.2% (n=11) of the patients and absent in 73.8% (n=31). Comorbidities were identified in 47.6% (n=20) of the patients, while 52.4% (n=22) had no associated conditions. Among the patients, 21.4% (n=9) had diabetes mellitus, 31.0% (n=13) had obesity, 7.1% (n=3) had peripheral arterial disease, and 16.7% (n=7) had hyperhidrosis (Table 2). No predisposing factors were identified in 11.9% (n=5) of the 42 patients.

An analysis of the clinics where the initial treatments were performed revealed that 38.1% (n=16) of the patients were treated in the general surgery clinic, 28.6% (n=12) in the dermatology clinic, 19.0% (n=8) in the plastic and reconstructive

Table 1. Demographic characteristics of patients with recurrent ingrown toenails.

Variables	n (%)
Gender	
Female	14 (33.3)
Male	28 (66.7)
Age (years)	
Mean ± Standard Deviation	26.8±10.1
Median (1st quartile-3rd quartile)	25.5 (18.7-35.0)
Minimum - Maximum	12.0-49.0
Total	42 (100.0)

A total of 42 patients with recurrent ingrown toenails were included in the study. Of the patients, 33.3% (n=14) were female, and 66.7% (n=28) were male. The age distribution of the cases was tested for normality using the Shapiro-Wilk test, and the ages were found to follow a normal distribution. (p=0.126) The mean age of the patients was 26.8 ± 10.1 years, with the youngest being 12.0 years and the oldest 49.0 years.

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Table 2. Characteristics of patients with recurrent ingrown toenails.

Variables	n (%)
Foot Hygiene	
Good	34 (81.0)
Bad	8 (19.0)
Nail Trimming	
True	15 (35.7)
False	27 (64.3)
Footwear Usage	
True	24 (57.1)
False	18(42.9)
History of Additional Deformity or Trauma	
Present	11 (26.2)
Absent	31 (73.8)
Presence of Comorbidities	
Present (DM*, Obesity, Peripheral Vascular Disease, Hyperhidrosis)	20 (47.6)
Absent	22 (52.4)
Total	42 (100.0)

*DM: Diabetes Mellitus. Among the patients, 81.0% (n=34) had good foot hygiene, while 19.0% (n=8) had poor hygiene. Correct nail trimming was observed in 35.7% (n=15) of the patients, whereas 64.3% (n=27) had incorrect nail trimming practices. Proper footwear usage was noted in 57.1% (n=24) of the patients, while 42.9% (n=18) used improper footwear. A history of additional foot deformities or trauma was present in 26.2% (n=11) of the patients and absent in 73.8% (n=31). Comorbidities were identified in 47.6% (n=20) of the patients, while 52.4% (n=22) had no associated conditions. Among the comorbidities, 21.4% (n=9) of the patients had Diabetes Mellitus, 31.0% (n=13) had obesity, 7.1% (n=3) had peripheral vascular disease, and 16.7% (n=7) had hyperhidrosis Of the total 42 patients, 5 (11.9%) had no identifiable predisposing factors.

Table 3. Initial clinic visits and treatment methods for patients with recurrent ingrown toenails.

Variables	n (%)
Initial Clinic Visited	
General Surgery	16 (38.1)
Dermatology	12 (28.6)
Plastic and Reconstructive Surgery	8 (19.0)
Orthopedics and Traumatology	6 (14.3)
Initial Treatment Method	
Orthonyxia	17(40.5)
Chemical Partial Matricectomy	9 (21.4)
Spicule Excision	9 (21.4)
Partial Matricectomy	7 (16.7)
Total	42 (100.0)

An analysis of the clinics initially visited by the patients revealed that 38.1% (n=16) presented to the general surgery clinic, 28.6% (n=12) to the dermatology clinic, 19.0% (n=8) to the plastic and reconstructive surgery clinic, and 14.3% (n=6) to the orthopedics and traumatology. An evaluation of the initial treatment methods showed that 40.5% (n=17) of the patients underwent Orthonyxia, 21.4% (n=9) received Chemical Partial Matricectomy, 21.4% (n=9) underwent Spicule Excision, and 16.7% (n=7) underwent Partial Matricectomy.

surgery clinic, and 14.3% (n=6) in the orthopedics and traumatology clinic (Table 3).

An evaluation of the initial treatment methods indicated that 40.5% (n=17) of the patients underwent Orthonyxia, 21.4% (n=9) underwent Chemical Partial Matricectomy, 21.4% (n=9) underwent Spicule Excision, and 16.7% (n=7) underwent Partial Matricectomy (Table 3).

DISCUSSION

Ingrown toenails are a common and painful condition that can significantly impair function. In addition to external factors like mechanical trauma, incorrect nail cutting, and ill-fitting footwear, individual predisposing factors play a crucial role in their development. These include excessive nail plate curvature (pincer nail deformity), excessive sweating (hyperhidrosis), obesity, genetic predisposition, and structural foot deformities like hallux valgus. A more active lifestyle in younger people and recurrent microtraumas are also known risk factors [6]. The aim of this study is to evaluate the clinical and sociodemographic characteristics of patients with recurrent ingrown toenails and the effectiveness of previous treatments on recurrence. Thorough investigation of the clinical and sociodemographic features of ingrown toenails and the contributing factors, followed by appropriate treatment planning, can help eliminate these factors, prevent the disease, and reduce recurrence rates. The high recurrence rates, despite various treatments, underscore the importance of addressing both these individual predispositions and post-treatment care. Effective management requires not only symptom relief but also the identification and, if possible, elimination of underlying predisposing factors. This study provides a comprehensive overview of the demographic, hygienic, and treatment practices of patients with recurrent ingrown toenails. A significant portion of patients exhibited poor nail care, which may have contributed to their recurrence. The presence of comorbidities highlights the need for a multidisciplinary approach to patient management. The varied treatment methods and their distribution across clinics indicate a broad spectrum of management strategies for this condition.

The primary aim of this study is to evaluate the clinical and sociodemographic characteristics of patients with recurrent ingrown toenails and the effectiveness of their previous treatments in preventing recurrence. A thorough investigation into these features and contributing factors can help clinicians develop appropriate treatment plans to prevent the disease and reduce recurrence rates.

Ingrown toenails significantly impair a patient's quality of life due to pain, deformity, and the inability to wear comfortable footwear. The condition negatively affects daily life, sports, and work activities, potentially impacting emotional and mental well-being [7]. While studies on the epidemiology of ingrown toenails are limited, most focus on treatment approaches [2]. Inadequate data repositories, particularly in developing countries, make it challenging to accurately evaluate prevalence and recurrence rates.

Several studies have shown that primary ingrown toenails are more common in females compared to males [2]. However, there are also studies reporting higher prevalence in males [8].

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In our study, 33.3% (n=14) of the patients were female, while 66.7% (n=28) were male. Contrary to primary ingrown toenails, recurrent cases in our study showed a higher prevalence in males than females.

Several studies report that primary ingrown toenails are more common in females than males [2], though others report a higher prevalence in males [8]. In our study, 33.3% (n=14) of patients were female and 66.7% (n=28) were male. Contrary to primary cases, recurrent ingrown toenails in our study were more prevalent in males.

The incidence of ingrown toenails typically follows a bimodal age distribution, with peaks around 15 and 50 years [9]. In our study, the mean age was 26.8 ± 10.1 years, ranging from 12 to 49 years. This is consistent with the mean ages reported in the literature [2,10].

The etiology of ingrown toenails involves various risk factors, including improper nail trimming, inappropriate footwear, poor foot hygiene, obesity, hyperhidrosis, foot/toe deformities, onychomycosis (fungal nail infection), diabetes mellitus, and peripheral arterial diseases [11]. However, the specific influence of these factors on recurrence is unclear. This study evaluated the frequency of these variables in patients with recurrent cases.

The prevalence of poor foot hygiene as a predisposing factor varies widely in recent studies (0.97%-58.5%) [2, 11]. In our study, the rate was 19%. This suggests that while poor hygiene may predispose patients to infections that negatively affect treatment success, its impact on recurrence might be less significant than other factors. Proper nail trimming—cutting nails straight across—is crucial. Trimming nails with rounded or V-shaped cuts, or cutting them too deep, can cause the nail to grow into the surrounding soft tissue, increasing the risk of ingrown toenails [12]. In our study, 64.3% of patients trimmed their nails improperly, and many believed these methods would correct the condition. This was the most frequent risk factor among recurrence cases.

Inappropriate footwear and socks are also major contributors. Tight or pointed shoes cause repetitive trauma and are among the leading causes of ingrown toenails [13]. In our study, 42.9% of patients used inappropriate footwear. Trauma is another factor [14]. A case-control study by Cho et al. concluded that foot and toe deformities are significant risk factors [15]. In our study, 26.2% of patients had a history of trauma and/or additional deformities.

Obesity is a well-known factor in the pathogenesis of ingrown toenails, with a reported prevalence ranging from 34.1% to 69.5% [2,16]. It is believed to increase pressure on the nail and contribute to hypertrophy of the lateral nail fold. Diabetes mellitus is a significant risk factor, particularly due to its long-term vascular and neurological complications, which can impair wound healing and predispose patients to infections [17,18]. Hyperhidrosis creates a risk for ingrown toenails through skin maceration [19]. In our study, 47.6% of patients had comorbidities. Of these, 21.4% had diabetes mellitus, 31.0% had obesity, 7.1% had peripheral arterial disease, and 16.7% had hyperhidrosis.

Several clinical specialties, including general surgery, dermatology, plastic and reconstructive surgery, and orthopedics, manage the treatment of ingrown toenails. We investigated the clinics where patients received initial treatment and the specific treatments administered. Both conservative and surgical options are available. While conservative treatments are effective for mild cases, surgical procedures are more effective for severe ones. The most suitable procedure depends on the condition's severity, patient history, and associated risk factors [1].

In our study, the initial treatments for recurrent cases were predominantly Orthonyxia, followed by Chemical Partial Matricectomy, Spicule Excision, and Partial Matricectomy. A comprehensive literature review reported no significant difference in recurrence rates among different treatment methods [4,20], although some studies noted higher recurrence rates with Spicule Excision and lower rates with Partial Matricectomy, Chemical Partial Matricectomy, and Orthonyxia. Regardless of the technique, proper application and minimizing risk factors are critical for reducing recurrence rates.

Limitations

This study has several limitations. It is a descriptive, single-center study with a limited sample size, and its findings can only be generalized to the included patients. The lack of a control group further restricts the study's scope. Despite these limitations, it provides valuable information about the characteristics of patients with recurrent ingrown toenails and their treatment practices. Future research with larger samples, multiple centers, and a prospective design is recommended.

CONCLUSION

We believe that predisposing factors play a significant role in the recurrence of ingrown toenails. In the current literature, recurrent cases are generally evaluated from the perspective of treatment. However, greater emphasis should be on the risk factors, which are overseen. Preventive methods should be part of all treatment strategies. Furthermore, recurrences can occur even in the absence of any predisposing factors. This highlights the necessity of thoroughly understanding treatment techniques and applying them correctly.

Ethics Committee Approval: This study was approved by the Ethics Committee of Kafkas University Faculty of Medicine with the Approval No: 19 and Date: 30/04/2024.

Informed Consent: Both verbal and written (informed consent) approval was obtained from the participants.

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Determination of density ranges to be used in grading hepatosteatosis using computed tomography

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MAIN POINTS

- This retrospective study analyzed a cohort of 666 individuals to establish computed tomography (CT) density thresholds for quantifying hepatic steatosis.
- Patients were initially classified based on the grade of hepatosteatosis determined by ultrasound.
- Subsequent CT density measurements of the liver were performed to define precise Hounsfield Unit (HU) ranges that can differentiate between these steatosis grades.
- A key anatomical finding was that Segment I (the caudate lobe) demonstrated the highest attenuation values, identifying it as the liver segment most resistant to fatty infiltration.

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ABSTRACT

Aim: To determine the density ranges to evaluate the degree of hepatosteatosis on computed tomography (CT) grades.

Materials and Methods: Patients who were diagnosed with hepatosteatosis by ultrasonography and those who subsequently underwent tomography were included in the study. Measurements were made from each segment of the liver and the spleen in the CT images of the graded groups. Liver/spleen density ratios were compared.

Results: In total 666 patients were included for evaluation in the present study. Liver/spleen density ratios for Grade 1, Grade 2, and Grade 3 were 0.94 ± 0.19, 0.70 ± 0.16, and 0.37 ± 0.13, respectively. There was a statistically significant difference in the Liver/spleen density ratios throughout all grades (p=.001). The cut-off value separating Grade 1 and Grade 2 was calculated as 0.77, and the cut-off value separating Grade 2 and Grade 3 was calculated as 0.47. Segment 1, which had the least fat accumulation, was significantly different from all the other segments.

Conclusion: In the present study, it was determined that both contrast-enhanced and non-contrast-enhanced tomography can be used for the evaluation of hepatosteatosis. However, contrast-enhanced tomography has been found to distinguish Grade 1 from Grade 2 more effectively than unenhanced CT.

Keywords: Hepatosteatosis, Density range, Computed tomography, Ultrasonography

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INTRODUCTION

Liver steatosis, or fatty liver, is the accumulation of triglycerides in hepatocytes over time [1-4]. Hepatosteatosis is considered when 5% or more fat makes up its weight [5]. The prevalence is quite high, affecting more than 16-31% of the world's population [3,6-8]. Hepatosteatosis is significant because it involves an inflammatory process that can lead to chronic liver disease [2,4,7,8]. It is often diagnosed incidentally during abdominal ultrasonography (US) examination [3].

Liver biopsy is considered the gold standard for diagnosing and classifying hepatosteatosis [1,4,6,9,10]. However, it has several disadvantages, such as being an invasive procedure, the possibility of sampling error [1,4,6,10]. In cases of heterogeneous steatosis, a biopsy can yield misleading results [4]. For these reasons, various imaging methods and laboratory parameters have been used to detect fat accumulation [4,9,10].

Ultrasonography is the most common diagnostic method because of its noninvasive nature, low cost, and absence of ionizing radiation [1,3,5,6,8,11]. The sensitivity for detecting steatosis ranges from 60-94%, and the specificity ranges from 84-95% [1,5]. Sensitivity increases when steatosis is moderate to severe [5,7]. However, the accuracy of diagnosis decreases in patients with low fat accumulation (below 20%) [1,3-6,8]. The main disadvantage of US is that it is dependent on the operator and the equipment used [1-4,7]. US can also be used to grade the extent of steatosis [4-6,8,11-13].

Grade 1 (G1) steatosis is defined as a slight increase in liver echogenicity compared with the adjacent renal parenchyma. The borders of the intrahepatic vessels remain sharp. Grade

2 (G2) steatosis is defined as a moderate increase in liver echogenicity, accompanied by a reduction in the echogenicity of the intrahepatic vascular structures and distortion of the diaphragm contour. Grade 3 (G3) steatosis is defined as a marked increase in liver echogenicity leads to blurring of the diaphragm contour, inability to distinguish the vessel walls, and difficulty in visualizing the posterior segments of the liver [4,6,8,11-13].

The clinical utility of this nonquantitative ultrasonographic assessment, which is based on operator-dependent echogenicity increases, is controversial [4,11]. Computed tomography reveals liver steatosis as a diffuse or heterogeneous decrease in parenchymal density [1,8,11]. Increased fat accumulation correlated with a greater decrease in density [1,3,4]. While the accuracy of CT in detecting liver steatosis varies, its sensitivity is reported to be 93%, with a positive predictive value of 76% [2,7]. Although CT is very sensitive in detecting moderate to severe steatosis, it is less effective for mild cases [7,11]. The use of non-contrast CT in clinical practice for detecting liver steatosis [1,4,7,10,11]. Some studies suggest that measurements taken during the portal venous phase in contrast-enhanced CT are more specific than those in non-contrast CT [14,15].

To assess liver steatosis, the liver parenchymal density, liver-spleen density difference (L-S), or liver-spleen density ratio (L/S) are measured [4,7,9,11]. The literature indicates that in healthy individuals, liver parenchymal density on non-contrast CT ranges from 45-65 hounsfield unit (HU), 50-57 HU, or 50-65 HU, with a liver density 8-10 HU higher than the spleen density [3,4,16]. A liver density less than 40 HU suggests presence of more than 30% steatosis [3,8]. One study defined a normal L-S range as 1-18 HU, where patients with a liver density of 48 HU and an L-S difference of -2 were identified as having moderate to severe steatosis [7]. Iwasaki et al. determined the L/S ratio in patients with no or mild steatosis to be approximately 1.184±0.091 and set a threshold of 1.1 for distinguishing between mild and moderate to severe steatosis [9]. An L/S ratio less than 1 indicates hepatosteatosis [3]. Additionally, an L/S ratio less than 0.8 or an L-S difference greater than 9 HU indicates more than 30% hepatosteatosis [8].

Proton density fat fractionation MRI derivative (MRI-PDFF) has emerged as the most prevalent method for fat quantification in recent years, as it facilitates simultaneous whole organ imaging and organ tissue quantification. The MRI-PDFF technique facilitates the evaluation of individual hepatic segments [17,18]. The Quantitative Imaging Biomarkers Alliance (QIBA) MRI PDFF committee has presented data that confirms the accuracy of MRI in determining fat fraction over a wide range [19].

The objective of this study was to ascertain the HU ranges that facilitate grading by conducting density measurements on CT images of patients diagnosed with hepatosteatosis via US.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Fırat University (date: 01.02.2024/ session number 02-37). Since the study was retrospective and no personal data were used, informed consent was not obtained. Patient lists were obtained by searching the term "hepatosteatosis" in US reports from our hospital database. To reduce operator variability, only patients reported by a single radiologist were evaluated. A total of 10,320 patients diagnosed with hepatosteatosis on USG were included for analysis. A total of 1,504 patients who underwent re-imaging were excluded from the study. The remaining patients were examined for the presence of CT images. CT imaging was available for 3,560 patients. Of these patients, 2011 underwent a CT scan in close temporal proximity to the US procedure (±2 Weeks). Patients were excluded from the study if they did not undergo equilibrium phase imaging or if they underwent arterial phase imaging, im cases with a lesion in the liver, and if the imaging field did not include the entire liver or spleen. Patients suffering from chronic liver parenchymal disease and known alcohol abuse were also excluded from the study. The remaining 666 patients constituted the study cohort. Of these patients, 105 had contrast and non-contrast CT images obtained during the same period. The images of 105 patients with contrast and non-contrast imaging were dynamic images, and the non-contrast and equilibrium phases were used in the examination. The selected patients were classified according to the grades specified in their US reports.

The US assessments were conducted by a radiologist with 13 years of experience using a Philips Affiniti 50 device with a convex probe at 6-2 MHz. Liver echogenicity was graded based on the visibility of the vascular walls and diaphragm contours (Figure 1).

CT examinations were performed via a 128-slice CT scanner (Ingenuity Core 128; Philips Medical Systems, Best, Netherlands). Regions of interest (ROI) measuring 100-150 mm^2 were placed separately in the 8 segments of the liver. Three separate measurements were taken from the spleen parenchyma (Figure 2). The averages of these measurements were calculated, and the L/S ratios were determined. The HU values of each segment were also recorded. When placing the ROIs, care was taken to avoid artefacts, and blood vessels. In cases of heterogeneous density reductions, measurements were taken from more hypodense areas.

Since our measurements were taken from both contrast-enhanced and non-contrast images, we found that it was more appropriate to use the L/S ratio for evaluation. To compare the results of patients with both contrast-enhanced and non-contrast imaging, we performed calculations on both sets of images.

Statistical analysis

The data were analyzed via IBM SPSS 22.0 software (IBM SPSS Corp.; Armonk, NY, USA). The descriptive statistics of

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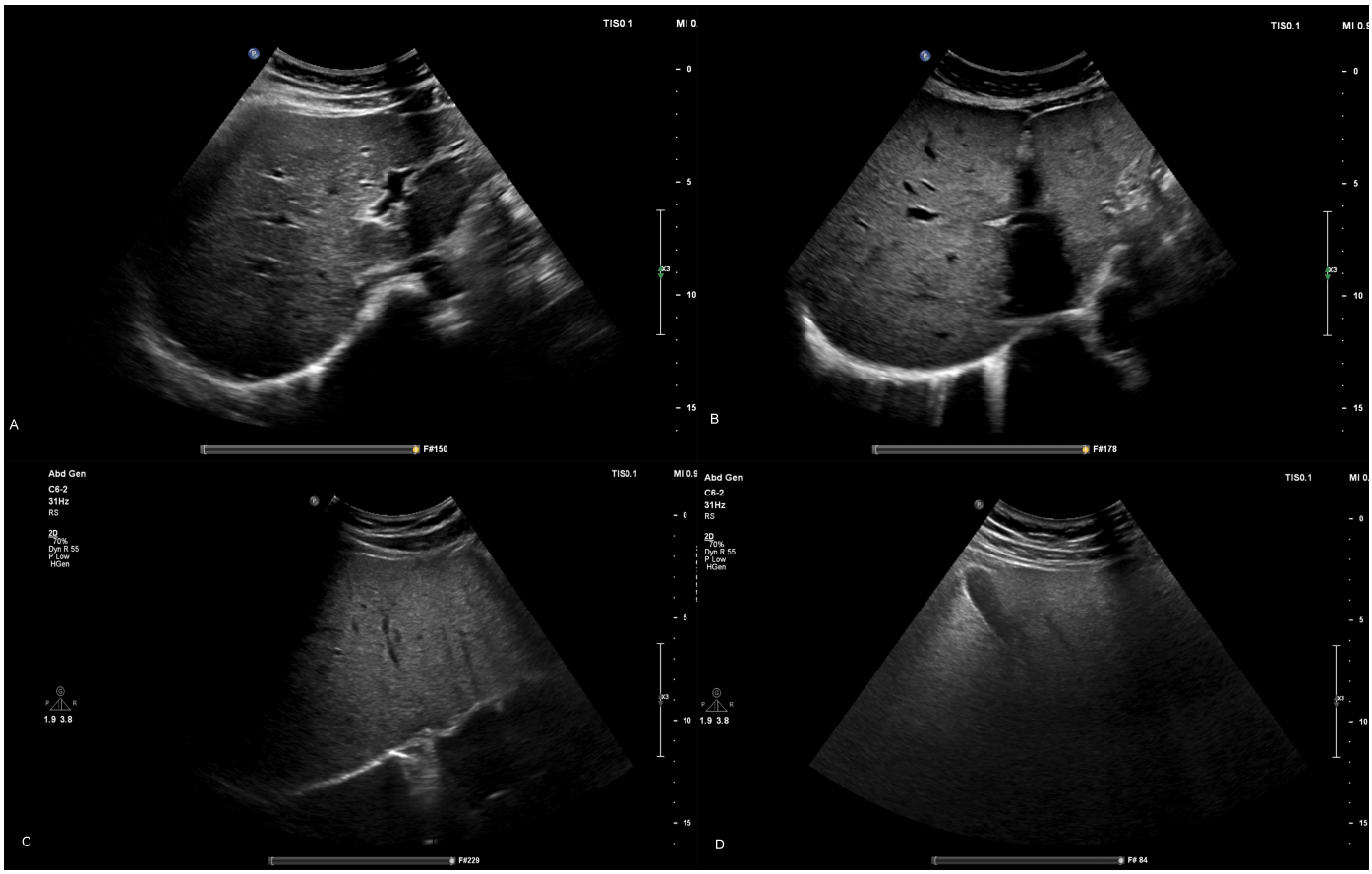

Figure 1. Liver US images according to grade. Grade 0 (A), Grade 1 (B), Grade 2 (C), Grade 3 (D).

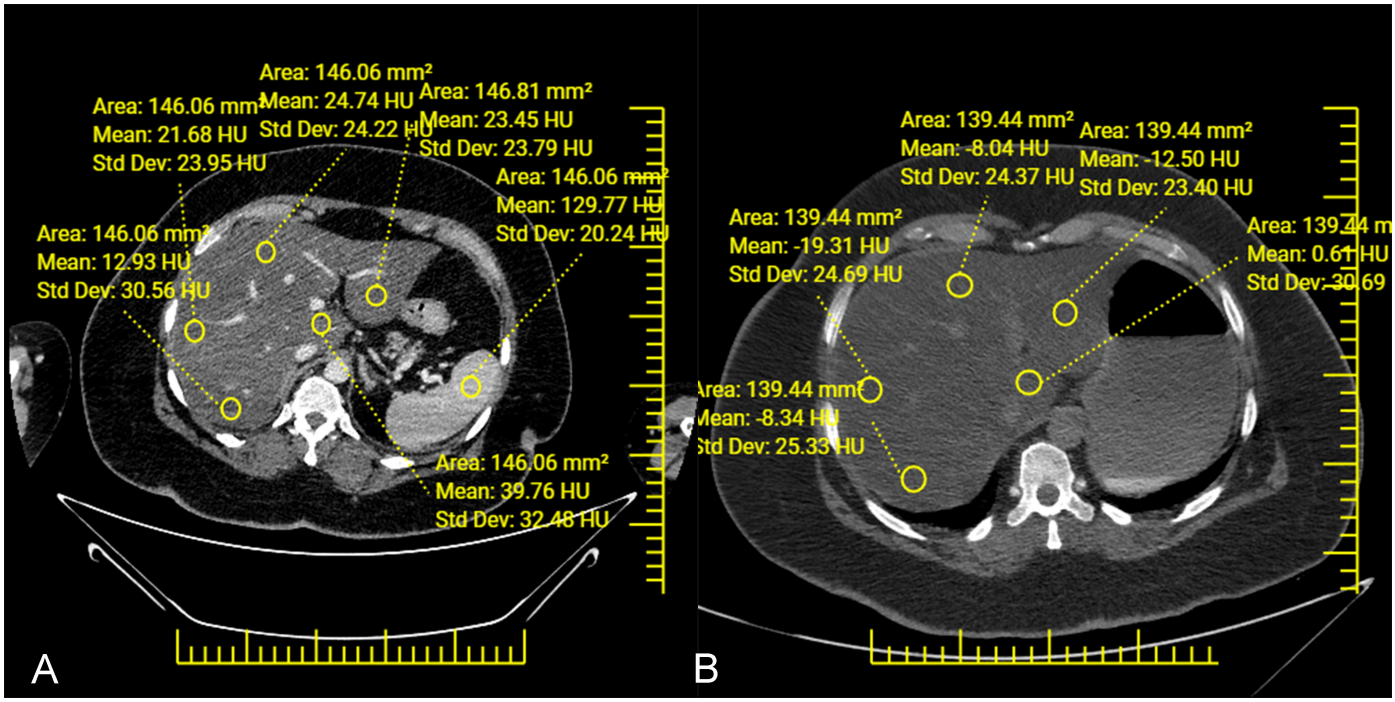

Figure 2. Placement of ROIs for computed tomography density measurement. (A) Axial CT image showing standard ROI placement in spleen and liver segments 1, 3, 4b, 5, and 6. (B) A supplemental image showing ROI placement in liver segments 1, 2, 4a, 8, and 7. ROIs were positioned to avoid visible vessels and bile ducts and to ensure representative sampling of parenchymal density.

the data are presented as the mean ± standard deviation, median (minimum–maximum), frequency, and percentage values. The normal distribution of variables was assessed via the Kolmogorov-Smirnov test. For the analysis of quantitative re-

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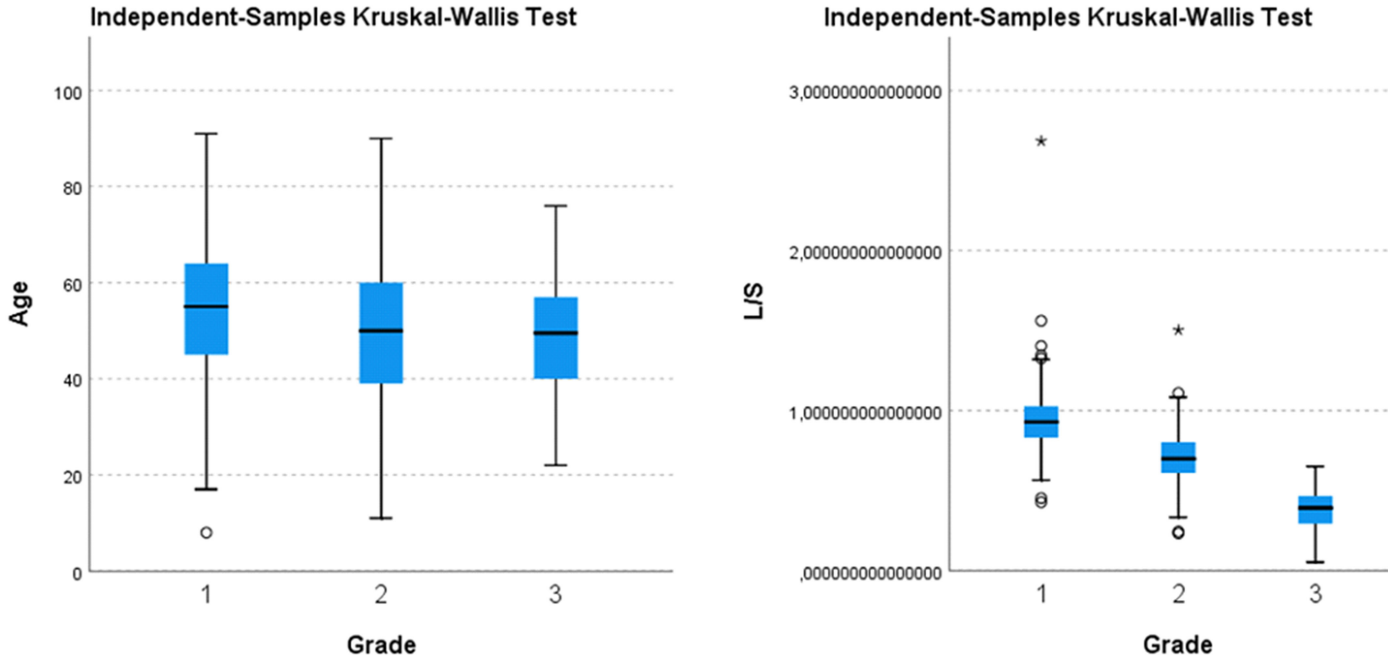

Figure 3. Comparison of age and L/S ratio of groups shown with a graph.

peated measures, the Friedman test was used, followed by the Dunn-Bonferroni correction as a post-hoc test. For the analysis of independent quantitative measurements, the Kruskal-Wallis test was used, followed by the Dunn-Bonferroni post-hoc correction. ROC analysis was used to determine the cutoff value, and the results are presented with the cutoff value calculated based on the area under the curve (AUC) and Youden index. A p value of 0.05 was considered statistically significant.

RESULTS

A total of 666 individuals, including 349 men and 317 women, met the inclusion criteria and were analyzed in the study. The characteristics of the patients, categorized by grade, are presented in Table 1. The average age of patients in G1 was significantly different from those in G2 and G3 (p<.008). The L/S ratios for G1, G2, and G3 were 0.94 ± 0.19, 0.70 ± 0.16, and 0.37 ± 0.13, respectively. There was a statistically significant difference in the L/S ratios among all the groups (p=.001) (Figure 3). A ROC analysis was conducted to determine the threshold L/S values distinguishing the groups. For G1-G2, the area under the curve (AUC) was 0.857, with a sensitivity of 86%, specificity of 71%, and cutoff value of 0.77. For G2-G3, the AUC was 0.954, with a sensitivity of 94%, specificity of 82%, and cutoff value of 0.47 (Figure 4).

The HU values for all eight liver segments were recorded for each patient (Table 2). Segment 1 had the highest average value (66.72 HU), whereas segment 7 had the lowest (58.65 HU). Comparisons revealed no significant difference in HU values between segments 7-8 (p<.068), segments 5-6, segments 4-3, segments 4-2, and segments 3-2 (p=1). Significant differences were observed in other comparisons (p<.001). Segment 1, which had the least fat accumulation, was significantly different from all the other segments.

Additionally, 105 patients with both contrast-enhanced and non-contrast abdominal CT scans taken within close time frames or on the same day were classified by grade. Measurements were taken from both types of CT scans to calculate L/S values. Statistical comparisons of contrast-enhanced and non-contrast CT data were made, and a ROC analysis was

Table 1. Characteristics of patients classified according to degree of hepatosteatosis.

	n
Total cases	666
Gender (male/female)	349/317
Age (mean)	51.62
Contrast CT/non-contrast CT	360/306
Grade 1	337
Gender (male/female)	164/173
Contrast CT/non-contrast CT	185/152
Grade 2	249
Gender (male/female)	134/115
Contrast CT/non-contrast CT	137/112
Grade 3	80
Gender (male/female)	51/29
Contrast CT/non-contrast CT	38/42
CT with and without contrast	105
Grade 1	48
Grade 2	47
Grade 3	10

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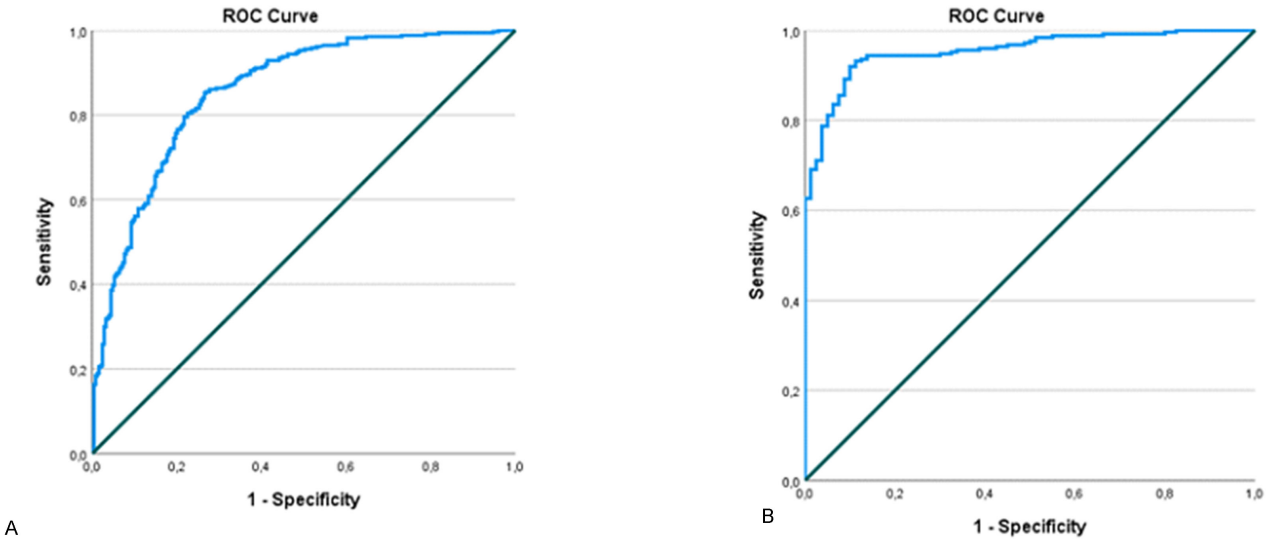

Figure 4. Determine the threshold L/S values separating the groups ROC analysis graphs. Areaunder the curve (AUC) for G1-G2 was 0.857 (A). AUC for G2-G3 was 0.954 (B).

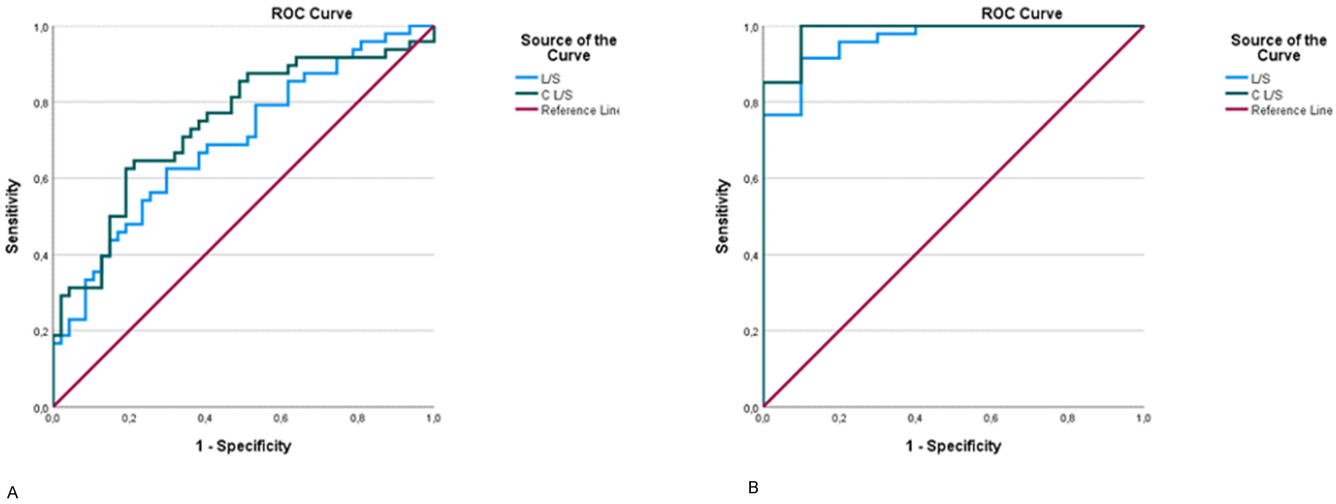

Figure 5. ROC analysis graphs of contrast and non-contrast CT data of the same patient. (A) For Grade 1-2, (B) For Grade 2-3. In both graphs, the AUC of contrast images is higher. L/S: Liver spleen HU ratio on noncontrast CT, CL/S: Liver spleen HU ratio on contrast enhanced CT.

Table 2. HU values of eight liver segments.

Liver segments	Minimum HU	Maximum HU	Mean HU	Std. Deviation
1	1	142	66.72	25.607
2	0	146	64.29	26.560
3	0	162	63.77	26.092
4	0	155	63.54	26.634
5	0	151	61.25	26.904
6	0	137	61.55	26.747
7	0	160	58.65	26.854
8	0	137	59.83	27.279

performed. The analysis of values from contrast-enhanced and non-contrast-enhanced imaging revealed significant differences between the groups. However, contrast-enhanced images exhibited a higher degree of significance in distinguishing G1 and G2 (L/S p .003, L/S with contrast p .001). In the ROC analysis, the AUC for the G1-2 comparison was 0.695 for L/S and, 0.742 for L/S with contrast, indicating that contrast-enhanced imaging was more discriminative (Table 3, Figure 5).

Segment 1 was found to be the least affected by fat accumulation. During the US evaluations, we observed focal, segmental, and lobar steatosis types. In the tomographic sections, lobar and segmental fatty deposits were observed in the G1 and G2 groups, while diffuse involvement was predominantly observed in the G3 group. It was also noteworthy that fatty deposits were more prevalent in the central parts.

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Table 3. Comparison of measurements of patients who had CT scans with and without contrast.

	L/S			Contrast L/S		
	Mean HU	Min-Max HU	Std. Deviation	Mean HU	Min-Max HU	Std. Deviation
G1	0.98	0.57-1.32	0.168	0.86	0.42-2.68	0.300
G2	0.85	0.39-1.16	0.165	0.73	0.50-0.96	0.109
G3	0.31	0.02-0.73	0.252	0.40	0.23-0.62	0.112
	p			p		
G1-2	**.003**			**.001**		
G1-3	.001			.001		
G2-3	.001			.001		
	AUC	%95 Confidence Interval		AUC	%95 Confidence Interval	
G1-2	0.695	0.591	0.800	**0.742**	0.641	0.842
G2-3	0.962	0.910	1.000	**0.985**	0.954	1.000

DISCUSSION

Liver biopsy is the best diagnostic method for evaluating hepatosteatosis. However, for the diagnosis of simple hepatosteatosis, more non-invasive methods should be used instead of biopsy [6].

Hepatosteatosis is a condition that is common in all societies and is often detected incidentally with US. US, which has high sensitivity in detecting moderate and severe steatosis, has limited accuracy in detecting mild steatosis. Additionally, the detection of mild steatosis is variable because of user dependency. When there is less than 33% fat infiltration in the biopsy sample, the sensitivity of US decreases [7,13].

In daily practice, abdominal CT iamges are taken with contrast. Non-contrast CT is recommended especially for hepatosteatosis. Studies have shown that non-contrast and contrast-enhanced shots have similar accuracy rates [10].

In the study conducted by Kim et al. with 179 liver donors, contrast-enhanced CT was shown to be more successful than non-contrast CT [15].

In the study conducted by Johnston et al., contrast-enhanced CT detected hepatosteatosis with a sensitivity of 54-71% [10].

In this study, we performed measurements on existing CT images of patients with hepatosteatosis that we diagnosed and graded with US and determined the threshold HU value that separates the groups. We also performed measurements on contrast and non-contrast CT images of the same patient and examined which technique separated the groups better. Although there are many studies in literature, the measurements we made have not been made in any previous study.

Non-contrast CT is generally preferred because of contrast material delivery methods and scanning timing problems. We created our working groups by paying attention to this. Since we used images with and without contrast, it would not be correct to use only the liver HU value. Therefore, we used the liver HU/spleen HU value.

Although CT has high accuracy in the diagnosis of moderate and severe steatosis, it is not as sensitive in detecting mild steatosis [3,7].

Iwasaki et al used various parameters to evaluate hepatosteatosis (L/S, BMI, GGTP, ALT, AST, Che, and T-CHO). These authors reported that the L/S ratio was strongly associated with steatosis. A single biopsy sample represents a very small part of the liver and cannot represent the entire liver. Therefore, CT allows the evaluation and measurement taken from every part of the liver [9].

In our study, we found a significant difference in the L/S values among the groups and calculated the threshold values that separate the grades. When comparing images with and without contrast, there was no significant difference in distinguishing G3 from G1 and G2, whereas CT with contrast was more significant in distinguishing G2 from G1. When the groups were compared, the area under the curve was greater in contrast-enhanced images. Some studies have shown that hepatosteatosis reduces hepatic blood flow [15]. This finding may explain why fatty segments are more hypodense during portal phase CT imaging. As a result, the increased fat lowers the average density of the liver and delays its contrast enhancement. In this case, we think that fatty segments become more prominent.

In addition, CT allowed us to measure each segment separately, and we found that segment 1 (Caudate lobe) had the least steatosis and that segment 7 had the highest. During the investigation, it was observed that the liver in patients G1 and G2 was partially fatty rather than diffusely. Liver biopsy is performed from the left lobe of the liver by a subcostal approach or from segments 5-6 by an intercostal approach. It is obvious that it is difficult to perform a biopsy from segment 7, where the most pronounced steatosis is seen. This finding suggests that not all biopsies will show the degree of hepatic steatosis with absolute certainty.

CT taken in the portal phase can detect hepatosteatosis with the same or even greater accuracy than non-contrast CT [15].

Several cross-sectional studies have reported heterogeneous steatosis among different lobes and segments. Research has been conducted on the alterations in fat distribution in re-

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sponse to weight gain and loss [17,20]. In the study conducted by Syvari et al. [17] with MRI-PDFF, mean liver and segmental steatosis values were calculated. Segment 1 had the least steatosis and segment 8 had the most. Segment 7 was the second most steatotic segment. Our study showed similar results with this study. In our study, the second most steatotic segment was 8 and the most diffusely steatotic segment was 7. We found very close results to MRI-PDFF measurements, which is reported to give the most accurate results for steatosis measurement in the literature. This also shows the accuracy of our US evaluation.

Limitations

The current study is not without limitations. Due to the retrospective nature of the study, it was not possible to obtain tissue diagnosis for the cases. There were limited number of G3 cases. Additionally, laboratory data from the imaging period were not available for each patient. It should be noted that weight and height data were not available for most patients.

CONCLUSION

As a result, hepatosteatosis is a disease of increasing concern. US examinations are routinely used to determine the degree of fatty liver disease detected on CT images obtained for various reasons. MRI is not an easily accessible imaging modality. In this study, we determined grade-separating thresholds for grading hepatosteatosis detected on CT without the need for USG or any other imaging technique. We believe that this approach will be useful for radiologists in grading and reporting hepatosteatosis detected on CT and will eliminate the need for additional imaging.

Ethics Committee Approval: Ethical approval was obtained for the study from the Fırat University Non-Interventional Research Ethics Committee (No: 2024/02-37). This retrospective study was conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent: Not necessary for this manuscript.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Functional neurological (conversion) symptoms mediate the effect of self-stigma in women seeking psychological help on their psychological well-being

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MAIN POINTS

- In functional neurological symptom disorder, self-stigma of seeking psychological help is higher and psychological well-being is lower than that in healthy controls.
- A significant relationship exists between self-stigma of seeking psychological help and psychological well-being.
- The level of functional neurological symptom disorder symptoms indirectly mediates the relationship between self-stigma and psychological well-being.

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ABSTRACT

Aim: This study aimed to examine the effect of self-stigma of seeking psychological help on psychological well-being in patients diagnosed with functional neurological symptom disorder (formerly conversion disorder) through conversion symptoms.

Materials and Methods: In this cross-sectional study, the Self-Stigma of Seeking Psychological Help Scale (SSPHS), Psychological Well-Being Scale (PWBS), and Somatoform Dissociation Questionnaire (SDQ-20) were administered to the FNSD and HC groups.

Results: The FNSD group consisting of 31 females (12 motor (M)-FNSD, 9 somatosensory (SS)-FNSD, and 10 mixed-FNSD) and the HC group consisting of 32 females were similar in terms of age ($p = 0.350$), education level ($p = 0.386$), marital status ($p = 0.579$), and working status ($p = 0.136$). Significant differences were observed between the FNSD and HC groups in terms of SSPHS ($p<0.001$), PWBS ($p<0.001$), and SDQ-20 ($p<0.001$). Significant differences were observed between the M-FNSD, SS-FNSD, and Mix-FNSD subgroups in terms of SDQ-20 ($p = 0.034$), SSPHS ($p = 0.028$), and PWBS ($p = 0.015$). The comparison that caused significant differences in terms of SDQ-20, SSPHS, and PWBS scores among the FNSD subgroups was between M-FNSD and Mix-FNSD. The mediating role of the FNSD symptom level (SDQ-20) in the relationship between SPH and PW was examined. The indirect effect of SPH on PW was determined as -0.436 (49.65%). The direct effect of SPH on PW was determined as -0.442 (50.35%). In the correlation analysis performed in the FNSD group, a significant relationship was found between SSPHS and SDQ-20 ($r=0.921$, $p<0.001$), between SSPHS and PWBS ($r=-0.879$, $p<0.001$), and between PWBS and SDQ-20 ($r=-0.882$, $p<0.001$).

Conclusion: This study demonstrates that SPH increases and PW decreases in FNSD and that FNSD symptoms mediate the relationship between SPH and PW.

Keywords: Functional neurological symptom disorder, Conversion disorder, Psychological well-being, Self-stigma, Mediation analysis

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INTRODUCTION

Neurological symptoms or other medical conditions that cannot be attributed to a neurological disease are referred to as functional neurologic symptom disorder (formerly conversion disorder/hysteria). These symptoms are real and cause significant distress or impairment of functioning. Signs and symptoms vary and may include specific patterns [1]. FNSD affects sensations and movements, and the symptoms cannot be intentionally produced or controlled. Motor (M) FNSD refers to symptoms such as abnormal movement, paralysis, loss of balance, and non-epileptic seizures, and somatosensory (SS) FNSD refers to symptoms such as inability to speak, numbness, blindness, deafness, and cognitive difficulties. Motor and somatosensory symptoms are present together in a group of patients and are defined as mixed (Mix) FNSD [1, 2].

FNSD, which manifests itself in the form of physical/somatic symptoms, leads individuals to reject or have difficulty accepting the psychogenic nature referred to after subsequent examinations. Individuals are likely to avoid psychiatric treatment

and remain deprived of treatment during this process. One of the most important reasons for this reaction is stigmatization and related situations [3]. Stigma, represented by three forms, including public stigma, self-stigma, and label avoidance, is eminently present in those with FNSD [4]. Results of an online survey showed that 85% of patients diagnosed with FNSD feel rejected and disrespected because of their symptoms [5]. In addition to the stigmatizing attitudes of the public [6], it is known that health care professionals are not happy to serve patients with FNSD and describe them as difficult patients [7]. Many clinicians believe that patients have voluntary control over their symptoms or that they are acting out [8].

Patients with FNSD who internalize negative stereotypes and stigmatize themselves may subsequently exhibit negative emotional reactions. Psychiatric symptoms are more common in those who stigmatize themselves, and this situation harms PW [9]. Although stigma-related situations in FNSD have been partially examined [5, 6], self-stigma and a more specific form of self-stigma, i.e., self-stigma of seeking psychological help (SPH), have not yet been examined. The relationship between SPH and PW in patients with FNSD and the effect of FNSD symptoms on this relationship are unknown.

The relationships between stigma and psychological well-being in various medical illnesses and with each other and with the illness have been investigated, and significant relationships have been found [10]. Furthermore, some concepts have been demonstrated to play a moderating and mediating role in the relationship between stigma and psychological well-being [11-13]. The presence and severity of psychiatric symptoms also negatively affect psychological help-seeking behavior [14]. Considering all this information, this study aimed to evaluate and compare the SPH and PW of patients with FNSD and to reveal the mediator effect of FNSD symptoms. Our hypothesis is that FNSD symptom severity indirectly mediates the relationship between SPH and PW.

MATERIALS AND METHODS

This cross-sectional study was conducted at Elazig Fethi Sekin City Hospital between February 6, 2025, and April 18, 2025. Ethics committee approval was obtained (Elazığ Fethi Sekin City Hospital Non-Interventional Research Ethics Committee, Decision number: 2024/4-12; Decision date: 21/11/2024).

Sample and setting

After fulfilling the requirements (examination, treatment, prescription, report, etc.) regarding the admissions of female patients who applied to the psychiatric outpatient clinic and were diagnosed with FNSD according to DSM-5-TR [15], those who met the inclusion and exclusion criteria of the study were invited to the study as the FNSD group in the order of admission.

The topic, content, design, and ethical implications of the study were explained to the invited female patients. Informed consent was obtained from all those who agreed to participate in the study.

The HC group consisted of healthy first-degree relatives of patients with various psychiatric diagnoses who were admitted to the same outpatient psychiatry clinic. Explanations regarding the study were also provided to the HC group, and informed consent was obtained from them. The FNSD group was divided into three subgroups according to symptom types [motor (M)-FNSD, somatosensory (SS)-FNSD, and mixed (mix)-FNSD].

Inclusion/Exclusion criteria

The type, frequency, and severity of symptoms in patients diagnosed with FNSD may vary, which explains the fluctuating clinical course of FNSD. Although it is known that CR is difficult to achieve despite treatment, psychotherapy is associated with longer remission periods by increasing cognitive awareness. Psychotherapy was accepted as an exclusion criterion due to its role in reducing the negative effects of stigmatization-related situations [16]. Current comorbid psychiatric disorders, alcohol use, illicit drug use, and benzodiazepine use are other exclusion criteria. Neuropsychiatric diseases and conditions such as epilepsy and MS were accepted as exclusion criteria. The lack of control of medical conditions such as diabetes mellitus, essential hypertension, and hypothyroidism has been associated with cognitive decline [17]. However, such controlled medical conditions were not considered exclusion criteria because their effect on cognitive functions was limited, and thus, no patients were excluded.

DÖ collected the data in a single outpatient psychiatry clinic. The number of patients diagnosed with FNSD who were admitted to this outpatient clinic between the specified dates was 48 (46 females and 2 males). Three patients with FNSD symptoms who were admitted to psychiatry for the first time did not accept participating in the study. The three patients who were included in the psychotherapy sessions were excluded from the study.

One patient with epilepsy and four patients using benzodiazepines were excluded from the study. One patient with uncontrolled diabetes mellitus and two patients with hypothyroidism who were using medication for this condition were excluded from the study. Three patients who were currently under FNSD treatment and met the inclusion and exclusion criteria did not participate in the study. As a result, no male patients accepted to participate in the study.

The HC group comprised first-degree female relatives of patients who were admitted to the psychiatry outpatient clinic for any reason. In this group, exclusion criteria were as follows: past and current FNSD diagnosis, current psychiatric disorder diagnosis, alcohol and substance use, uncontrolled general medical disease, and neurological diseases with cognitive impairment.

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Measurements

Sociodemographic and Clinical data

This form included questions regarding age, education level, marital status, and working status. In addition, the characteristics related to the FNSD diagnosis were queried.

Self-Stigma of Seeking Psychological Help Scale (SSPHS) score

Vogel et al. [18, 19] developed the SSPHS. Acun-Kapkıran and Kapkıran [20] conducted the Turkish validity and reliability study of the scale. Some items of the scale are reverse-scored (items 2, 4, 5, and 7), and a high score indicates high self-stigma in seeking psychological help.

Psychological Well-Being Scale (PWBS) score

Diener et al. [21] developed the PWBS. Telef [22] conducted the The Turkish validity and reliability study of the scale. According to this scale, a high score indicates high psychological well-being.

Somatoform dissociation questionnaire (SDQ-20)

Nijenhuis et al. [23] developed the SDQ-20 and Turkish validity and reliability study of the scale was conducted by Şar et al. [24]. A high SDQ-20 score indicates high somatoform symptom severity.

Statistical analysis

IBM SPSS Statistics for Windows, Version 26.0 (Armonk, NY: IBM Corp.) was used for the statistical analysis. Continuous variables and descriptive statistics are presented as mean ± standard deviation, whereas categorical variables are presented as frequency and percentage. Categorical data were analyzed using the chi-square test (p-value adjusted using the Bonferroni method). If the expected frequency of one or more cells was less than five and this rate was above 25%, the Fisher's exact test was used instead of the chi-square test. Kolmogorov-Smirnov test determined the compliance with normal distribution. In comparing two groups, Mann–Whitney U test was used for variables that did not show normal distribution and the independent samples t-test for variables that showed normal distribution. In comparing numerical data across FNSD subgroups, Levene's statistics were determined using the test of homogeneity of variances. One-way ANOVA was used because the Levene's statistic was >0.05 for all variables. The post-hoc Bonferroni test was used to reveal differences between the means of the FNSD subgroups. The Pearson correlation analysis was used. Cohen's d was calculated for continuous variables and Cramer's V/Phi for categorical variables.

Linear regression analysis was used in the mediation analysis of the FNSD group. The assumptions required for linear regression analysis were checked (linearity, homoscedasticity, normality, and no multicollinearity). The significant effect of SSPHS on PWBS was first investigated using linear regression analysis to determine the appropriateness of the mediation analysis (unstandardized B=-0.987, standard error=0.099, standardized coefficients β=-0.879, t=-9.942, p<0.001, 95% Confidence Interval for B=-1.190 (lower bound), -0.784 (upper bound)). The effect of SSPHS on FNSD severity (partial mediator variable) was then examined using linear regression analysis. Subsequently, the combined effects of SSPHS and FNSD severity on PWBS were examined. The sum of the direct (c) and indirect (axb) effects of SSPHS on PWBS was expressed as the total effect (total effect = (axb) + c, Figure 1).

A p value of 0.05 was considered statistically significant.

When calculating the sample size, since there was no previous study with similar characteristics, the data obtained from the pilot administration conducted on ten participants (five FNSD and five HC) were used, and it was seen that there should be at least 20 subjects in each group (SSPHS score of FNSD=20.35±5.03; SSPHS score of HC=14.11±3.01; alpha=0.05; beta=0.20; power=0.80). After including 31 subjects in the FNSD group and 32 subjects in the HC group, the obtained data were subjected to power analysis again, and the adequacy of the sample size was confirmed (SSPHS score of FNSD group=19.29±4.72; SSPHS score of HC group =13.21±2.56; alpha=0.05; beta=0.20; power=0.80).

RESULTS

The FNSD group consisted of 31 females (M-FNSD, 12 females; SS-FNSD, 9 females; Mix-FNSD, 10 females), and the HC group consisted of 32 females. Tables 1 and 2 show the sociodemographic and clinical characteristics of the FNSD and HC groups.

While the FNSD and HC groups were similar in terms of age (p = 0.350), education level (p = 0.386), marital status (p = 0.579), employment status (p = 0.136), and smoking status (p = 0.836), there were significant differences between the groups in terms of SDQ-20 (p<0.001), SSPHS (p<0.001) and PWBS (p<0.001) scores. Significant differences in SDQ-20 (p = 0.034), SSPHS (p = 0.028), and PWBS (p = 0.015) scores were found between the M-FNSD, SS-FNSD, and Mix-FNSD groups. The comparison that caused significant differences in terms of SDQ-20, SSPHS, and PWBS scores among FNSD subgroups was between SS-FNSD and Mix-FNSD. All patients in the FNSD group were using antidepressants. No subjects were on psychotherapy.

Figure 1 shows the mediating role of the FNSD symptom level (SDQ20) in the relationship between SPH and PW. The indirect effect of SPH on PW was found to be -0.436 (standardized coefficient β of "a" [0.921] x standardized coefficient β of "c" [-0.474], Figure 1). This indicates that SPH reduces PW through FNSD symptoms. The ratio of the indirect effect (-0.436) to the total effect (-0.878) was 49.65%. The direct effect of SPH on PW was found to be -0.442 (standardized coefficient β of "c," Figure 1). This result shows that SPH reduces PW. The ratio of the direct effect (-0.442) to the total effect (-0.878) was 50.35%. The total effect of SPH on PW was found

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Table 1. Comparison of the FNSD and HC groups.

Variables	FNSD (n=31) Mean±SD or Median (mean rank)	HC (n=32) Mean±SD or Median (mean rank)	p-value (Kolmogorov-Smirnov Z)	Cohen's d and Cramer's V/Phi
Age (years)	37.61±8.87	35.5(mean rank)0±8.91	0.350[a]	0.237[e]
Education level (years)	8.00 (30.02)	8.00 (33.92)	0.386[b] (0.920)	0.185[e]
Marital status (married, single, widowed, divorced)	20/7/4	24/6/2	0.579[c]	0.900[f]
Working status (housewife/paid worker)	27/4	23/9	0.136[d]	0.882[g]
Smoking status (no/yes)	23/8	23/9	0.836[d]	0.643[g]
SDQ-20	52.00 (48.00)	24.50 (16.50)	<0.001*[b](3.968)	3.709[e]
SSPHS	20.00 (43.34)	13.00 (21.02)	<0.001*[b] (2.200)	1.601[e]
PWBS	17.06±5.29	33.31±4.76	<0.001*[a]	3.229[e]

*p<0.05; Statistical analysis was performed using the independent samples t-test[a], Mann-Whitney U test[b], chi-square analysis[c], Fisher's exact test[d], Cohen's d[e], Cramer's V[f], Phi[g].

Table 2. Comparison of the FNSD subgroups.

Variables	M-FNSD (n=12) Mean±SD (Median)	SS-FNSD (n=9) Mean±SD (Median)	Mix-FNSD (n=10) Mean±SD (Median)	p value
Age (years)	39.08±8.47 (40.00)	36.11±9.77 (34.00)	37.20±9.17 (37.00)	0.750[a]
Education level (years)	7.33±4.24 (6.50)	8.55±2.96 (9.00)	7.60±2.75 (7.00)	0.716[a]
Marital status (married, single, widowed, divorced)	8/2/2	5/3/1	7/2/1	0.900[b]
Working status (housewife/paid worker)	10/2	8/1	9/1	0.882[b]
Smoking status (no/yes)	10/2	6/3	7/3	0.643[b]
History of psychiatric hospitalization (no/yes)	11/1	8/1	8/2	0.706[b]
Antipsychotic use (no/yes)	10/2	7/2	8/2	0.949[b]
Age of FNSD onset	27.08±6.77 (24.50)	28.33±6.32 (26.00)	26.40±6.86 (24.50)	0.818[a]
SDQ-20	54.83±10.92[xy] (49.50)	49.88±9.70[x] (46.00)	62.20±8.41[y] (63.50)	0.034*[a]
SSPHS	18.33±5.08[xy] (19.00)	17.11±3.51[x] (17.00)	22.40±3.86[y] (23.00)	0.028*[a]
PWBS	17.33±4.53[xy] (18.00)	20.44±5.52[x] (22.00)	13.70±4.13[y] (12.50)	0.015*[a]

*p<0.05; tatistical analysis was performed using one-way ANOVA[a] (post-hoc Bonferroni) and Fisher's exact test[b] (adjusted p value using the Bonferroni method). The letters [x] and [y] indicate statistical significance in the two comparisons. The presence of the same exponent letter in two compared groups indicates that the groups are similar (p > 0.05) for that variable, whereas different exponent letters indicate that the groups are different (p<0.05) for that variable.

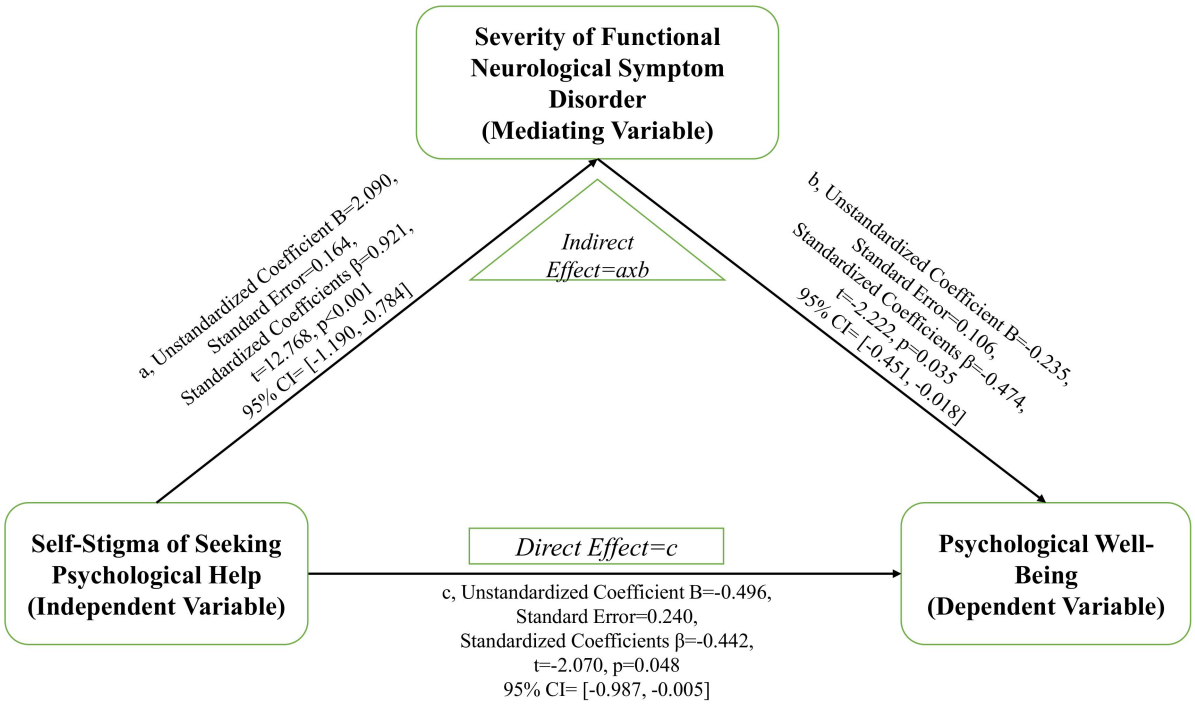

Figure 1. Mediation Model Diagram.

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to be -0.878. This shows that SPH generally reduces PW (total effect of 100.00%).

In the correlation analysis performed in the FNSD group, a significant relationship was found between SSPHS and SDQ-20 (r=0.921, p<0.001), between SSPHS and PWBS (r=-0.879, p<0.001), and between PWBS and SDQ-20 (r=-0.882, p<0.001).

DISCUSSION

This study examines the concepts of SPH and PW in FNSD across FNSD symptoms. The findings demonstrated that patients diagnosed with FNSD had higher SPH scores and lower PW scores than healthy individuals, a negative relationship between SPH and FNSD symptom scores and PW, and a mediating role of FNSD symptoms in half of the relationship between SPH and PW.

Symptoms of FNSD, a biopsychosocial disorder, are common in patients with non-psychiatric illnesses [25, 26]. This symptomatic overlap highlights the importance of a thorough differential diagnosis and careful consideration of its clinical features, natural history, and treatment reaction in distinguishing FNSD from other nonpsychiatric illnesses [27]. Patients referred to psychiatry after a series of unsuccessful attempts at non-psychiatric treatment avoid admission due to stigmatization concerns [27, 28]. A recent survey showed that 81.6% of respondents felt that they had been treated poorly due to stigmatization [28]. New psychiatric symptoms are added to the existing psychiatric symptoms of patients whose psychiatric treatment has been delayed or the severity of existing symptoms increases [6]. There are various ways to conceptualize stigmatization, which is a multifaceted social process [27, 29]. According to Link and Phelan's [29] sociological model, stigmatization is the result of labeling, stereotyping, separation, status loss, and discrimination in a power-based environment. Additionally, stigmatization has been viewed as an interpersonal process that involves discrimination, stereotyping, and prejudice [28, 30]. Cognitive errors, such as labeling, play a role in the emergence of stigma [29, 31], and cognitive errors in interpersonal relationships are higher in patients with FNSD than in healthy individuals [2]. In the present study, the SPH level was higher in patients with FNSD than in healthy individuals and was significantly higher in patients with motor and somatosensory FNSD symptoms (mix FNSD) than in patients with only motor and somatosensory symptoms. The SPH level of patients with motor FNSD symptoms was higher than that of patients with somatosensory symptoms, although not significantly. In the study conducted by Örüm and Atmaca [2], the cognitive error levels of FNSD subtypes in interpersonal relationships were compared, and an increased cognitive error level was reached in M-FNSD compared to SS-FNSD. Although stigmatization and related situations were not directly investigated in this study, this may facilitate the study's understanding. Studies investigating cognitive errors and SPH together will allow a more accurate interpretation of our findings.

Depending on the symptom characteristics, FNSD causes negative changes in psychological, physical, social, and functional areas and harms PW [32, 33]. The quality of life of patients with impaired PW is also negatively affected over time. The quality of life of patients diagnosed with FNSD has been examined in various studies. In the study conducted by Özenli et al. [34], the quality of life of patients diagnosed with FNSD was worse than that of healthy controls. The deterioration of quality of life may result in the deprivation of the required treatment for FNSD symptoms. Ultimately, since FNSD and negative life outcomes have a two-way relationship, the period in which the patient remains untreated may be extended. Studies on FNSD subtypes or symptom dimensions are insufficient, and most studies have focused on nonepileptic seizures [28]. However, recent studies have shown that FNSD subtypes differ in various characteristics and that patients may exhibit more than one symptom dimension. In other words, the majority of studies in this sphere relate to nonepileptic seizures and do not cover the full spectrum of FND symptoms [2, 35].

This study is valuable because it reveals the relationship between SPH and PW in FNSD. A negative relationship exists between SPH and PW in patients with FNSD. Rose et al. [36] conducted a study on healthy high school students and reported that self-stigma was associated with overall well-being and five well-being subscales, including environmental mastery, self-acceptance, autonomy, personal growth, and positive relations. The findings of Rose et al. [36] point to the need for greater awareness of self-stigma along with an explicit focus on the promotion of protective well-being in prevention work and interventions designed to alleviate the tendency for young people to internalize stigma.

The most important finding of this study is that FNSD symptoms mediate the relationship between SPH and PW. FNSD treatment should be approached with a biopsychosocial approach. The combination of psychopharmacological agents and psychotherapy provides the best results. The family, caregivers, and social environment should be included in the treatment process as a whole. Possible additional psychiatric symptoms accompanying FNSD should also be considered during treatment [1]. Reducing FNSD symptoms with various interventions may positively affect the relationship between high SPH and low PW through the mediating effect of FNSD symptoms.

Limitations

This study has several limitations. The limited sample size of FNSD subgroups. Its cross-sectional nature does not allow for a strong establishment of the findings' cause-and-effect relationships. The factors affecting SPH and PW in FNSD will be revealed more clearly with longitudinal studies. The possible effect of personality traits on the findings was not separately investigated. It is recommended to reveal the possi-

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ble effects of factors such as social support, culture, economic conditions, and personality traits on the relationship between SPH and PW for a better understanding of the subject (as an intermediary or regulator). Only female participants were included in this study. Conducting studies that include male patients would eliminate unintentionally raised questions about recruitment bias. Although the HC group excluded participants with past or current FNSD diagnoses or any active psychiatric disorder, patients may have influenced them in terms of SPH and PW [37]. Studies that include participants with no relatives with any active or past psychiatric disorder can be expected to eliminate this limitation.

CONCLUSION

In conclusion, this study shows that in patients diagnosed with FNSD, the level of SPH is higher and the level of PW is lower compared to healthy individuals, that there is a significant relationship between SPH and PW, and that the level of FNSD symptoms indirectly mediates the relationship between SPH and PW. Reducing FNSD symptoms with biopsychosocial interventions may indirectly affect the relationship between SPH and PW and produce positive results.

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Informed Consent: Informed consent was obtained from all participants.

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The relationship between health literacy and digital healthy diet literacy and dietary habits of pregnant women in different trimesters

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MAIN POINTS

- Health literacy and digital healthy diet literacy are positively correlated with women who are pregnant.
- Pregnant women with higher health literacy tend to make healthier dietary choices and use reliable sources of information.
- Educational interventions during prenatal care can help improve both health and digital diet literacy, thereby enhancing maternal and fetal outcomes.

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ABSTRACT

Aim: This study aimed to investigate the relationship between health literacy, digital healthy diet literacy, and dietary habits of pregnant women in different trimesters.

Materials and Methods: This study included 189 pregnant women who had registered for routine prenatal care. The participants were interviewed about their demographic characteristics, general health, smoking and alcohol consumption, medical history, and general dietary habits. In addition, a questionnaire with the Health Literacy Scale and the Digital Healthy Diet Literacy Scale was completed.

Results: A positive, weak, and statistically significant correlation was found between prepregnancy body mass index (BMI) and the Health Literacy Scale ($p<0.05$). A positive, weak, and statistically significant relationship was found between health literacy and digital healthy eating literacy ($r = 0.278$; $p = 0.007$).

Conclusion: As the health literacy of pregnant women improves, so does their digital healthy diet literacy. These results demonstrate the importance of promoting health literacy to support healthy dietary behaviors during pregnancy.

Keywords: Pregnancy trimesters, Health literacy, Diet, Obesity, Women health

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INTRODUCTION

Pregnancy is a critical time for women to experience physiological and psychological changes. Healthy lifestyle and dietary habits during pregnancy are important for both the mother and the baby to reduce risks such as gestational hypertension, diabetes, premature birth, low birth weight, macrosomia, and cesarean delivery both in the short and long term [1,2]. Pregnancy is a period in which health services are frequently used and weight gain and changes in dietary habits are observed. Various health information that pregnant women receive from different sources during this period may also cause confusion [3–5].

General literacy forms the basis of health literacy. On average, 26% of the adult population in the world does not have basic literacy skills, and two-thirds of this population are women [6,7]. A study conducted in Austria, Bulgaria, Germany, Greece, Ireland, the Netherlands, Poland, and Spain within the scope of the European Health Literacy Survey (HLS-EU) showed that the average health literacy index was 33.78 out of 50 points, and 47.60% of individuals had limited health literacy [8–10]. In Turkey, a health literacy study was conducted with the participation of 4924 adults in 23 provinces in 12 regions. The study found that the average health literacy index was 30.4, and people with limited (inadequate or problematic) health literacy made up 57.9% of society [11].

Increasing women's educational level in the reproductive period contributes to increasing health literacy rates and thus reducing infant/child mortality rates [12]. Low health literacy is now viewed as a global problem. Promoting health literacy is a public health goal that has a significant impact on soci-

ety's health and well-being [5,10]. During pregnancy, health literacy encompasses cognitive and social skills that enable women to access health information and prepare for childbirth and parenthood [13,14]. Pregnant women with high levels of health literacy receive parental care earlier and more frequently and are knowledgeable about birth control, fertility, prenatal screenings, correct use of prescription drugs, folic acid-vitamin use, and many issues related to reproductive health [6,7,12]. It is crucial to create strategies that will raise pregnant women's health literacy because the mother's lifestyle during pregnancy has an impact on the child's health later in life, ensuring the mother and the child stay healthy [15,16].

Improving the quality of daily nutrition and changing unhealthy dietary habits play a vital role in preventing CNRDs. Inadequate nutritional education and healthy dietary habits can lead to significant problems during pregnancy [17,18]. Web-based resources are mostly used to obtain information about a healthy lifestyle and proper dietary habits. Healthcare professionals and healthcare organizations actively use social media platforms to share their experiences and opinions. However, health and diet information from nonscientific and unreliable sources can often be perceived as reliable by the public, which may lead to the spread of low-quality content on websites [19–21]. Studies in the literature have evaluated dietary habits and health literacy during pregnancy. However, very few studies have examined health literacy and digital literacy for healthy eating and dietary habits of women during pregnancy.

Studies in the literature have examined dietary habits and health literacy during pregnancy. However, very few studies have examined the general health literacy, digital health literacy, and dietary habits of women during pregnancy, especially with trimester-specific comparisons. Therefore, the present study was designed to assess the health literacy and digital health literacy of pregnant women for healthy eating, compare these measures across trimesters, and examine their association with age and pre-pregnancy BMI. This approach fills a gap in the literature by incorporating DNL into prenatal research and providing trimester-by-trimester stratified analyses in a primary care setting.

MATERIALS AND METHODS

The study included 189 pregnant women aged 20–45 years with a live singleton fetus, without diagnosed psychiatric or chronic illness, who presented to the Gynecology and Obstetrics Outpatient Clinic of Ankara Koru Sincan Hospital between January and February 2024 for routine pregnancy check-ups and agreed to participate in the study. This study excluded pregnant women with pregnancy complications, maternal or fetal risks, or other diseases.

The "Informed Volunteer Consent Form" was given to each study participant, and their verbal and written consent was obtained. The Ankara Medipol College Ethics Committee for Non-Interventional Clinical Research approved the study (decision no:1, date: 09.01.2024). The Declaration of Helsinki was followed in the study.

Data collection

The questionnaire drawn up by the researchers was presented to the participants at the start of the study in a personal interview that lasted around 15 minutes. The questionnaire includes questions about the demographic characteristics, general health information, medical history, general dietary habits, and anthropometric measurements, as well as the Health Literacy Scale (HLS) and Digital Healthy Diet Literacy Scale Short Form (DDL-SF).

HSL-SF: Duong et al created the scale in 2019 [22]. The scale is scored according to the following formula: index = (average-1) x 50/3). To determine the average, the total score of the scale is divided by the number of scale points. The method produces an index score ranging from 0 to 50, with a higher score indicating greater HLL. The scale comprises 12 questions [22] with 4-point Likert response options ranging from 1 (very difficult) to 4 (very easy). Karahan et al. examined the validity and reliability in Turkey in 2021 [22].

Duong et al created the scale in 2019 [22]. The scale is scored according to the following formula: index = (average-1) x 50/3). To determine the average, the total score of the scale is divided by the number of scale points. The method produces an index score ranging from 0 to 50, with a higher score indicating greater HLL. The scale comprises 12 questions with 4-point Likert response options ranging from 1 (very difficult) to 4 (very easy) [22]. Karahan and his colleagues examined the validity and reliability of the study in Turkey in 2021 [23].

DDL-SF: The HLS, which evolved from the original "Digital Healthy Diet Literacy" Scale, was developed by Duong et al. in 2020 and includes four diet-related questions [24]. The scale is scored using the following formula: Index = (Average-1) x 50/3). The algorithm results in an index score ranging from 0 to 50, with a higher score indicating more knowledge about healthy eating. The scale comprises four items with 4-point Likert response options ranging from 1 (very difficult) to 4 (very easy) [24]. Karahan and his colleagues conducted the Turkish validity and reliability study in 2021 [23].

Anthropometric measurements

At the beginning of the study, the researcher dietitian measured body anthropometric measurements and recorded them in the questionnaire form.

Body weight: The participants' weights were measured with a fixed weighing device on an empty stomach without consuming any liquids. Prepregnancy weights were taken verbally from the participants.

Height: The participants' height was measured using a non-stretchable measuring tape while standing upright with closed

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feet. The participants' heights were measured in "cm" form from the top of the head to the ground without shoes, with the individuals standing against a flat wall and their head, body, hips, and heels leaning against the wall.

Body Mass Index (BMI): Normal is defined as 18.50–24.99 kg/m^2, overweight is defined as 25.00–29.99 kg/m^2, and obesity is defined as ≥30.00 kg/m^2 [7]. Before pregnancy, the BMI of individuals was determined by dividing body weight by the square of height, and the World Health Organization (WHO) standards were used to assess BMI categorization. The reference range for BMI is 18.50–24.99 kg/m^2, overweight is 25.00–29.99 kg/m^2, and obesity is ≥30.00 kg/m^2 [24].

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 27.0 (Armonk, NY: IBM Corp.). Descriptive statistics (n, %, median [IQR]) and frequency tables were used to summarize the data. Non-normally distributed variables were analyzed using nonparametric methods. Comparisons across three independent groups were performed using the Kruskal–Wallis H test (χ^2 test statistic). Correlations between two quantitative variables were evaluated using Spearman's rank correlation coefficient. A p-value < 0.05 was considered statistically significant.

Sample size and power: The minimum sample size was determined a priori using G*Power (version 3.1) for a two-tailed correlation test (H_0: $\rho = 0$), with $\alpha = 0.05$, power $(1-\beta) = 0.80$, and an expected effect size of r = 0.40 based on prior literature reporting moderate associations between eHealth/health literacy and HRBs [25]. This analysis indicated a required sample of N = 46 participants. Our final sample (N = 189) exceeded this threshold; therefore, the study was adequately powered. Additionally, for three-group comparisons analyzed with nonparametric methods (Kruskal–Wallis), we used the common ANOVA approximation in G*Power (F tests → fixed effects, omnibus, one-way). Assuming a medium effect size (f = 0.25), $\alpha = 0.05$, and power = 0.80, the required total sample size was N = 158, which was also exceeded by our study sample.

RESULTS

24.9%, 33.9%, and 41.3% of the pregnant women were in the second trimester, and 41.3% in the third trimester. Of the pregnant women, 36% had a normal BMI class and 49.2% were between 25 and 29 years old. Of the pregnant women who participated in the study, 41.8 were found to have been pregnant only once overall, 36.5% had a bachelor's degree, 48.7% were employed, and 59.3% earned enough money to cover their expenses (Table 1).

Of the pregnant women who took part in the survey, 54.5% stated that they had received nutritional information, 43.7% received it from doctors or nutritionists, 31.1% from television, newspapers, magazines and other sources and 23.3% from other medical professionals. It was found that the appetite of 38.1% decreased in the 1st trimester, 43.8% increased in the 2nd trimester, and 35.7% increased/did not change in the 3rd trimester, and 54% of them ate 3 main meals and 40.7% consumed 1.500-2.499 ml of water daily (Table 2).

Table 3 shows the change distribution of foods consumed during the pregnancy period. The products with increased consumption were milk (33.3%), yogurt/ayran/kefir (45.2%), egg (40.9%), cheese (44.1%), oilseeds (54.8%), vegetables (51.6%), fresh fruits (63.4%), dried fruits (48.4%), and mineral water (30.1%). The products with decreased consumption were white bread and its types (38.7%), rice, bulgur, pasta, etc. (33.3%), biscuits, crackers, chips (52.7%), desserts (49.4%), pita bread, lehmann, pizza, etc. (54.8%), sugary and carbonated beverages (44.1%), and tea and coffee (51.6%). The products not consumed due to pregnancy were offal, suzuki, salami, sausages, etc. (62.4%), and sugary and carbonated drinks (46.2%) (Table 3).

The digital measure of healthy eating and the health literacy scale did not change significantly between the trimesters

Table 1. Distribution of participants' sociodemographic characteristics.

Variable (N=189)	n	%
Trimester		
1st	61	24.9
2nd	72	33.9
3rd	56	41.3
Age class ($\overline{\chi} \pm SD \rightarrow 29.62 \pm 4.58$ years)		
≤24	47	20.6
25-29	64	40.2
≥30	78	30.2
Prepregnancy BMI category		
Slim	31	16.4
Normal	68	36.0
Overweight	49	25.9
Obese	41	21.7
Total number of pregnancies		
1	79	41.8
2	60	31.7
3 and above	50	26.5
Educational level		
Primary school	17	9.0
Secondary school	21	11.1
High school or equivalent	34	18.0
College	25	13.2
Undergraduate	69	36.5
Postgraduate	23	12.2
Working status		
Working	92	48.7
Not working	97	51.3
Economic level		
Income is below the expenses	38	20.1
Income equals expenses	112	59.3
Income exceeds expenses	39	20.6

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Table 2. Distribution of participants' nutritional status.

Variable (N=189)	n	%
Status of receiving nutritional information		
Received	103	54.5
Did not receive	86	45.5
Person from whom nutritional information is obtained		
Doctor/dietitian	45	43.7
Other health care personnel	24	23.3
Social media, TV, newspaper, or magazine	32	31.1
Other (Specify)	2	1.9
1st trimester appetite status		
Increased	50	26.5
Decreased	72	38.1
Unchanged	67	35.4
1st trimester appetite status		
Increased	56	43.8
Decreased	31	24.2
Unchanged	41	32.0
1st trimester appetite status		
Increased	20	35.7
Decreased	16	28.6
Unchanged	20	35.7
Number of main meals consumed		
2	87	46.0
3	102	54.0
Water consumption		
<1.500 ml	46	24.3
1.500-2.499 ml	77	40.7
≥2.500 ml	66	34.9

(p>0.05). The trimesters are similar in terms of the aforementioned characteristics. Health literacy and prepregnancy BMI scores were positively, weakly, and statistically significantly correlated (p<0.05). As prepregnancy BMI values increased, health literacy scale scores increased (Table 4).

The digital healthy eating scale and health literacy were positively, weakly, and statistically significantly correlated (r = 0.278; p = 0.007). The health literacy scale scores increased in parallel with the digital healthy eating scale (Table 5).

DISCUSSION

The most notable finding of this study is that the health literacy and digital healthy diet literacy scores of pregnant women varied by trimester and were positively associated with prepregnancy BMI, while no significant association was found with age. In addition, pregnant women usually ate three main meals, and their appetite often increased in the second and third trimesters. The consumption of milk and dairy products, eggs, fresh vegetables, and fruits increased; the consumption of white bread, rice, bulgur, pasta, biscuits, crackers, chips, desserts, pita bread, lehmann, and pizza, which led to rapid weight gain, decreased; and products such as offal, suzuki, salami, and sausage were not consumed during pregnancy.

Pregnant women's interest in health literacy varies depending on many factors, such as number of pregnancies, age, socioeconomic status, educational level, dietary habits, nutritional knowledge level, and physical activity status. Pregnant women who are employed, have higher incomes, and have higher education levels have higher levels of health literacy. The number of pregnancies, number of children alive, increasing gestational age, and level of health literacy is often inversely correlated. This could be because fewer people are using health services and more pregnancies and children are present [26,27]. The participants in this study were found to have a high level of education and above average scores in digital literacy for healthy eating and health literacy.

Health care providers aim to reduce postpartum hospital stays. In this context, women's self-care skills and health literacy are becoming increasingly important. In a study of 258 pregnant women in China, higher health literacy positively impacted postpartum health behaviors, self-care skills, and healthy lifestyles [28]. A study of 323 pregnant women in Iran found that high health literacy levels were associated with positive pregnancy outcomes. Women with excellent (34.1%) and adequate (33.1%) health literacy were significantly more aware of prenatal care, folic acid intake, exercise before and during pregnancy, pregnancy symptoms, and breastfeeding [16]. In a study conducted with 238 pregnant women in Turkey, the average health literacy score was found to be 30.45±6.56, and the importance of improving pregnant women's health literacy and knowledge and attitudes about being healthy was emphasized [29]. In this study, the health literacy knowledge of pregnant women was at a sufficient level, consistent with the literature. The health literacy scale showed no statistically significant differences between the trimesters.

Research has shown that there is either no correlation between health literacy and BMI in pregnant women or a negative correlation between the two [30,31]. In this study, an inverse relationship was observed between the participants' health literacy scores and BMI, and health literacy scale scores increased as pregnancy weight gain and pre-pregnancy BMI values increased. The reason for the inverse relationship may be that awareness about health increases as BMI increases.

Nutritional literacy is affected by sociodemographic characteristics and dietary habits. Nutritional knowledge and nutrition literacy are related. Individuals can access and apply nutrition information using digital technology as the level of nutrition knowledge increases, which increases e-healthy nutrition literacy [19,21,32].

Individuals can access and apply nutrition information using digital technology as the level of nutritional knowledge increases, which increases e-healthy nutrition literacy [19,21,32]. Carolan et al. found that underweight, obese, and under 18-year-old women had a lower level of knowledge compared with women in other age groups (25–29, 30-34 and

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Table 3. Distribution of foods consumed during pregnancy.

Variable (N=189)	No change		Consuming less		Consuming more		Consumption started during pregnancy		Not consuming due to pregnancy	
	n	%	n	%	n	%	n	%	n	%
Milk	79	41.9	16	8.6	63	33.3	26	14.0	4	2.2
Yogurt,ayran, kefir	73	38.6	14	7.5	85	45.2	12	6.5	4	2.2
Cheese	94	49.5	6	3.2	83	44.1	6	3.2	-	-
Egg	79	41.9	22	11.8	77	40.9	8	4.3	2	1.1
Red meat	101	53.7	18	9.7	65	34.4	2	1.1	2	1.1
Chicken/turkey meat	94	49.5	47	24.7	41	21.5	-	-	8	4.3
Fish	100	52.7	26	14.0	45	23.7	2	1.1	16	8.5
Offal (liver, etc.)	39	20.4	30	16.1	2	1.1	-	-	118	62.4
Sujuk, salami, sausage, etc.	35	18.3	30	16.1	6	3.2	-	-	118	62.4
Dried legumes	101	53.7	12	6.5	63	33.3	10	5.4	2	1.1
Oilseeds (e.g., hazelnuts)	65	34.4	-	-	104	54.8	18	9.7	2	1.1
Vegetables	75	39.8	8	4.3	98	51.6	8	4.3	-	-
Fresh fruits	57	30.1	6	3.2	120	63.4	6	3.2	-	-
Dried fruits	67	35.4	8	4.3	91	48.4	20	10.8	2	1.1
White bread and its types	71	37.6	73	38.7	18	9.7	2	1.1	24	12.9
Types of Whole-Grain Bread	79	41.9	41	21.5	45	23.7	22	11.8	2	1.1
Rice, bulgur, pasta, etc.	83	44.1	63	33.3	33	17.2	-	-	10	5.4
Biscuits, crackers, and chips	20	10.8	100	52.7	18	9.7	-	-	51	26.9
Desserts	55	29.0	93	49.4	12	6.5	-	-	29	15.1
Pekmez	100	52.7	45	23.7	16	8.6	14	7.5	14	7.5
Pita, lehmann, pizza, etc.	45	23.7	104	54.8	2	1.1	-	-	39	20.4
Sugary, carbonated beverages	12	6.5	83	44.1	6	3.2	-	-	87	46.2
Fresh fruit juices	91	48.4	37	19.4	22	11.8	12	6.4	26	14.0
Mineral water	59	31.2	47	24.7	57	30.1	16	8.6	10	5.4
Tea, coffee	73	38.7	98	51.6	-	-	-	-	18	9.7

Table 4. Comparison of scale scores according to age, BMI, and trimester.

Variable	1st trimester (n = 61) Median (IQR)	2nd trimester (n = 72) Median (IQR)	3rd trimester (n = 56) Median (IQR)	p-value
Health Literacy Scale	33.3 (13.2--60)	35.9 (6.6--85)	40.4 (16.7--85)	0.126
Digital Healthy Diet Literacy Scale	33.3 (27.1--52.1)	30.6 (27.1--46.9)	35.4 (15.6--53.4)	0.286
Correlations				
Variable		Age (year)	Prepregnancy BMI (kg/m²)	
Health Literacy Scale	r	-0.094	0.259	
	p	0.369	**0.012**	
Digital Healthy Diet Literacy Scale	r	0.042	0.097	
	p	0.692	0.353	

The Kruskal–Wallis H test was used for comparisons among the three independent groups. Spearman's correlation coefficient was used to examine the relationships between two non-normally distributed quantitative variables.

Table 5. Examining the relationships of the scales.

Correlation*		Health Literacy Scale	Digital Healthy Diet Literacy Scale
Health Literacy Scale	r	1.000	0.278
	p	-	**0.007**
Digital Healthy Diet Literacy Scale	r	0.278	1.000
	p	0.007	-

"Spearman" correlation coefficient was used to examine the relationships between two quantitative variables that do not have a normal distribution.

≥35 years old) and with normal BMI [33]. In this study, a very weak relationship was found between digital healthy diet literacy and weight gain.

Although individuals frequently consult physicians for health issues, health information is widely accessed through social media and the internet. The ability to find, understand, and evaluate health information using digital services and technologies is a prerequisite for health literacy [34,35]. In a study conducted on pregnant and lactating women, the media sources that the participants most frequently used

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to obtain nutritional or dietary information were television (57.0%), newspapers/magazines (50.0%), and the Internet (20.0%). Doctors/health professionals and television are the most trusted non-print sources to obtain nutritional information, and those with low nutritional literacy use television and newspapers/magazines less than those with sufficient levels of nutrition [30]. The sources people used to obtain health-related information and the medical professionals they consulted did not differ significantly from the levels they achieved on the digital healthy diet. However, individuals who most frequently preferred a doctor/dietitian to access health-related information had higher digital healthy diet literacy scores.

Nutritional information and nutrition literacy are integral to health literacy. Studies have shown that high health literacy and digital healthy nutrition literacy scores are associated with healthier eating behaviors, and there is a positive relationship between health literacy and e-healthy diet literacy [24,31,36]. Our study found a positive relationship between the scales. The higher the scores on the healthy eating scale, the higher the scores on the HLS.

One of the strengths of this study is that it is one of the few studies that simultaneously assesses general health literacy and digital healthy eating literacy in pregnant women and compares these scores across trimesters. Second, the use of validated and culturally adapted measurement tools (HLS and DDL-SF) increases the results' reliability and comparability. Finally, trained researchers conducted face-to-face interviews to collect data, minimizing the risk of missing or incorrect responses. However, certain limitations should be noted. No causal relationship between education level and dietary behavior can be established in the cross-sectional design. The study was conducted at a single center, which may limit the generalizability of the results to other regions or health facilities. In addition, dietary behavior and prepregnancy weight are based on self-reporting, which is subject to recall and reporting errors.

The low health and diet literacy levels found in previous studies emphasize the need for targeted interventions during pregnancy. Our findings support the development of evidence-based strategies to improve general and digital diet literacy in prenatal care, which can contribute to better maternal health and optimal weight management.

CONCLUSION

This study found that the health literacy and digital healthy diet literacy of pregnant women were positively correlated, and the scores varied across trimesters. The mother should increase her health literacy because this can be a warning sign for the mother and the unborn child. Nutrition education and health literacy should be included as subjects in prenatal care and workshops to help pregnant women who lack health literacy and increase their knowledge of healthy eating. Future research on the variables that may influence the dietary habits and digital healthy eating and health literacy of pregnant women needs to be conducted on larger samples.

Ethics Committee Approval: Ethical approval for the study was obtained from the Ankara Medipol University Ethics Committee (decision no: 2024/1, date: 08.01.2024).

Informed Consent: Written informed consent was obtained from all participants prior to their inclusion.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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Impact of reflux, bruxism, age, and plaque index on anterior tooth wear: A cross-sectional clinical evaluation

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MAIN POINTS

- Gastroesophageal reflux disease increases the risk of erosive wear on the palatal surfaces of maxillary anterior teeth.
- Anterior Clinical Erosive Classification is an effective tool in evaluating the severity of dental erosion and the need for clinical intervention.
- Plaque index did not show a significant difference between groups, and dental erosion is thought to be mainly associated with chemical and mechanical factors.
- As the duration of reflux increases, ACEC scores increase, indicating that dental erosion intensifies depending on the duration of the condition.

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ABSTRACT

Aim: This study aims to evaluate the effect of variables such as gastroesophageal reflux disease (GERD), bruxism, plaque index, and age on erosive wear occurring on the palatal surfaces of maxillary anterior teeth, and to objectively measure this wear using the Anterior Clinical Erosive Classification (ACEC).

Materials and Methods: A total of 507 individuals were included. Participants completed self-report questionnaires regarding the presence, previous diagnosis, disease duration, and medication use. Bruxism was assessed through self-report and clinical examination. Erosive wear on maxillary anterior teeth palatal surfaces was measured using ACEC, and plaque accumulation using the Silness and Löe Plaque Index. Statistical analyses included independent sample t-tests and Spearman/Pearson correlation coefficients. Significance was set at $p<0.05$.

Results: Reflux disease was detected in 20.9% of the participants in the study. ACEC scores of individuals reporting reflux symptoms were found to be significantly higher compared to healthy individuals ($p<0.05$). ACEC scores were also found to be significantly higher in individuals with bruxism than those of without bruxism. In contrast, the plaque index did not show a significant difference between the groups. Additionally, a significant and positive relationship was found between the duration of reflux and ACEC scores ($r=0.281$, $p<0.01$). ACEC scores were observed to be higher in individuals receiving reflux treatment compared to those not using medication.

Conclusion: These findings indicate that reflux affects not only the gastrointestinal system but also oral and dental health and emphasize the importance of early diagnosis and intervention for dental erosion in individuals with reflux symptoms. Our study reveals the usability of the ACEC in large populations and sheds light on the multifactorial etiology of dental erosion. It also highlights the need to consider the potential abrasive effects of medications used in reflux treatment.

Keywords: Gastroesophageal reflux disease, Dental erosion, Anterior clinical erosive classification, Tooth wear

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INTRODUCTION

Erosive wear of the teeth and Gastroesophageal Reflux Disease (GERD) are two conditions are two interrelated conditions [1]. GERD, characterized by the backward movement of stomach acid, has heartburn and regurgitation as its main systemic symptoms [2]. Heartburn is described as a burning sensation in the retrosternal area. Clinical symptoms are very common and affect a significant portion of the general population [3]. It has been reported that 20% of the adult population experiences heartburn at least once a week, and 40% at least once a month [4]. According to data from another study, this incidence has been reported as 10-20% in Europe and North America, and 5% in Asia. A study from Turkey showed that its incidence was 33% [5].

Dental erosion is defined as the dissolution of hard dental tissues by acidic factors without bacterial activity. The etiology of erosion may be attributed to extrinsic factors, such as acidic foods, beverages, or medications, or intrinsic factors like stomach acid [6]. The erosive process begins on the tooth surface. Initially, acids or chelating agents remove the tooth's protective pellicle layer, followed by the dissolution of the organic structure and demineralization. In cases of GERD, the

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palatal and incisal surfaces of maxillary teeth and the occlusal surfaces of mandibular teeth are most affected due to the entry of acidic material into the oral cavity [7]. As the disease progresses, erosion may also be observed on the chewing surfaces of the posterior teeth in both jaws. Concurrently, the labial and buccal surfaces generally experience wear in long-term and severe reflux cases. The palatal surfaces of the maxillary teeth are the earliest affected areas because of the limited protective effect of the salivary glands and continuous exposure to gastric acid. Furthermore, the force of regurgitation reaching the mouth from the pharynx can also increase the severity of dental erosion [7, 8]. Studies have shown a significant relationship between GERD and dental erosion [9]. However, the development of erosion does not progress identically in every individual; its progression can be significantly affected by the duration and severity of reflux, diet, medications, and oral hygiene habits [10, 11]. The damaged tooth surface becomes more susceptible to wear from mechanical friction during chewing, swallowing, tongue and cheek movements, or brushing. Tooth brushing performed after an acid attack is particularly damaging, since it can further increase wear on the softened and demineralized tooth surface.

Clinicians often prefer a wait-and-see approach for dental erosion, whereas they tend to proceed directly to treatment for dental caries [8, 12]. Erosion observed in asymptomatic teeth is initially considered insignificant and often left untreated until later ages or until significant symptoms develop. However, it is crucial to determine whether these teeth will eventually require minimally invasive treatment or more invasive procedures at advanced stages. In advanced cases, serious complications such as pulp chamber exposure, complete loss of the tooth crown, vertical dimension loss, and temporomandibular joint dysfunction may develop. Despite these risks, awareness among general physicians is limited; one study found that only 40% were aware that GERD can cause dental erosion [13]. This indicates a clear need for this knowledge to be more widely addressed in medical and dental education.

There is still no definitive consensus in the literature on how to clinically evaluate and determine the causes of tooth wear. While acid erosion is considered the most important cause of tooth wear in many European countries, in some other countries, mechanical wear (attrition, abrasion) is still regarded as the predominant factor. These different approaches can cause confusion in the assessment of tooth wear. Researchers today emphasize the multifactorial etiology of tooth wear and state that attributing it to a single cause can be misleading [14, 15]. This multifactorial perspective is also highly important when evaluating wear on the palatal surfaces of maxillary anterior teeth. Not only GERD, but also factors such as tooth brushing habits, oral hygiene level, clenching and grinding activities (bruxism), and medications can contribute to wear on these surfaces. The Anterior Clinical Erosive Classification (ACEC) systematically grades erosive wear, particularly that arising from intrinsic acid sources, and helps determine the need for clinical intervention [16]. To our knowledge, no comprehensive study in the literature has simultaneously examined reflux, oral hygiene index, and bruxism to evaluate wear on the palatal surfaces of maxillary anterior teeth using the ACEC.

In this context, the aim of our study was to evaluate the tooth wear occurring in the maxillary anterior teeth of patients who presented to the Restorative Dentistry Clinic of Inonu University Faculty of Dentistry using the ACEC and to reveal its relationship with reflux, oral hygiene, and bruxism. The null hypothesis for this study was that the variables of reflux presence, bruxism presence, age, and plaque index had no significant effect on the level of erosive wear occurring on the palatal surfaces of maxillary anterior teeth (ACEC score).

MATERIALS AND METHODS

This study is cross-sectional and observational research. It was conducted at the Restorative Dentistry Clinic of the Faculty of Dentistry, Inonu University, between June and July 2025.

Power analysis

When the effect size was calculated as 0.19, evaluating at least 436 participants was deemed sufficient with a 95% confidence interval and a 5% margin of error. However, in the study, 507 participants were examined, ensuring a reliable estimation of reflux prevalence among individuals attending the clinic.

Participants

Individuals aged between 16 and 70 years who could read and understand Turkish, who did not have missing maxillary anterior teeth, who had at least 20 healthy and clinically controllable teeth in the mouth, and who did not use fixed or removable prostheses were included in the study. Individuals with systemic diseases other than reflux were excluded from the study.

Procedure

Before the study was conducted, volunteer candidates were taken to the waiting room and informed about the study. Those who agreed to participate signed the informed consent form and were admitted to the examination room. For participants under the age of 18, informed consent was additionally obtained from their parents. In this study, adult patients who had previously been diagnosed with gastroesophageal reflux disease (GERD) by a gastroenterologist based solely on typical symptoms, responded to treatment with antisecretory therapy, and had no alarm symptoms were included. Since advanced diagnostic tests for GERD (such as pH monitoring or endoscopy) are only required in suspicious cases or when there is no response to treatment, the individuals included in this study were those diagnosed based on clinical evaluation and response to therapy alone [17,18]. Participants were

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administered a self-report questionnaire regarding the presence of GERD and were asked whether they had previously been diagnosed with reflux. Subsequently, the Anterior Clinical Erosive Tooth Wear Classification index and the Silness & Löe Plaque Index were applied by the dentist. Participants were also administered a self-report questionnaire regarding the presence of bruxism. In addition to the questionnaire results, masseter muscle examination, intraoral examination, and temporomandibular joint evaluation were performed. The masseter muscles were examined by palpation, tooth surfaces were assessed for wear (enamel loss, dentin exposure), and the presence of pain or clicking sounds in the jaw joint was recorded and diagnosis of bruxism was established based on participants' self-report responses and clinical examination findings.

Tests used in the study

Participants were asked to complete the following tests.

Reflux assessment questionnaire

In the study, a questionnaire was administered to evaluate participants' symptoms related to gastroesophageal reflux disease (GERD), questioning whether they had previously been diagnosed with reflux, the duration of the diagnosis, medication use, and lifestyle impacts related to reflux. The questionnaire was prepared based on methods widely used in clinical research that rely on symptomatic assessment rather than diagnostic tests to determine the presence of reflux. In this context, the presence of reflux was evaluated based on the individual's self-report, history of reflux diagnosis, and frequency of symptoms.

Anterior clinical erosive classification (ACEC)

This classification is an objective system that enables the clinical assessment of acid erosion occurring on the palatal surfaces of maxillary anterior teeth [16]. This system assigns a score from 0 to 5 to each of the six anterior teeth in the upper jaw. Scores are determined according to the amount of wear observed at the enamel and dentin levels; a score of 0 indicates no wear, while a score of 5 represents wear characterized by pulp exposure or significant structural loss (Table 1). The average of the scores determined for each tooth is calculated to obtain individual's overall ACEC score. This system allows for the clinical classification of both early and advanced stages of erosive tooth wear and is recognized as a reliable method, especially for assessing wear caused by intrinsic acid sources such as reflux.

Plaque index (PI)

Developed by Silness and Löe in 1964, this index aims to assess the severity of plaque present on the tooth surface [19]. The plaque index, divided into four scores, is performed by evaluating teeth numbered 16, 12, 24, 36, 32, and 44 in the mouth. Each of the four surfaces of these teeth (buccal, lingual, mesial, and distal) is scored between 0 and 3. The scores from the four regions of the tooth are summed and divided by four to provide the plaque index for the tooth according to the scores and criteria below.

Calibration

All examiners underwent a theoretical training period initially conducted on study models and subsequently through practical sessions with dental students. The training included recording indices individually by each of the three examiners on subjects, discussing the findings, and then re-evaluating several subjects to compare results. All examiners scored the same areas and compared their results, discussing their experiences. This process continued until they consistently assigned the same values for each surface and achieved a 90% agreement for the entire mouth.

Statistical analysis

Data were analyzed using IBM SPSS Statistics, version 27.0 (IBM Corp.; Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine the distribution of the data. For comparing independent groups, the Independent Samples t-Test was applied for parametric data, while the Mann-Whitney U Test was used for non-parametric data. The homogeneity of variance was assessed with Levene's test. Any p value less than 0.05 was considered statistically significant. For correlation analyses, Spearman's rho correlation coefficient was used to assess the relationships between variables. Finally, linear regression analysis was performed to evaluate the predictive effect of independent variables on the dependent variables.

RESULTS

This study involving 507 individuals found that the prevalence of gastroesophageal reflux disease (GERD) was 20.9% and bruxism was 27.6%. Both the GERD and bruxism groups had significantly higher median ages and Anterior Clinical Erosive Classification (ACEC) scores compared to healthy controls, with correlations of r=0.18 and r=0.13 for the GERD group, and r=0.27 and r=0.2 for the bruxism group, respectively (Table 2). A higher plaque index was also found in males (d=0.15), who also had significantly higher ACEC scores (r=0.19). Among those with reflux, individuals on medication had significantly higher ACEC scores (r=0.2) than those not using medication (Table 3). Linear regression analysis identified age as a significant predictor of ACEC scores (R^2 =0.248,p<0.001), while correlation analysis showed a significant positive relationship between the duration of reflux and ACEC scores (r=0.281, p<0.01) (Table 4).

DISCUSSION

This study confirms that both GERD and bruxism are associated with increased dental erosion, with a notable finding

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Table 1. ACE classification

Classification	Palatal enamel	Palatal dentin	Insizal edge length	Facial enamel	Pulp vitality	Suggested therapy
Class I	Reduced	Not exposed	Preserved	Preserved	Preserved	No restorative treatment
Class II	Lost in contact areas	Minimally exposed	Preserved	Preserved	Preserved	Palatal composites
Class III	Lost	Distinctly exposed	$\leq$ 2 mm lost	Preserved	Preserved	Palatal onlays
Class IV	Lost	Extensively exposed	> 2 mm lost	Preserved	Preserved	Sandwich approach
Class V	Lost	Extensively exposed	> 2 mm lost	Distinctively reduced/lost	Preserved	Sandwich approach (experimental)
Class VI	Lost	Extensively exposed	> 2 mm lost	Lost	Lost	Sandwich approach (highly experimental)

Table 2. The summary of the age, ACEC score, and plaque index values according to reflux status, gender, and presence of bruxism among the participants.

	Reflux		p value*	Gender		p value*	Bruxism		p value*
	Present	Absent		Male	Female		Present	Absent	
n	106 (20.9%)	401 (79.1%)		229 (45.2%)	278 (54.8%)		140 (27.6%)	367 (72.4%)	
Age	46(20)A	34(26)B	<0.001	37(27)	36(29)	0.48	46(31)A	35(24)B	<0.001
ACEC	1.66(1)A	1(1)B	0.003	1.33(1)	1.16(1)	0.18	1.66(1.17)A	1(1)B	<0.001
PI	1.37(0.59)	1.29(0.58)	0.29	1.33(0.65)A	1.25(0.59)B	<0.001	1.25(3)	1.29(0.58)	0.259

Groups denoted by different superscript letters (A, B) in the same row are significantly different (p<0.05). All comparisons were performed using the Mann–Whitney U test. Data are presented as median (interquartile range, IQR).

Table 3. The summary of the age, reflux duration, ACEC score, and plaque index values according to medication use, bruxism, and gender status in the reflux group.

	Medication Use		p value*	Bruxism		p value*	Gender		p value*
	Yes	No		Present	Absent		Male	Female	
n	42	64		46	60		40	66	
Age	44.29(2.28)	43.5(1.87)	0.791*	47.09(2.29)A	41.30 (1.79)B	0.046*	48.1(2.44)A	41.21(1.72)B	0.02*
Duration of Reflux (years)	4(9)	5(5)	0.835**	5(7)	2.5(5)	0.005**	5(8)A	4(4)B	0.046**
ACEC	1.83(0.71)A	1.33(0.96)B	0.037**	1.83(1.17)A	1.41(1)B	0.05**	1.91(1.25)A	1.5(0.87)B	0.049**
PI	1.33(0.55)	1.39(0.68)	0.338**	1.25(0.71)	1.47(0.54)	0.082**	1.56(0.56)A	1.29(0.67)B	0.004**

Variables with a normal distribution are presented as mean ± standard deviation (SD) and were analyzed using the independent samples t-test (*). Variables without a normal distribution are presented as median (interquartile range, IQR) and were analyzed using the Mann–Whitney U test (**). Groups denoted by different superscript letters (A, B) in the same row are significantly different (p < 0.05). *p<0.05: independent samples t-test; **p<0.05: Mann–Whitney U test.

Table 4. Correlation and regression analyses of age, reflux duration, and ACEC scores.

Correlation					
		Age	ACEC	PI	Duration of Reflux (years)
Spearman's rho	Age	1	0.488**	0.159**	0.242*
	ACEC	0.488**	1.00	.230**	0.281**
	PI	0.159**	0.230**	1	0.07
	Duration of Reflux (years)	0.242*	0.281**	0.069	1

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

that the ACEC classification, typically used in case reports, is an effective tool for large-scale epidemiological studies. The prevalence of GERD found in this cohort (20.9%) is consistent with reported rates in Turkey and globally, and the mean age of GERD patients was around 43 years [5, 20, 21].

The use of the ACEC is a key strength of this research, as it offers a systematic and quantitative approach to evaluating intrinsic acid-related wear [16]. This classification assesses each palatal surface of the anterior teeth individually for enamel and dentin loss, incisal edge level, presence of facial enamel, and pulp vitality, thus helping to determine not only the presence of wear but also its severity and the need for treatment [16]. In the literature, the ACEC has generally been used in individual case reports and for justifying restorative treatment plans; however, no published studies have been found in which it was systematically applied for data collection in large populations. Various indices have been used by researchers to investigate the presence of dental erosion [22,23]. In this re-

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gard, our study is, to our knowledge, the first clinical research in which the ACEC has been used quantitatively in a large group of individuals to evaluate erosive wear on anterior teeth. Through comprehensive data analysis and simultaneous assessment of factors such as GERD, bruxism, age, and plaque index, the ACEC is considered a valid and applicable tool for epidemiological studies. In this way, the study demonstrates both the practical potential of the ACEC and contributes to the literature on how this classification can be appiled in clinical research into the causes of dental erosion.

In our study, individuals reporting GERD symptoms and those with a history of bruxism had higher ACEC scores on their anterior teeth compared to healthy individuals, whereas the plaque index did not show significant differences between groups. These findings suggest that, in addition to chemical destruction due to intrinsic acid exposure, mechanical stress factors (such as clenching and grinding) may also play a role in the progression of erosive wear. It is known that acidic material reaching the oral cavity due to reflux can cause early-stage wear, especially on the palatal surfaces of the maxillary anterior teeth [24,25]. Indeed, it has been reported that poor eating habits starting in childhood and factors such as bruxism contribute to dental erosion, which often persists into adulthood [26]. The literature also emphasizes that tooth surface damage is more severe in cases where chemical erosion coexists with mechanical wear [15,27]. Our findings that both GERD and bruxism were linked to higher ACEC scores, while the plaque index was not, reinforce the concept of dental erosion as a multifactorial process. This suggests that while classic oral hygiene is crucial for preventing caries, it has little impact on erosion caused by chemical and mechanical factors such as acid reflux and tooth grinding [28,29]. The positive correlation between reflux duration and ACEC scores suggests that the chronicity of reflux is a key driver of progressive erosive wear.

The observation that individuals on GERD medication had higher ACEC scores is particularly interesting. While these medications neutralize stomach acid, some, such as calcium carbonate, may cause abrasive effects on tooth surfaces, contributing to wear [30,31]. This highlights the need for a holistic, interdisciplinary approach to managing patients with both medical conditions and dental erosion.

Correlation analysis revealed a statistically significant and positive relationship between reflux duration and ACEC scores ($r = 0.281$, $p<0.01$). This indicates that as the duration of reflux increases, erosive wear on the anterior teeth also tends to increase. In other words, in individuals with longer-standing reflux symptoms, the acidic wear observed on the palatal surfaces of the maxillary anterior teeth is more severe. Researchers have reported that individuals who have had reflux disease for a longer time experience greater erosive wear on their teeth [32].

Limitations

A primary limitation of this study is its retrospective and cross-sectional design. The data on GERD and bruxism were collected through self-reports and clinical examinations rather than objective diagnostic methods like pH monitoring or polysomnography. This reliance on subjective reporting can introduce bias. Additionally, the study used the ACEC, which focuses exclusively on the palatal surfaces of maxillary anterior teeth, excluding erosion in other parts of the mouth. Future longitudinal studies with more objective diagnostic tools would provide a more robust understanding of the causal relationships between these factors and dental erosion.

CONCLUSION

In conclusion, this study demonstrates that intrinsic and mechanical factors such as GERD and bruxism are strongly linked to the development and severity of dental erosion on the palatal surfaces of maxillary anterior teeth. The lack of a significant relationship with the plaque index suggests that the etiology of erosion is distinct from that of periodontal pathologies. The findings also underscore the importance of a holistic approach to patient care, considering both systemic conditions and the potential abrasive effects of some medications.

Ethics Committee Approval: Ethical approval for this study was granted by the Scientific Research Ethics Committee of Inonu University, Faculty of Health Sciences (Decision number: 2025/7710).

Informed Consent: Participants were informed about the study and their written consent was obtained. For participants under the age of 18, both verbal and written consent were obtained from their parents.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare no conflict of interest.

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