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Image	200	No abstract	3	No table	3

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ORIGINAL ARTICLES

Zeynep Kamil Med J 2025;56(4):179–183
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ORIGINAL ARTICLE

Hormonal interplay in hyperprolactinemia: Insights from a large-scale study of reproductive-age patients

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ABSTRACT

Objective: This study examined serum prolactin and reproductive hormone levels in women with elevated prolactin levels, with a particular focus on fertility status. The objective was to understand how prolactin affects reproductive hormones in infertile women, aiming to improve diagnostic and therapeutic strategies.

Material and Methods: The study involved 847 women aged 18–46 years who visited gynecology outpatient clinics between January and October 2019. Participants with prolactin levels ≥26 µg/L underwent hormone testing on the second or third day of menstruation. Patients were categorized based on fertility status and prolactin levels, specifically into groups of 26–100 µg/L and >100 µg/L. Demographics, symptoms, medical history, and hormone profiles were analyzed using NCSS 2007 software, employing descriptive methods, the chi-squared test, and Spearman's correlation.

Results: A statistically significant yet very weak negative correlation was identified between prolactin and estradiol levels in patients with moderate hyperprolactinemia (26–100 µg/L), as well as in both infertile and non-infertile subgroups. No significant associations were found between prolactin and gonadotropins (FSH=follicle-stimulating hormone, LH=luteinizing hormone) or progesterone, regardless of prolactin level or fertility status. In patients with highly elevated prolactin levels (≥100 µg/L), no statistically significant correlation was observed between prolactin levels and any measured reproductive hormone levels.

Conclusion: This cross-sectional study provides insights into the hormonal interplay in hyperprolactinemia, showing that serum prolactin levels are weakly correlated with estradiol levels and are not significantly associated with gonadotropin levels in clinical settings. These findings suggest that prolactin may impair reproductive function through indirect mechanisms not captured by static hormone measurements. Future research should incorporate longitudinal designs and clinical outcomes to further elucidate the relationship between prolactin and reproductive function.

Keywords: Estradiol, gonadotropins, hyperprolactinemia, infertility, reproductive hormones.

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INTRODUCTION

Hyperprolactinemia, the most prevalent endocrine disorder affecting the hypothalamic-pituitary axis, is a significant concern in gynecological endocrinology owing to its association with hypogonadism and infertility.[1] Pathological hyperprolactinemia is characterized by elevated serum prolactin (PRL) levels resulting from excessive prolactin secretion, excluding physiological causes. The diagnosis is confirmed when serum PRL levels, measured on two separate occasions, exceed the normal range established by the laboratory, typically with an upper limit of 20 ng/mL (20 µg/L SI units) or 400–500 mU/L.[2] The prevalence is 5% among individuals attending family planning clinics, 9% among those with primary amenorrhea, and 17% among women diagnosed with polycystic ovary syndrome.[3]

Prolactin is known to adversely affect the reproductive axis by reducing gonadotropin-releasing hormone (GnRH) secretion.[4] Animal studies have shown that elevated PRL levels lead to a decrease in both the amplitude and frequency of luteinizing hormone (LH) pulsations.[5,6] However, despite reports indicating that most GnRH-secreting neuronal cells lack PRL receptors,[7] it has been discovered that GnRH release is not directly influenced by PRL levels. Instead, it is indirectly regulated by kisspeptin, a regulatory neurocell type.[8–10] An increase in the frequency of GnRH pulsation is correlated with a predominance of LH secretion, whereas a decrease in pulsation results in hypothalamic amenorrhea characterized by dominant follicle-stimulating hormone (FSH) gonadotropin secretion.[11] Studies have indicated that causes of hyperprolactinemia that do not result in structural changes in pituitary gonadotroph cells, such as drugs or functional causes, lead to dominant FSH secretion.[11,12] In contrast, organic causes such as adenomas directly reduce both FSH and LH levels. These findings suggest that PRL levels could serve as a predictor of changes in gonadotropin levels, aiding in determining both the etiology and severity of symptoms such as amenorrhea and infertility.[12]

Although hyperprolactinemia is a well-recognized cause of reproductive dysfunction, the relationship between elevated prolactin levels and other reproductive hormones—particularly gonadotropins, estradiol, and progesterone—remains unclear. Existing data are limited and often inconsistent, largely owing to the complex hormonal interplay and variability in the underlying causes of hyperprolactinemia.[12,13] Most studies lack stratification by fertility status and often do not explore hormonal correlations in a clinically meaningful manner. Understanding how prolactin interacts with key reproductive hormones in infertile individuals is essential for improving diagnostic accuracy and treatment planning. This large-scale study aimed to address this gap by examining the correlation between serum prolactin and gonadotropin levels (FSH and LH), as well as estradiol, progesterone, and thyroid-stimulating hormone (TSH) levels, in patients with hyperprolactinemia, with a focus on infertility.

MATERIAL AND METHODS

The study included women who attended the gynecology outpatient clinics at Zeynep Kamil Women and Children's Diseases Training and Research Hospital from January to October 2019. These participants sought consultation for infertility, characterized by the inability to conceive after 12 months of regular intercourse, or for other conditions related to menstrual disorders such as oligomenorrhea or amenorrhea. The participants underwent serum hormonal profile tests on the second or third day of their menstrual cycle. Patients with serum prolactin levels ≥26 µg/L, indicative of hyperprolactinemia, were included in this study. Demographic data, symptoms and findings, history of chronic diseases, and hormone profiles (FSH, LH, estradiol, progesterone, and TSH) of the patients were reviewed and recorded through the hospital data system following the Zeynep Kamil Women and Children's Diseases Training and Research Hospital's ethics committee approval (18.09.2019/86). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients with chronic illnesses, a history of systemic drug use, or treatments that could affect their hormone profiles were excluded. The remaining patients were categorized into two groups: infertile and other diagnoses; the latter included menstrual cycle-related disorders such as oligomenorrhea and amenorrhea. They were further divided based on prolactin levels into those with slightly elevated levels (26–100 µg/L) and those with highly elevated levels (>100 µg/L). The results were statistically analyzed to explore the contribution of endocrine profile changes to hyperprolactinemia, to correlate PRL levels with LH, FSH, estradiol, and progesterone levels, and to identify their relationship with infertility. The patient selection process and exclusion criteria are summarized in a flow chart (Fig. 1).

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software was used for statistical analyses. To evaluate the study data, descriptive statistical methods such as mean, standard deviation, frequency, percentage, minimum, and maximum were utilized. The normality of the distribution of quantitative data was assessed using the Shapiro–Wilk test and graphical analyses. Pearson's chi-square test was applied for comparing qualitative data, while Spearman correlation analysis was conducted to examine relationships between quantitative variables. Statistical significance was set at $p<0.05$.

RESULTS

The initial cohort comprised 1,153 patients. Of these, 36 pregnant women (due to physiological hyperprolactinemia), 67 patients with a diagnosis of endometriosis (owing to the potential impact on reproductive hormone balance), and 203 patients with incomplete hormonal profiles (lacking data on parameters other than prolactin) were excluded. The final study population included 847 patients aged 18–46 years, with a mean age of 30.9±6.6 years. Serum prolactin levels in this group ranged from 26.13 to 258.14 µg/L, with a mean of 43.07±23.25 µg/L. Comprehensive hormonal measurements, including estradiol (E2), progesterone, thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and the LH/FSH ratio, are presented in Table 1. Notably, 75.3% (n=638) of the patients were diagnosed with infertility.

In patients with moderately elevated prolactin levels (26–100 µg/L), a statistically significant but very weak negative correlation (0.084) was observed between prolactin and E2 levels ($r=-0.084$, $p=0.018$). A statistically significant positive correlation at a very

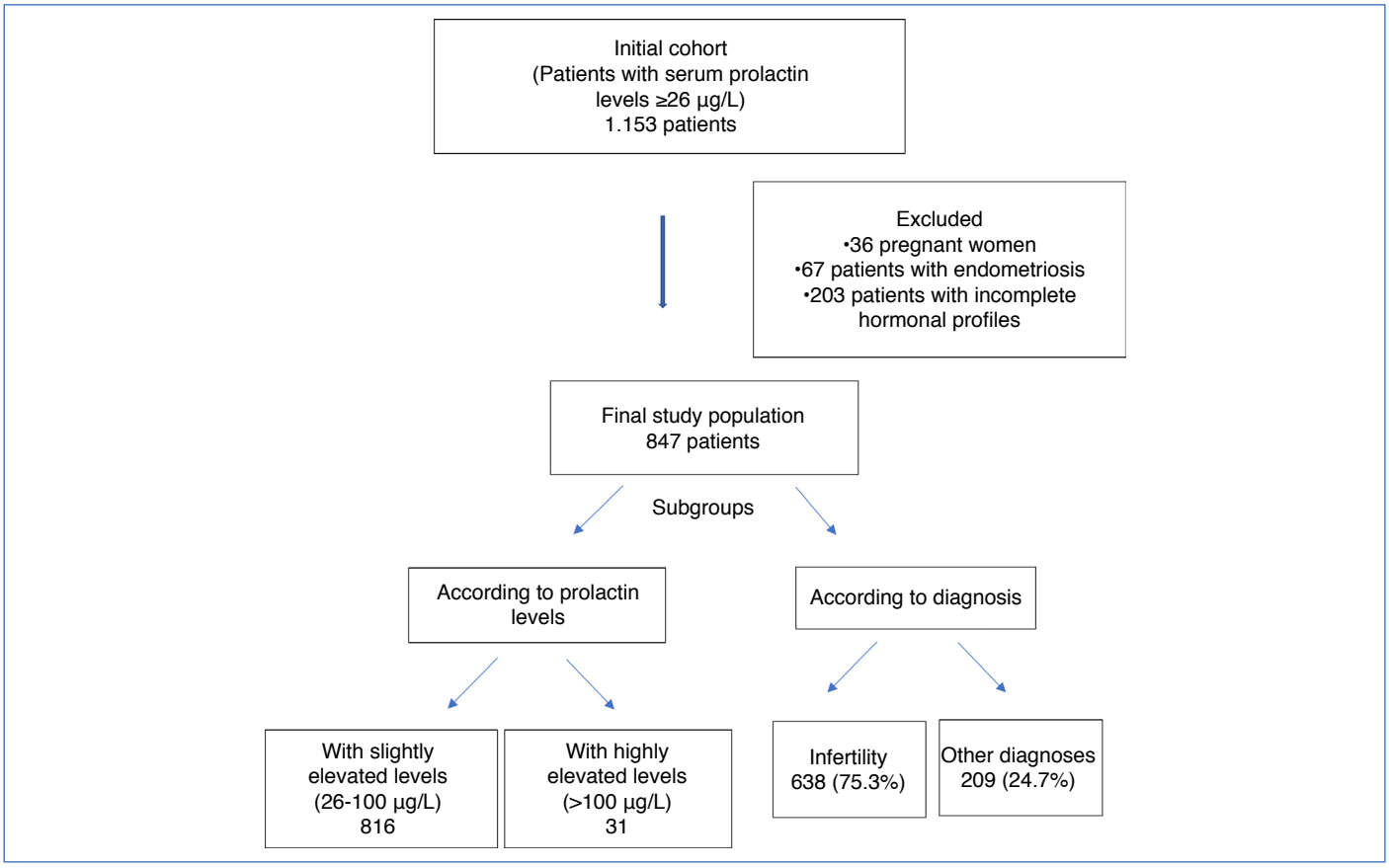

Figure 1: Flow chart of patient selection and exclusion criteria.

weak level (0.074) was found between prolactin and progesterone levels (r=0.074, p=0.042). No statistically significant correlation was found between prolactin levels and TSH, LH, FSH, or LH/FSH levels (p>0.05) (Table 2).

In patients with highly elevated prolactin levels (≥100 µg/L), no statistically significant correlation was observed between prolactin levels and E2, progesterone, TSH, LH, FSH, or the LH/FSH ratio (p>0.05) (Table 2).

In patients diagnosed with infertility, a very weak yet statistically significant negative correlation was observed between prolactin and E2 levels, with a correlation coefficient of -0.100 and a p-value of 0.012. However, no statistically significant correlations were identified between prolactin levels and progesterone, TSH, LH, FSH, or the LH/FSH ratio (p>0.05) (Table 3).

In patients with other diagnoses, a very weak yet statistically significant negative correlation of -0.166 was observed between prolactin and E2 levels (r=-0.166, p=0.021). However, no statistically significant relationships were identified between prolactin levels and progesterone, TSH, LH, FSH, or the LH/FSH ratio (p>0.05) (Table 3).

DISCUSSION

This large-scale cross-sectional study explored the correlation between serum prolactin levels and reproductive hormones (FSH, LH, estradiol, progesterone, and TSH) in women with hyperprolactinemia stratified by both fertility status and degree of prolactin elevation. Our findings revealed a statistically significant yet very weak negative correlation between prolactin and estradiol levels, particularly among patients with moderate hyperprolactinemia, as well as within both the infertility and other diagnoses subgroups. Notably, no significant associations were found between prolactin and gonadotropins or progesterone, irrespective of prolactin levels or fertility status.

These findings are consistent with previous evidence suggesting that prolactin suppresses the hypothalamic–pituitary–gonadal axis primarily by reducing GnRH pulsatility rather than by directly acting on gonadotrophs, given that GnRH neurons largely lack prolactin receptors. Instead, this suppression is likely mediated by kisspeptin inhibition, as demonstrated in both animal and human models.[14–17] Furthermore, animal studies have shown that hyperprolactinemia impairs LH pulse frequency and amplitude, which can, in turn, affect ovulatory function.[5,18] However, the absence of a strong or consistent correlation between prolactin and gonadotropins in our study suggests that these effects may not be reliably captured using single-point hormone measurements in clinical practice.

One of the primary strengths of this study was its large sample size and well-defined patient population, which allowed for robust statistical analysis and subgroup stratification. The inclusion of infertile individuals adds to the clinical depth, as most previous studies did not consider fertility status when evaluating prolactin-related hormonal changes. Furthermore, the strict

Table 1: Descriptive information and hormonal results

	Min–Max	Average±SD
Age	18–46	30.9±6.6
Prolactin	26.13–258.14	43.07±23.25
E_2	5.44–1677	60.48±89.98
P_4	0.01–28	0.68±2.07
TSH	0–40.55	2.29±2.54
LH	0.05–52	5.15±4.15
FSH	0.01–95.49	7.4±7.74
LH/FSH	0.02–25	0.87±1.05
	n	**%**
Diagnosis		
Infertility	638	75.3
Other	209	24.7

Min: Minimum; Max: Maximum; SD; Standard deviation; E_2: Estradiol; P_4: Progesterone; TSH: Thyroid-stimulating hormone; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone.

Table 2: Correlation between prolactin and other hormones, including LH/FSH levels associated with prolactin concentrations

(n=847)	Prolactin 26–100 mcg/L (n=816)		Prolactin ≥100 mcg/L (n=31)	
	r	p	r	p
E2	-0.084	0.018*	-0.277	0.131
P4	0.074	0.042*	-0.206	0.274
TSH	0.034	0.331	-0.304	0.097
LH	-0.047	0.189	0.105	0.581
FSH	-0.026	0.463	-0.052	0.779
LH/FSH	-0.013	0.713	0.071	0.708

Spearman correlation coefficient *p<0.05. E_2: Estradiol; P_4: Progesterone; TSH: Thyroid-stimulating hormone; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone.

exclusion of patients with confounding factors such as pregnancy, endometriosis, or incomplete hormonal data increased the internal validity of our results.

However, this study had several limitations. First, its cross-sectional design limits its ability to infer causal relationships or dynamic hormonal interactions. Serum hormone levels were measured at a single time point, which may not accurately reflect the pulsatile nature of GnRH and LH secretion. Second, our study did not include advanced hormonal markers such as kisspeptin or anti-Müllerian hormone (AMH), nor did it evaluate clinical outcomes such as ovulation or pregnancy rates. Finally, etiological subtyping of hyperprolactinemia (e.g., prolactinoma vs. drug-induced vs. idiopathic) was not performed, which may have further clarified hormonal patterns.

Table 3: The correlation between prolactin, other hormones, and LH/FSH levels in relation to infertility

(n=847)	Infertility Prolactin		Other diagnoses Prolactin	
	r	p	r	p
E_2	-0.100	0.012*	-0.166	0.021*
P_4	0.031	0.441	0.077	0.338
TSH	0.066	0.095	0.013	0.854
LH	-0.057	0.150	-0.134	0.066
FSH	0.010	0.806	-0.128	0.071
LH/FSH	-0.064	0.108	-0.029	0.695

Spearman correlation coefficient *p<0.05. E_2: Estradiol; P_4: Progesterone; TSH: Thyroid-stimulating hormone; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone.

CONCLUSION

This study provides valuable insights into the hormonal interplay in hyperprolactinemia by demonstrating that, despite its well-known suppressive effect on the reproductive axis, serum prolactin levels are only weakly correlated with estradiol and not significantly associated with gonadotropin levels in routine clinical settings. These findings suggest that prolactin may impair reproductive function through indirect mechanisms that are not fully captured by static hormone measurements. Future studies should include longitudinal designs, dynamic testing (such as GnRH stimulation or kisspeptin challenge), and clinical outcomes such as ovulation and pregnancy rates to provide a more comprehensive understanding. Stratifying patients according to the etiology of hyperprolactinemia is also critical for identifying subgroup-specific hormonal profiles and guiding individualized therapeutic strategies.

Statement

Ethics Committee Approval: The University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 18.09.2019, number: 86).

Informed Consent: Written informed consent was not required due to the retrospective design and ethics committee regulations.

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ORIGINAL ARTICLE

Motherhood shaped by the pandemic: Do pandemic-related anxiety and obsession play a role in postpartum parenting behavior?

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ABSTRACT

Objective: This study aimed to examine the impact of COVID-19 pandemic-related anxiety and obsessive thoughts on parenting behaviors during the postpartum period.

Material and Methods: A descriptive, cross-sectional design was employed, including 300 postpartum women, to evaluate the impact of COVID-19 pandemic anxiety and obsession on parenting behaviors. Data were collected between June and December 2020 at a tertiary hospital in the Marmara region of Türkiye. Instruments included a sociodemographic information form, the COVID-19 Anxiety Scale (CAS), the Obsession with COVID-19 Scale (OCS), and the Postpartum Parenting Behavior Scale (PPBS).

Results: Participants' mean age was 29.3±5.8 years, with an average marriage duration of 6.9±5.3 years. Over half (58%) reported that giving birth during the COVID-19 pandemic had a negative psychological impact. Statistical analyses revealed a significant interaction effect between CAS and OCS on PPBS scores (p=0.015).

Conclusion: The findings suggest that postpartum parenting behaviors are shaped by the complex interaction between COVID-19-related anxiety and obsessive thoughts. These psychological constructs should be understood not as isolated factors but as interrelated processes that collectively influence maternal behavioral outcomes during the postpartum period. To better understand these dynamics, future studies employing longitudinal and intervention-based designs are recommended to reveal causal pathways and underlying mechanisms. In addition, even in the post-pandemic context, the development and implementation of targeted mental health interventions for postpartum women remain essential public health priorities.

Keywords: Anxiety, COVID-19, obsession, pandemic, parenting behavior.

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INTRODUCTION

The COVID-19 pandemic has exerted widespread biopsychosocial, spiritual, and economic effects on individuals and communities.[1–3] While the pandemic has affected all age groups, its psychological burden has disproportionately impacted vulnerable populations, including women in the perinatal period. A growing body of evidence documents significant increases in anxiety, depression, and stress across diverse demographic groups during the pandemic. Evidence suggests that women appear more susceptible than men to psychological distress during this period.[4] Recent studies further demonstrate that the pandemic and related public health restrictions have heightened the risk of mental health problems, particularly among vulnerable groups such as postpartum women.[5,6] The postpartum period is a uniquely sensitive phase characterized by profound psychological, emotional, and physiological changes, as well as increased caregiving responsibilities.[7] These challenges can increase maternal vulnerability to a range of psychopathological symptoms, indicating the need for targeted mental health support and early interventions during this critical window. In addition, psychological symptoms in mothers may be exacerbated during acute stressors such as the COVID-19 pandemic.[8] Emerging evidence indicates that maternal mental health difficulties during crises not only impact maternal well-being but may also adversely affect cognitive, emotional, and behavioral development.[9,10] Parenting challenges exist even under optimal conditions; the added stressors of the pandemic have intensified maternal fears and concerns related to safety and security.[11] Previous research links maternal mental health conditions—such as anxiety, stress, and depression—with adverse perinatal outcomes, including preterm birth, low birth weight, impaired maternal perception of parenting, and difficulties in mother–infant attachment.[9,10] In this context, exploring the relationship between pandemic-specific stressors and postpartum parenting behaviors, particularly in relation to anxiety and obsessive thoughts, is essential. Accordingly, this study was designed to examine the impact of COVID-19-related anxiety and obsessive thoughts on parenting behaviors during the postpartum period.

Research Question

To what extent do COVID-19-related anxiety and obsessive thoughts influence parenting behaviors among postpartum women?

MATERIAL AND METHODS

Study Design

This study employed a descriptive, cross-sectional design to examine the impact of COVID-19-related anxiety and obsessive thoughts on postpartum parenting behaviors.

Population and Sample

This study was conducted between June and December 2020 with postpartum women attending the obstetrics outpatient clinics of a tertiary hospital in the Marmara region of Türkiye. The sample consisted of volunteers who met the following inclusion criteria: aged 18 years or older, in the postpartum period, having delivered a healthy singleton infant (i.e., no multiple pregnancy), self-reported good physical and mental health, literate in Turkish, and capable of completing the data collection forms independently. Only participants who completed all sections of the questionnaire were included in the final analysis. The required sample size was calculated based on a 90% confidence level and a 5% margin of error, resulting in a minimum target of 231 participants.[12] A total of 300 postpartum women who fully completed the data collection forms and met the inclusion criteria were included in the final analysis. Data were collected through face-to-face interviews conducted by trained researchers. Participants who did not meet the inclusion criteria were excluded from the study.

Data Collection Instruments

A sociodemographic information form was developed by the researchers based on a review of relevant literatüre.[13–18] This form collected participants' background characteristics, including age, educational level, self-reported mental health status, and experiences related to the COVID-19 pandemic. The COVID-19 Anxiety Scale (CAS), originally developed by Lee et al.[19] to assess anxiety symptoms related to the COVID-19 pandemic, was used to measure participants' pandemic-specific anxiety levels. The CAS distinguishes between those experiencing dysfunctional anxiety and those experiencing no anxiety using an optimized cutoff score of 9 with 90% sensitivity and 85% specificity.[19] The Turkish adaptation and validation of the scale were conducted by Evren et al.,[20] confirming its cultural and linguistic appropriateness for use in the Turkish population. The internal consistency of the scale in the Turkish adaptation study was reported with a Cronbach's alpha coefficient of 0.80. In the present study, the CAS demonstrated good reliability, with a Cronbach's alpha of 0.83. Participants were asked to indicate how often they experienced the symptoms described in the scale items over the preceding two weeks. Each item is scored from 0 to 4, with total scores ranging from 0 to 20. Higher scores indicate greater severity of COVID-19-related anxiety.[20]

The Obsession with COVID-19 Scale (OCS) was developed by Lee [19] as a brief self-report instrument designed to identify individuals experiencing functional impairment due to persistent and intrusive COVID-19-related thoughts. This scale serves as a mental health screening instrument to assess obsessive thinking patterns specifically associated with the pandemic.[21] The Turkish adaptation study by Evren et al.[20] reported acceptable internal consistency with a Cronbach's alpha of 0.71. In the present study, the OCS demonstrated good reliability, with a Cronbach's alpha of 0.79. The scale consists of four items rated on a five-point Likert scale, with participants indicating the frequency of obsessive COVID-19-related thoughts over the preceding two weeks. Total scores range from 0 to 16. A total score of 7 or higher on any single item suggests the need for further clinical evaluation.[19]

The Postpartum Parenting Behavior Scale (PPBS) was developed by Britton et al.[22] to assess parental behaviors during the initial interaction with the infant immediately following birth. The Turkish adaptation was conducted by Çalışır et al.,[23] who reported reliability coefficients ranging from 0.80 to 0.83, indicating good internal consistency. The scale is applied by observing the mother's

Table 1: Descriptive characteristics of the participants

	n	%		n	%
Age (Mean±SD)	29.3±5.8 (Min: 18–Max: 44)		General mood		
Duration of marriage (Mean±SD)	6.9±5.3 (Min: 1–Max: 22)		Poor	6	2.0
Number of pregnancies (Mean±SD)	2.5±1.4 (Min: 1–Max: 7)		Neutral	70	23.3
Educational status			Good	177	59.0
High school education or lower	235	78.3	Very good	47	15.7
University graduate	65	21.7	History of prior COVID-19 diagnosis		
Employment status			Yes	11	3.7
Unemployed	228	76.0	No	289	96.3
Employed	72	24.0	Family history of COVID-19 diagnosis		
Occupation			Yes	60	20.0
Worker	24	33.3	No	240	80.0
Government officer	39	54.2	COVID-19–related death in the family		
Self-employed	9	12.5	Yes	17	5.7
Family type			No	283	94.3
Nuclear family	225	75.0	Frequency of following news related to the COVID-19 pandemic		
Extended family	75	25.0	Never	15	5.0
Smoking behavior			Occasionally	148	49.3
Smoker	27	9.0	Often	137	45.7
Non-smoker	273	91.0	Did giving birth during the COVID-19 pandemic have a negative impact on you?		
Parity			Yes	174	58.0
Primigravida	91	30.3	No	126	42.0
Multigravida	209	69.7	Change in delivery method choice influenced by the COVID-19 pandemic		
			Yes	24	8.0
			No	276	92.0

SD: Standard deviation; Min: Minimum; Max: Maximum; COVID-19: Coronavirus disease 2019.

behavior toward her infant during the first 10 minutes after birth. Each behavior is recorded as present (+) or absent (-). Observed behaviors receive a score of 1, while unobserved behaviors receive 0. The total scale score ranges from 0 to 6 points, with higher scores indicating more positive parenting behaviors. In this study, the PPBS demonstrated good internal consistency, with a Cronbach's alpha coefficient of 0.80.

Ethical Considerations

Ethical approval for the study was obtained from the Clinical Research Ethics Committee (Decision No: 127, dated 24 June 2020). Written informed consent was obtained from all participants after they were provided with comprehensive information about the study, including their right to withdraw at any time without any penalty. Permissions for the use of all measurement scales were obtained prior to data collection. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 16.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including means, standard deviations, and percentages, were used to summarize participant characteristics and scale scores. Factorial ANOVA was conducted to examine the main and interaction effects of COVID-19-related anxiety and obsession on postpartum parenting behaviors. A p-value of<0.05 was considered statistically significant.

RESULTS

Table 1 presents the descriptive characteristics of the study participants. The mean age was 29.3±5.8 years (Min: 18–Max: 44), and the average duration of marriage was 6.9±5.3 years (Min: 1–Max: 22). Among the participants, 78.3% had a high school education

Table 2: Analysis of the interaction between CAS, OCS and PPBS

Reference	F	p	η^2
CAS	1.02	0.314	0.003
OCS	3.22	0.074	0.010
OCS*CAS	5.94	**0.015***	0.020
Error	807.58		
Total	7133.00		

*: P<0.05; CAS: COVID-19 Anxiety Scale; OCS: Obsession with COVID-19 Scale; PPBS: Postpartum parenting behavior scale.

or lower, 76.0% were homemakers, and 75.0% lived in a nuclear family structure. In addition, 91.0% reported being non-smokers, and 59.0% described their general mood as good. Regarding obstetric characteristics, the mean number of pregnancies was 2.5±1.4 (Min: 1–Max: 7), with 69.7% being multiparous. Furthermore, 58.0% reported that giving birth during the COVID-19 pandemic negatively affected them, and 8.0% stated that they had changed their decision about the mode of delivery due to the pandemic.

Table 2 presents the factorial ANOVA results examining the interaction between CAS, OCS, and PPBS. The analysis showed that neither CAS nor OCS individually had a statistically significant effect on postpartum parenting behavior (p=0.314 and p=0.074, respectively). The partial eta squared value (η^2=0.020) indicated a small effect size based on Cohen's (1988) criteria. However, a statistically significant interaction effect between CAS and OCS on PPBS was observed (p=0.015).

DISCUSSION

This study aimed to examine whether COVID-19-related anxiety and obsession influence parenting behavior during the postpartum period. The findings revealed a statistically significant interaction effect between the CAS and the OCS on postpartum parenting behavior, as measured by the PPBS (p=0.015). Although individual effects of CAS and OCS on PPBS were not statistically significant (p=0.314 and p=0.074, respectively), the significant interaction (p=0.015) suggests a more complex, independent relationship between these psychological factors. Specifically, the effect of one variable on parenting behavior appears to depend on the level of the other, indicating a non-linear interaction between COVID-19-related anxiety and obsessive thoughts. The significant interaction (p=0.015) supports the conclusion that certain combinations of anxiety and obsession levels differentially impact postpartum parenting behavior, rather than these factors acting independently (p=0.314 and p=0.074, respectively). This is consistent with the literature suggesting that maternal perfectionism can contribute to increased anxiety and stress, potentially triggering anxiety-related symptoms.[24] The findings of the present study also support this result, indicating that elevated anxiety and obsessive thought patterns—potentially shaped by internalized expectations of perfect parenting—are associated with variations in postpartum parenting behavior.

The postpartum period is marked by physical recovery, the assumption of new parenting responsibilities, and adjustment to profound life changes. This transitional phase places considerable demands on a woman's psychological health and can contribute to the emergence of anxiety symptoms.[25] Indeed, anxiety is recognized as one of the most common psychological challenges in the postpartum period, with reported prevalence rates ranging from 13% to 40%.[26] Postpartum anxiety has been linked to difficulties in maternal adaptation, sleep disturbances, breastfeeding challenges, and adverse maternal-infant outcomes such as depression, all of which may compromise maternal and infant health.[26,27] Furthermore, the COVID-19 pandemic has introduced an additional layer of stress, potentially disrupting the mother-infant attachment process.[28] It is well documented that fear of the unknown elevates anxiety levels in individuals regardless of their prior mental health history.[29] During the pandemic, increased psychological distress—particularly anxiety and obsessive-compulsive symptoms—has been observed among pregnant and postpartum women.[30–34]

The most common obsessive-compulsive symptoms observed during the postpartum period typically involve safety-related concerns, such as fears of harming the infant, excessive online information-seeking, and compulsive cleaning behaviors.[35] Although pandemic-related fears and hygiene behaviors differ from clinically diagnosed germ-related obsessions, the physiological and psychological changes associated with pregnancy may increase women's vulnerability to such symptoms. The fear of contagion, combined with heightened hygiene vigilance, may develop into obsessive thoughts and compulsive behaviors. These manifestations have been associated with adverse outcomes, including reduced breastfeeding rates and diminished maternal enjoyment of parenting.[36] Maternal fears of inadvertently harming the infant may lead to emotional distancing, which can negatively impact both breastfeeding motivation and success.[36,37] Previous studies have shown that breastfeeding rates are lower among mothers diagnosed with obsessive-compulsive disorder.[37] Hormones such as oxytocin and prolactin, which are released during breastfeeding, play a vital role in fostering mother-infant attachment and promoting positive parenting behaviors.[38] However, obsession related to COVID-19—particularly those involving fears of infection or harm—may disrupt these attachment processes and influence the mother's engagement with her infant.[37,39–42] Specifically, intrusive thoughts related to contamination or infant safety may cause mothers to avoid physical contact, engage in excessive cleaning, or demonstrate reduced sensitivity in their caregiving behaviors. Given the interconnected nature of obsession and anxiety, these symptoms may also extend beyond parenting to impact other aspects of maternal functioning, including sexual behavior.[37]

The findings of the present study are consistent with the broader literature, highlighting the importance of recognizing and addressing these psychological dimensions in postpartum care.

Limitations

The single-center design of this study represents a limitation, as the sample may not be fully representative of the broader postpartum maternal population. Consequently, the generalizability of the findings may be restricted.

CONCLUSION

This study examined the interactive effects of COVID-19-related anxiety and obsessive thoughts—measured using the COVID-19 Anxiety Scale (CAS) and the Obsession with COVID-19 Scale (OCS), respectively—on postpartum parenting behaviors, assessed using the Postpartum Parenting Behavior Scale (PPBS). The findings revealed that while CAS and OCS scores individually did not significantly affect parenting behaviors, their interaction produced a statistically significant effect. This suggests that specific combinations of anxiety and obsession levels may jointly impact maternal behaviors during the postpartum period. Although the observed effect size was small, the statistical significance of the interaction underscores the importance of considering these psychological constructs as interrelated, rather than isolated, impacts on maternal behavior. These findings point to the need for a more nuanced understanding of postpartum mental health, particularly in contexts of heightened stress such as the COVID-19 pandemic.

Future research should expand on these results by incorporating additional psychological variables—such as fear of infection, adaptability to life changes, and sociodemographic factors—to explore more complex interaction models. Longitudinal and intervention-based studies are especially recommended to establish causality and identify effective prevention and support strategies. The statistically significant interaction found in the study (p=0.015) indicated that postpartum parenting behaviors in the context of the COVID-19 pandemic are shaped by a complex combination of anxiety and obsession. While the study findings point to the complex role of anxiety and obsessive thoughts on postpartum parenting behaviors, the reported effect size of η^2=0.020 suggests that the significance of this effect may be limited.

These findings suggest that future researchers should consider and include in the model other variables that may influence parenting behaviors, in addition to anxiety and obsession, such as cultural factors, environmental stressors, birth experience, self-efficacy, spousal support, and coping strategies. In addition, even in the post-pandemic context, the development and implementation of targeted mental health interventions for postpartum women should remain a public health priority to support maternal well-being and foster healthy parenting behaviors.

Statement

Ethics Committee Approval: The by Zeynep Kamil Women and Children Diseases Traning and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 24.06.2020, number: 127).

Informed Consent: Written informed consent was obtained from all participants after they were provided with comprehensive information about the study, including their right to withdraw at any time without any penalty.

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

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ORIGINAL ARTICLE

Evaluation of high sensitive C-reactive protein levels in patients with polycystic ovary syndrome

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ABSTRACT

Objective: The aim of this study was to investigate high sensitive C-reactive protein (hsCRP) levels in patients with polycystic ovary syndrome (PCOS) without insulin resistance (IR) and metabolic syndrome (MS).

Material and Methods: This retrospective study involved 90 patients aged 18–35 years who applied to a tertiary clinic between March 2022 and December 2023. A total of 45 PCOS patients without IR and MS and 45 healthy women were enrolled in the study. All participants underwent medical history review, clinical physical examination, gynecological ultrasonographic evaluation, and laboratory testing. Laboratory screening tests included measurements of follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (T), free testosterone, sex hormone-binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), and low-density lipoprotein (LDL), which is a cardiovascular risk factor. Normal insulin sensitivity was defined on the basis of fasting serum glucose, fasting insulin level, serum insulin response to the oral glucose tolerance test, and the homeostatic model of insulin resistance. hsCRP levels were evaluated using the enzyme-linked immunosorbent assay (ELISA) technique.

Results: There were no significant differences between the groups in terms of age, systolic and diastolic blood pressure, FSH, LH, free T, total T, DHEAS, or SHBG. PCOS patients had increased hsCRP, waist-to-hip ratio (WHR), body mass index (BMI), and LDL levels compared to the control group. hsCRP was positively correlated with WHR, BMI, and LDL. A strong correlation was found between hsCRP and PCOS.

Conclusion: Elevated hsCRP is associated with cardiovascular risk factors in PCOS patients without IR and MS.

Keywords: Cardiovascular risk factor, high sensitive c-reactive protein, polycystic ovary syndrome.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) affects approximately 5–10% of women of reproductive age. It is an endocrine and metabolic disorder with polygenic inheritance, modulated by both epigenetic and environmental factors. Although the exact etiology remains unclear, multiple pathophysiological mechanisms are thought to be involved.[1,2]

Intestinal microbiota plays an important role in human health and contributes to various diseases. It has been shown that microbiota imbalance leads to metabolic and immune system dysfunction.[3] Dysbiosis has been associated with several conditions, including pregnancy complications, endometriosis, cancer, and PCOS.[4] Recent research suggests that chronic low-grade inflammation in lean PCOS patients may result from altered gut microbiota, ovarian steroidogenic dysregulation, or hyperandrogenemia.[3,4]

PCOS is frequently associated with abdominal fat, obesity, insulin resistance (IR), mood disorders, metabolic disorders, and increased cardiovascular risk.[1–3] PCOS is associated with cardiovascular risk, and cardiovascular diseases (CVD) are the major cause of morbidity and mortality. Atherosclerosis, an inflammatory disease in the intima layer of the arterial wall, is the leading cause of cardiovascular diseases.[5,6] It is known that C-reactive protein (CRP) plays an active role in atherogenesis, causes plaque instability, contributes to thrombosis, and ultimately to the formation of acute coronary syndromes.[7] CRP is an important independent risk factor for myocardial infarction, stroke, and peripheral vascular diseases. High sensitive C-reactive protein (hsCRP) is an established marker of low-grade chronic inflammation and is especially elevated in patients with acute coronary syndrome.[8]

IR is a common pathogenetic factor in PCOS. Approximately 30–47% of patients with PCOS exhibit IR and meet the criteria for metabolic syndrome (MS), including obesity, hypertension, impaired glucose tolerance, dyslipidemia, and hypertriglyceridemia.[9,10]

There is an association between increased cardiovascular risk factors and PCOS. Patients with PCOS, even at an early age, have cardiovascular risk factors such as IR, dyslipidemia, hypertension, impaired cardiac and pulmonary functional capacity, autonomic dysfunction, and low-grade chronic inflammation. These risk factors increase with obesity. The risk of cardiovascular disease is higher in patients with obesity and PCOS.[11] hsCRP is closely related to MS criteria and has been shown to be increased in PCOS patients.[10,12] However, the relationship between hsCRP and PCOS in normoinsulinemic, non-obese women without MS remains underexplored. This study aims to evaluate hsCRP levels in such patients.

MATERIAL AND METHODS

This retrospective, single-center study included 90 women aged 18–35 years with a body mass index (BMI)<30 kg/m² who presented to the Kartal Lütfi Kırdar City Hospital Gynecology and Obstetrics Outpatient Clinic between March 2022 and December 2023. The study group consisted of 45 women with PCOS without IR or MS and 45 normoandrogenic, ovulatory women attending for routine gynecological examination. The study was approved by the İzmir Bakırçay University Ethics Committee, and informed consent was obtained from all participants before the start of the study. The study was conducted in accordance with the principles of the Declaration of Helsinki. Artificial intelligence (AI)-supported technologies were not used in this study.

Exclusion criteria included the presence of IR, MS, hypertension, hyperlipidemia, hyperprolactinemia, hypothalamic amenorrhea, premature ovarian failure, thyroid hormone dysfunction, congenital or acquired adrenal dysfunction, diabetes mellitus, pregnancy, smoking, alcohol or substance use, psychiatric illness, neoplastic disease, infections, autoimmune diseases, liver or kidney disease, diagnosed cardiovascular disease, a family history of early coronary artery disease, or the use of hormonal or psychoactive medications.

All participants underwent gynecological ultrasound evaluation. Mid-luteal phase progesterone measurements of less than 3 ng/mL in regular menstrual cycles were indicative of oligo/anovulation. Clinical hirsutism was defined as a score of ≥8 according to the modified Ferriman-Gallwey scoring system. Biochemical hirsutism was defined as total testosterone (T)>80 ng/dL or dehydroepiandrosterone sulfate (DHEAS)>350 ng/dL.[13] PCOS patients without hirsutism were included in the study. The diagnosis of PCOS was made according to the 2003 Rotterdam Consensus Criteria.[14] BMI was used as an assessment measure of obesity. BMI (kg/m²) was calculated using weight and height (weight divided by height squared). Abdominal obesity was calculated as the waist-to-hip ratio (WHR).[15]

Insulin sensitivity was defined according to serum fasting plasma glucose, serum fasting insulin level, serum insulin response to the oral glucose tolerance test (OGTT), and homeostatic model of insulin resistance (HOMA-IR). Fasting insulin and fasting plasma glucose levels were used for the calculation of HOMA-IR (insulin×glycemia in µmol/L/22.5). Patients with fasting insulin>25 μIU/mL, peak serum insulin>100 μIU/mL during OGTT, and HOMA-IR>4 were classified as IR. The 2-hour OGTT value was <140 mg/dL in all participants.[16–19]

All participants with normal serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, thyroid function tests, spontaneous menstruation, or a positive bleeding response to progestogen withdrawal were included in the study. All participants underwent clinical and ultrasonographic evaluation. Hormone and biochemical tests were performed by taking blood samples. Endocrine screening included serum assays for glucose, insulin, 75 g OGTT, prolactin, FSH, LH, thyroid function tests, estradiol, progesterone, free T, total T, sex hormone-binding globulin (SHBG), and DHEAS. All tests administered to the participants were performed between days 3 and 5 of the menstrual cycle. Fasting venous blood samples were taken after 12 hours of overnight fasting.

Statistical Analysis

Statistical analyses were performed using IBM SPSS for Windows version 25.0 software. Baseline characteristics of both groups were presented as mean±SD. Laboratory and anthropometric parameters of patients were compared using Student's t-test. Independent relationships between PCOS and hsCRP, BMI, WHR, and LDL were assessed by multiple linear regression analysis. Correlations between hsCRP and BMI, WHR, and LDL were assessed by Pearson correlation analysis, and the correlation between hsCRP and PCOS status was assessed by Spearman's rank test. Statistical significance was set at $p<0.05$.

Table 1: Clinical and laboratory parameters of women with normoinsulinemic PCOS and control group

Parameters	PCOS (n=45) Mean±SD	Controls (n=45) Mean±SD
Age (years)	27.5±4.1	27.3±4.0
Blood pressure (mmHg)	113.5±11.4	111.2±11.5
	74.1±8.6	73.5±9.0
BMI (kg/m^2)	28.1±1.7*	25.1±2.0*
WHR	0.82±0.0*	0.72±0.0*
FSH (mIU/mL)	4.8±2.0	4.9±2.1
LH (mIU/mL)	7.0±3.1	6.8±3.0
Free testosterone (ng/dL)	8.8±2.3	8.0±2.5
Testosterone (ng/dL)	61.1±11.7	55.5±11.9
SHBG (nmol/L)	58.8±12.4	63.3±12.3
DHEAS (μg/dL)	168.1±43.9	158.1±44.3
LDL (mg/dL)	110.2±20.9*	90.1±20.3*
hsCRP (mg/L)	1.7±0.7*	0.5±0.4*

PCOS: Polycystic ovary syndrome; SD: standard deviation; *: P<0.05; BMI: Body mass index; WHR: Waist to hip ratio; FSH: Follicle stimulating hormone; LH: Luteinizing hormone; SHBG: Sex hormone binding globulin; DHEAS: Dehydroepiandrosterone sulfate; LDL: Low density lipoprotein; hsCRP: High sensitive C reactive protein.

RESULTS

The clinical and laboratory parameters are shown and summarized in Table 1. No differences were observed between the groups in terms of age, systolic and diastolic blood pressure, FSH, LH, androgens, or DHEAS. SHBG levels were lower in PCOS patients compared to the control group, but this difference was not statistically significant. PCOS patients exhibited significantly higher BMI, WHR, LDL, and hsCRP levels than the control group. hsCRP was positively correlated with BMI, WHR, and LDL. A significant association was also found between hsCRP and PCOS status (p<0.05) (Table 1).

DISCUSSION

PCOS is a complex endocrine disorder that affects not only reproductive health but also long-term cardiometabolic health. There are data showing an increased incidence of cardiovascular disease in patients with PCOS. An increased risk of atherosclerotic heart disease has been reported multiple times in patients with PCOS compared to healthy controls. Previous studies have investigated the relationship between PCOS and coronary artery disease, and most have found that PCOS patients have more extensive coronary artery disease than controls. It has also been reported that PCOS patients have a higher risk of myocardial infarction than controls.[20]

Circulating inflammatory markers have been found to be elevated in PCOS compared with controls.[12] Markers of low-grade inflammation such as tumor necrosis factor-alpha (TNF-α), hsCRP, and white blood cell counts were increased in PCOS patients.[9] CRP was related to both BMI and PCOS.[21] It is known that hsCRP is a cardiovascular risk biomarker. hsCRP, one of the independent cardiovascular risk factors, is an indicator of chronic vascular inflammation and plays a role in the development of thrombovascular events.[22] Studies have shown that hsCRP is elevated in PCOS patients.[12] A meta-analysis of 48 studies concerning CRP levels in women with PCOS reported that CRP levels were significantly higher in the study group.[23] In this study, it was demonstrated that hsCRP levels were significantly higher in PCOS patients without IR or MS compared to normoandrogenic ovulatory women. Our findings suggest that low-grade chronic inflammation may be associated with PCOS independent of well-established risk factors such as obesity or IR. The presence of these biomarkers suggests that PCOS may not only be a hormonal disorder but also a systemic inflammatory condition.

Obesity is another contributing factor for CVD.[24] Obesity and excess abdominal fat are often associated with low-grade chronic inflammation. In adipose tissues, many proinflammatory cardiovascular risk markers such as interleukin-6 (IL-6) and hsCRP are secreted.[12] We also found significant positive correlations between hsCRP levels and BMI, WHR, and LDL cholesterol levels. Notably, since all PCOS patients included in our study were non-obese, our findings indicate that the inflammatory process may occur independently of IR or MS.

It has been previously shown that there is a strong association between hyperinsulinemia and an increased risk of cardiovascular disease in patients with PCOS.[25] IR is associated with atherosclerotic processes.[26] MS in women with PCOS is also associated with an increased risk of atherosclerosis, and this results in a higher risk of cardiovascular disease.[27] Cardiovascular risk factors in patients with PCOS without IR or MS have not been adequately studied before. Therefore, we conducted our study on this group to exclude the possible effects of these factors on cardiovascular risk. Dyslipidemia is very common in PCOS.[28] In our study, we found that LDL levels were higher in PCOS patients compared to controls. It is known that blood lipid levels are correlated with CRP levels.[21] Lipid-lowering therapy is known to be effective in reducing inflammatory markers.[29] In our study, we also found significant correlations between hsCRP and LDL.

One of the key strengths of this study is its design, which excluded major confounding cardiovascular risk factors such as IR and MS. This allowed us to isolate and directly assess the potential inflammatory contribution of PCOS itself. Our findings support the hypothesis that PCOS may be an independent inflammatory condition.

However, our study has several limitations. It was a single-center study with a relatively small sample size, and future studies with larger groups are needed. In addition, only hsCRP was evaluated as an inflammatory marker. Therefore, further multicenter, prospective studies with larger populations and comprehensive inflammatory profiling are warranted.

CONCLUSION

This study revealed that hsCRP levels were significantly higher in PCOS patients without insulin resistance or metabolic syndrome. These findings suggest that PCOS itself may act as an independent

inflammatory and cardiovascular risk factor. Therefore, even in the absence of classical risk indicators, cardiovascular risk assessment and regular monitoring should be considered in patients with PCOS. Preventive strategies based on early intervention and lifestyle modifications should be prioritized in this population.

Statement

Ethics Committee Approval: The İzmir Bakırçay University Ethics Committee granted approval for this study (date: 24.01.2024, number: 1441/1421)

Informed Consent: Informed consent was obtained from all participants before the study began.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Physical activity questionnaire (PPAQ) scores during pregnancy in a Turkish population with and without gestational diabetes mellitus: A prospective cohort study

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ABSTRACT

Objective: The risk of gestational diabetes mellitus increases in women with obesity and a sedentary lifestyle. Assessing quantitative physical activity in pregnant women with diabetes can help us better understand disease management. We report the characteristics of pregnant women who were screened and diagnosed with gestational diabetes, as well as the results of the Turkish version of the Pregnancy Physical Activity Questionnaire.

Material and Methods: A total of 292 pregnant women who completed the Pregnancy Physical Activity Questionnaire and underwent gestational diabetes screening were included in the study. Demographic characteristics, total and subscale scores of the Pregnancy Physical Activity Questionnaire were compared between women with positive and negative gestational diabetes mellitus screening and diagnostic test results.

Results: Total activity and subscale scores of the Pregnancy Physical Activity Questionnaire were similar between groups with positive and negative gestational diabetes mellitus screening and diagnostic test results. Age, weight, and body mass index differed significantly between groups (p=0.001, p=0.006, and p=0.001, respectively). Logistic multivariate binary analysis revealed no statistically significant differences between total activity and subscale scores.

Conclusion: Physical activity scores obtained from the Pregnancy Physical Activity Questionnaire, reflecting a 3-month period, were similar in cases with positive and negative gestational diabetes mellitus screening and diagnostic test results. Pregnant women should be encouraged to engage in more physical activity, as the frequency of gestational diabetes mellitus increases with age, body weight, body mass index, and number of pregnancies.

Keywords: Exercise, gestational diabetes mellitus, glucose tolerance test, obesity, physical activity questionnaire.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying levels that begins or is first diagnosed during pregnancy.[1] A greater prevalence of obesity and a sedentary lifestyle increases the prevalence of GDM in reproductive-aged women.[2] The aim of GDM management is to control blood glucose levels and improve pregnancy outcomes.[3] First-line treatment consists of dietary modification and exercise planning. Exercise plays an important role in the regulation of blood glucose levels, which in turn prevents or delays insulin treatment.[4] The American College of Obstetricians and Gynecologists (ACOG) recommends 20–30 minutes of moderate-intensity exercise on most or all days of the week.[5] Strong evidence demonstrates that moderate-intensity physical activity decreases the risk of excessive prenatal weight gain and gestational diabetes.[6] It has been reported that maternal epigenetic biomarkers are positively affected in physically active pregnant patients.[7]

Evaluation of quantitative physical activity (PA) in diabetic pregnant women may help to acquire a better understanding of the role of physical activity during treatment and may be useful in more effectively comparing the results of different studies conducted in different locations. There are subjective (questionnaires, interviews, diaries, direct observation) and objective techniques (pedometers, accelerometers, heart rate monitors, multicensors, indirect calorimetry, doubly labelled water method) to measure PA.[8] In assessing the intensity, duration, and frequency of activities, questionnaires are non-invasive, practical, and economical. Chasan-Taber et al.[9] established the Pregnancy Physical Activity Questionnaire (PPAQ), which is a simple and brief tool that measures the frequency, duration, and intensity of PA in pregnant women. The PPAQ evaluates 32 activities based on the time spent in each category. These activities are grouped into the following five categories: household/caregiving (13 activities), occupational (5 activities), sports/exercise (8 activities), transportation (3 activities), and inactivity (3 activities). The compendium-based metabolic equivalent (MET) values were used to estimate intensity. Each activity is classified as sedentary (<1.5 METs), light (1.5–3.0 METs), moderate (3.0–6.0 METs), or vigorous (≥6.0 METs) according to its intensity. Average weekly MET-hour values are calculated for each activity based on its intensity.

A Polish study analyzed the relationships between PA and quality of life using the PPAQ-PL and WHOQOL-BREF questionnaires in the second and third trimesters. Their study made an important contribution to understanding the correlations between PA and quality of life during pregnancy, and the results suggest the need for improvements in prenatal care and the promotion of PA programs for pregnant women.[10]

The Pregnancy Physical Activity Questionnaire provides a score based on a subjective assessment according to the activity type and intensity during the previous 3 months. GDM screening tests are applied at ≥24 weeks of gestation in standard practice. We hypothesized that pregnant women with positive GDM screening and diagnostic tests would have significantly lower PPAQ scores for the last 3 months than pregnant women with negative GDM screening and diagnostic test results. The validity and reliability of the Turkish version of the PPAQ (PPAQ-Tr) in GDM cases have been reported.[11] We aimed to evaluate characteristics and PA levels measured quantitatively with the PPAQ-Tr in cases with and without a diabetes diagnosis, as determined by gestational diabetes screening and diagnostic procedures performed during pregnancy.

MATERIAL AND METHODS

The Turkish reliability and validity version of the PPAQ was studied in the pregnant population of Zeynep Kamil Women's and Children's Diseases Training and Research Hospital between April 2015 and April 2017. The sample size calculation was made by predicting that the PPAQ "total activity of light-intensity and above" score in pregnant women without GDM would be 20% higher than in pregnant women with GDM. It was calculated that at least 256 cases were needed for 80% power and 95% CI. A total of 292 pregnant women over the age of 18 gave their consent for the study. Pregnant women who were referred for GDM screening at ≥24 gestational weeks were included in the study. Patients who had already been diagnosed with diabetes, had mobility issues, had multiple pregnancies, or were not Turkish literate were excluded from the study. Pregnant women who were diagnosed with a psychiatric disorder and receiving treatment were also excluded.

At the first follow-up, the age information of the pregnant women was verified using official identification. Height and weight measurements were taken by the outpatient clinic nurse before the examination. Body mass index values were calculated using the measurements taken at the patient's first visit. Obstetric history was obtained by the study team. Gestational age was determined using the last menstrual period and confirmed by first-trimester ultrasound measurements. A first-trimester ultrasound was used to establish gestational age in pregnant women whose last menstrual period was unclear. The patients were informed about the study and gave their consent prior to undergoing the 50-g glucose challenge test (GCT) for GDM screening. Gestational diabetes screening and diagnostic tests were performed with a two-step approach.[12]

At this first follow-up, the pregnant women were given the PPAQ-Tr and were asked to complete and bring it to the second follow-up. Those who did not fill out the PPAQ-Tr at the second follow-up were given it again and returned it the same day. The GCT results were assessed at the second follow-up. Pregnant women whose 50-g GCT result was ≥180 mg/dL were diagnosed with GDM. Cases with results between 140–180 mg/dL were referred for the 100-g oral glucose tolerance test (OGTT) for diagnosis.[12] The PPAQ-Tr scale's total and sub-dimension scores were calculated. The scores were compared between cases with positive and negative GDM screening results and between cases with positive and negative GDM diagnostic test results. After excluding primiparous cases, comparisons were also made for pregnant women who had and had not been diagnosed with GDM in their previous pregnancies.

The study protocol was approved by the Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital (2011-KAEK-25 2015/19-04). The study was conducted in accordance with the principles of the Declaration of Helsinki.

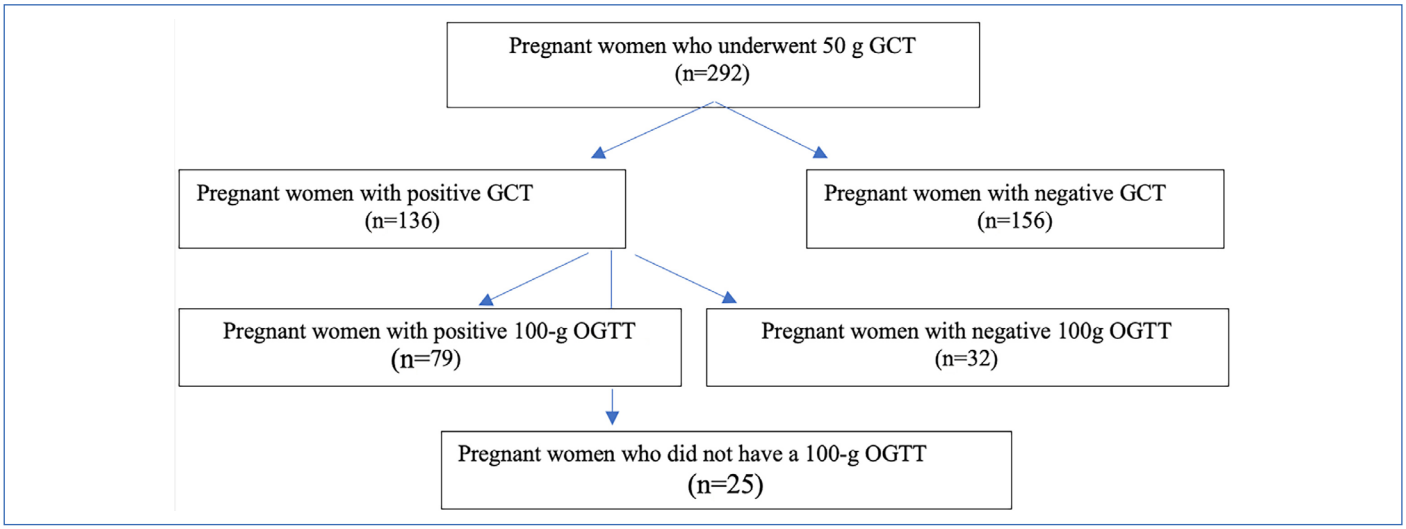

Figure 1: Flow diagram of case distribution according to GDM screening and diagnostic test results.

Statistical Analysis

Statistical analysis was performed using SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean±standard deviation (SD), percentiles (25th, median, 75th), and frequencies (number and percent). The compatibility of numerical variables with the normal distribution was examined using the Shapiro–Wilks test. Positive and negative OGTT results in terms of numerical characteristics were compared with the independent samples t-test or Mann–Whitney U test. A multiple binary logistic regression model was used to account for confounding variables. A p value of<0.05 was considered statistically significant.

RESULTS

The results of 292 pregnant women who completed the PPAQ-Tr before the screening test were evaluated. The test was positive in 136 of the 292 pregnant women who received the 50-g GCT. A 100-g OGTT was indicated for those with positive 50-g GCT findings, and the result was positive in 79 of 111 pregnant women who took the test, while 25 patients did not undergo a 100-g OGTT. Of the 267 pregnant women who obtained OGTT results, 79 (29.6%) were diagnosed with GDM. Among women who had previously given birth (n=179), GDM in a previous pregnancy was found in 14.5% (n=26) (Fig. 1).

Pregnant women with positive GDM screening test results had a statistically significantly lower mean height (p=0.018) and statistically significantly higher mean age (p=0.001), weight (p=0.002), body mass index (BMI) (p=0.001), and median gravida (p=0.005). The PPAQ-Tr scale scores showed no significant difference between pregnant women with positive or negative GDM screening test results (Table 1).

Pregnant women with positive GDM diagnostic test results (100-g OGTT) had statistically significantly higher mean age (p=0.001), mean weight (p=0.036), mean BMI (p=0.002), and median gravida (p=0.005) than pregnant women with negative GDM diagnostic test results. There was no statistically significant difference between pregnant women with positive or negative 100-g OGTT results in terms of PPAQ-Tr scale scores (Table 2).

Pregnant women who were diagnosed with GDM in their previous pregnancy had statistically significantly higher mean age (p=0.003), mean weight (p=0.029), mean BMI (p=0.009), and median gravida (p=0.025) compared with women whose previous pregnancies were not complicated by GDM. Evaluation of the PPAQ-Tr scale scores revealed that only the total score for the transportation activity subdimension was statistically significantly higher (p=0.025) in pregnant women who were diagnosed with GDM in their previous pregnancy (Table 3).

A multiple binary logistic regression model was created for confounding factors (age, BMI, gravidity, parity, and gestational age). The effects of these factors on the OGTT result at the time of diagnosis were eliminated, and the corrected effect of PA was examined. The model created for 'Total activity of light intensity and above' and 'Total activity of all questions' scores showed no significant relationship with GDM at the time of diagnosis after the baseline characteristic effects were eliminated.

DISCUSSION

In this study, no significant difference was found in PPAQ-Tr scale scores between pregnant women with positive and negative GDM screening and diagnostic test results.

Different GDM prevalences have been reported from various regions around the world. A meta-analysis reported the lowest prevalence of GDM in North America, with a rate of 7.1%, while the highest prevalence was reported in the Middle East and North Africa, with a rate of 27.6%.[13] Türkiye is located in the Middle East region. It has been reported that the prevalence of diabetes in the Turkish adult population increased by 90% over 12 years, reaching 13.7%. Diabetes was more common in women than in men (17.2% vs 16.0%).[14] These rates may explain the high prevalence of GDM among women of reproductive age. Lifestyle changes and predisposing conditions that contribute to the rising frequency of diabetes may also play a role in the increased prevalence of GDM in our country. In our study population, the GDM rate was found to be 29.6%.

Table 1: Comparison of pregnant women with positive and negative GDM screening test in terms of demographic characteristics and PPAQ-Tr scale scores

	GDM screening test negative (n=156)		GDM screening test positive (n=136)		p
	Mean	±SD	Mean	±SD	
Age (year)[a]	28.7	4.9	31.5	5.3	0.001
Height (cm)[a]	162.1	5.8	160.4	5.6	0.018
Weight (kg)[a]	71.2	11.9	76.4	12.4	0.002
BMI (kg/m²)[a]	27.2	4.2	29.8	4.7	0.001
Gestational age (weeks)[a]	26.7	3.0	27.0	4.1	0.494
	Median	IQR (25–75%)	Median	IQR (25–75%)	
Gravidity[b]	2	1–3	2	1–4	0.005
Parity[b]	1	0–1	1	0–2	0.103
Total activity of all questions[b]	139.8	101.3–188.0	139.4	97.3–212.8	0.883
Total activity of light intensity and above[b]	111.1	64.6–161.0	105.4	63.1–182.0	0.948
Sedentary activity[b]	29.4	14.0–44.8	29.4	7.6–44.8	0.870
Light-intensity activity[b]	95.1	58.0–129.5	90.6	55.7–141.8	0.879
Moderate-intensity activity[b]	10.6	3.5–33.0	13.7	1.9–45.7	0.851
Vigorous-intensity activity[b]	0.1	0.0.6	0.1	0–0.6	0.556
Household/caregiving activity[b]	71.4	41.9–126.4	70.2	35.4–116.5	0.526
Occupational activity[b]	0	0–0	0	0–11.5	0.342
Sports/exercise activity[b]	0.6	0.2–1.5	0.7	0.2–1.8	0.320
Transportation activity[b]	8.8	3.4–17.0	10.0	2.1–20.6	0.476
Inactivity[b]	30.4	15.0–56.5	31.0	14.0–46.8	0.979

a: Independent Samples t-Test. b: Mann-Whitney U test; GDM: Gestational diabetes mellitus; BMI: Body mass index; IQR: Intequartile range; SD: Standard deviation.

Advanced maternal age and pre-pregnancy BMI have been shown to be associated with an increased risk of GDM.[15] It has been reported that exercise interventions are effective in reducing the likelihood of developing GDM. Pregnant women should perform at least 600 MET-min of moderate-intensity exercise per week to reduce the likelihood of developing GDM by 25%.[16] In our study, pregnant women with positive GDM screening test results had a considerably lower mean height; in contrast, for both GDM screening and diagnostic tests, the mean age, mean weight, mean BMI, and median gravida were significantly higher. Increasing age, body weight, BMI, multiparity, and short stature play a role in the development of diabetes.[17] Height differences may be affected by ethnicity and environmental factors, which were not evaluated in our study. The pre-pregnancy weights of the cases were not recorded. It is noteworthy that the average BMI in our entire patient group was high. Body mass index was calculated as ≥25 kg/m² (overweight) in 90% of pregnant women diagnosed with GDM and 67.6% of pregnant women not diagnosed with GDM. The fact that our study was conducted in a tertiary center and the high rate of high-risk pregnancies may partially explain this result. Therefore, our results should not be interpreted as representative of the general population.

In a randomized trial, it was determined that higher acculturation was associated with a lower likelihood of meeting dietary guidelines but a greater likelihood of meeting PA guidelines during pregnancy.[18] Although immigrants were not included in our study, this approach was insufficient to exclude acculturation differences. Physical activity varies during pregnancy. A study that assessed PA using the visual analogue scale (VAS) for each trimester reported that PA decreased by 31% in the first trimester compared with the pre-pregnancy period, increased in the second trimester, and remained at the same level until birth.[19] In our study, gestational age was similar in all groups, and the gestational weeks at which the PPAQ-Tr was applied were comparable, with the majority being in the second trimester.

The examination of quantitative PA in diabetic pregnant women may help to acquire a better understanding of the role of PA throughout treatment and may be useful in more effectively comparing the results of previous studies. It can be considered that there may be differences between healthy pregnant women and those with GDM in terms of daily activities and caloric expenditure. Previous studies on PA in healthy pregnant women or those with GDM have reported varying

Table 2: Comparison of pregnant women with positive and negative diagnostic OGTT in terms of various demographic characteristics and PPAQ-Tr scale scores

	GDM diagnosis test negative (n=188)		GDM diagnosis test positive (n=79)		p
	Mean	±SD	Mean	±SD	
Age (year)[a]	28.9	5.0	32.4	5.5	0.001
Height (cm)[a]	161.9	5.8	160.8	5.2	0.058
Weight (kg)[a]	72.1	12.0	76.7	12.2	0.006
BMI (kg/m²)[a]	27.4	4.3	29.9	4.3	<0.001
Gestational age (weeks)[a]	26.8	3.127.6	4.0		0.103
	Median	IQR (25–75%)	Median	IQR (25–75%)	
Gravidity[b]	2	1–3	3	2–4	0.005
Parity[b]	1	0–1	1	0–2	0.287
Total activity of all questions[b]	146.2	102.5–204.0	136.3	93.9–187.6	0.265
Total activity of light intensity and above[b]	111.2	67.5–179.4	100.2	59.7–161.6	0.282
Sedentary activity[b]	29.4	14.0–44.8	28.2	7.4–43.4	0.263
Light-intensity activity[b]	97.2	60.0–136.5	85.2	53.6–128.8	0.191
Moderate-intensity activity[b]	11.9	3.5–38.2	15.4	1.6–39.2	0.857
Vigorous-intensity activity[b]	0.1	0.0.6	0.1	0–0.7	0.628
Household/caregiving activity[b]	78.1	42.0–128.0	64.0	32.6–110.2	0.096
Occupational activity[b]	0	0–0	0	0–0	0.769
Sports/exercise activity[b]	0.7	0.2–1.6	0.7	0.2–1.8	0.832
Transportation activity[b]	8.8	3.4–17.4	12.1	3.4–22.6	0.220
Inactivity[b]	30.9	14.9–56.7	28.7	7.4–45.9	0.161

a: Independent Samples t-Test. b: Mann-Whitney U test; GDM: Gestational diabetes mellitus; BMI: Body mass index; IQR: Interquartile range; SD: Standard deviation.

effects across different countries. In a study evaluating different types of PA using the PPAQ in 909 pregnant women in the first trimester, it was reported that sports/exercise and household/caregiving activities in early pregnancy significantly prevented the development of GDM, whereas other PPAQ subgroup dimension scores did not show significant differences.[20] Since the PPAQ evaluates the PA status of the last three months, first-trimester PA was not evaluated in our study. In the subgroup analyses of the groups diagnosed with and without GDM, no difference was found in the PA subgroup scores.

Another study conducted with 653 postpartum women reported that the overall means of PPAQ total and sub-scores were below average, and only the PPAQ sub-score "Vigorous Intensity Activity" was significantly higher among women without GDM than those with GDM. Additionally, PPAQ mean scores showed a significant positive correlation with women's pre-pregnancy BMI and birth weight, and a significant negative association with gestational systolic and diastolic blood pressure.[21]

Increased PA has been reported to improve insulin sensitivity through mechanisms such as anti-inflammatory changes, increased lipolysis, and enhanced fat oxidation.[22] However, it has also been reported that many women do not engage in PA at the currently recommended levels during pregnancy.[23] In a study conducted in Poland, the median PPAQ total activity score in the second trimester was reported as 166.8 MET-hour/week, and the median total activity of light intensity and above score was 143.3 MET-hour/week. A Greek version of the PPAQ translation and cross-cultural adaptation study reported the total activity score as 139.9 MET-hour/week, and the median score of total activity of light intensity and above as 78.4 MET-hour/week. A review including 18 systematic reviews and meta-analyses reported that PA is protective against GDM and that the risk of GDM is 24–38% lower in physically active women. The importance of starting and maintaining aerobic and strength exercises in early pregnancy was also emphasized.[24]

A prospective study conducted with women who had excessive gestational weight gain compared a group of pregnant women with low levels of PA with another group characterized by high levels of PA and high sedentary behavior. As a result, they reported that PA alone is not sufficient if sedentary behaviors accompany it. In fact, it was

Table 3: Comparison of demographic characteristics and PPAQ-Tr scale scores of pregnant women with and without GDM in their previous pregnancy

	No GDM diagnosis in previous pregnancy (n=153)		With GDM diagnosis in previous pregnancy (n=26)		p
	Mean	±SD	Mean	±SD	
Age (year)[a]	30.8	5.3	34.4	4.0	0.003
Height (cm)[a]	161.0	6.2	160.0	5.5	0.442
Weight (kg)[a]	72.9	11.5	78.3	12.2	0.029
BMI (kg/m^2)[a]	28.1	4.4	30.7	4.8	0.009
Gestational age (weeks)[a]	27.0	3.6	25.8	4.6	0.140
	Median	IQR (25–75%)	Median	IQR (25–75%)	
Gravidity[b]	2	2–3	3	2–5	0.025
Parity[b]	1	1–2	1	1–2	0.063
Total activity of all questions[b]	152.2	99.5–222.6	180.0	121.7–250.4	0.182
Total activity of light intensity and above[b]	115.8	71.2–192.3	138.6	93.5–241.4	0.170
Sedentary activity[b]	28.0	14.0–43.8	23.6	4.2–33.0	0.380
Light-intensity activity[b]	98.0	58.7–149.6	122.9	67.6–158.1	0.209
Moderate-intensity activity[b]	16.5	3.9–48.6	30.6	6.1–81.1	0.214
Vigorous-intensity activity[b]	0.1	0.0.6	0.2	0–1.8	0.317
Household/caregiving activity[b]	85.1	45.5–140.1	94.4	53.4–171.8	0.530
Occupational activity[b]	0	0–0.7	0	0–27.6	0.352
Sports/exercise activity[b]	0.6	0.2–1.4	0.6	0.2–2.6	0.389
Transportation activity[b]	8.8	2.1–17.4	15.0	6.4–27.5	0.025
Inactivity[b]	28.0	14.0–46.0	29.4	12.5–42.7	0.697

a: Independent Samples t-Test. b: Mann-Whitney U test; GDM: Gestational diabetes mellitus; BMI: Body mass index; IQR: Intequartile range; SD: Standard deviation.

reported that the risk of GDM increased despite increased PA in the second group. They concluded that reducing sedentary behavior is more effective than increasing PA in women with excessive gestational weight gain.[2] In our study, in a healthy pregnant population without a diagnosis of GDM, the median total activity score was found to be 139.8 MET-hour/week, and the median total activity of light intensity and above score was 111.1 MET-hour/week. PPAQ scores were similar between groups diagnosed with and without GDM. The low activity scores of our entire study population may explain why we could not detect a difference.

This study has several limitations. Although PA was assessed using a questionnaire, the patient's age, educational status, occupation, and socioeconomic level were all substantially related to how the questions were understood and answered—this being the main limitation of questionnaire-based studies. The study was conducted during a specific period of pregnancy, in which physiological changes related to GDM occur, and the diagnosis is determined by objective screening and diagnostic tests. Different results might have been obtained if PA levels had been evaluated in the first or third trimester.

CONCLUSION

This study did not reveal a significant difference between women with positive and negative GDM diagnostic and screening test results in terms of subjective PA scores reflecting the 3 months before GDM screening performed at 24 weeks and later. Pregnant women with positive GDM screening and diagnostic test findings had significantly higher mean age, weight, BMI, and gestational age than pregnant women with negative test results.

Statement

Ethics Committee Approval: The Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee granted approval for this study (date: 14.10.2015, number: 2011-KAEK-25 2015/19-04).

Informed Consent: Informed consent was obtained from all pregnant women. The patients filled out the questionnaire form with their own consent.

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

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Author Contributions: Concept – GAA, HAT, NUT; Design – GAA, HAT, NUT; Resources – GAA, HAT, NUT; Data Collection and/or Processing – HA, NUT; Analysis and/or Interpretation – HA; Literature Search – GAA, HAT, NUT, HA; Writing – GAA, HAT, NUT; Critical Reviews – GAA, HAT, NUT, HA.

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ORIGINAL ARTICLE

Comparison of maternal and perinatal outcomes between early-and late-onset preeclampsia

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ABSTRACT

Objective: Preeclampsia is a major cause of maternal and fetal-neonatal morbidity and mortality worldwide. The timing of onset–whether early (<34 weeks) or late (≥34 weeks)–may influence both maternal and perinatal outcomes. This retrospective study aimed to compare the clinical and perinatal outcomes of early- versus late-onset preeclampsia in singleton pregnancies.

Material and Methods: Medical records of 193 women with singleton pregnancies complicated by preeclampsia were retrospectively analyzed at a tertiary referral center between January 2013 and January 2014. Patients were categorized into early-onset (24–34 weeks) and late-onset (≥34 weeks) groups. Maternal demographic and clinical characteristics, laboratory parameters, obstetric complications, and neonatal outcomes (birth weight, Apgar scores, NICU admission, cord blood pH) were compared.

Results: Early-onset preeclampsia was associated with significantly higher AST, ALT, LDH, proteinuria, hypoalbuminemia, hypoproteinemia, magnesium sulfate therapy, cesarean delivery, oligohydramnios, fetal growth restriction, maternal complications, and NICU admissions. Compared with neonates in the late-onset preeclampsia group, those born to mothers with early-onset disease had significantly lower birth weights, reduced Apgar scores at 1 and 5 minutes, and more acidotic cord blood gases.

Conclusion: Early-onset preeclampsia represents a more severe form of the disease, characterized by higher maternal morbidity and adverse neonatal outcomes. The 34-week threshold appears to be a critical determinant of prognosis, with longer gestation positively influencing neonatal survival and health. Early detection, close monitoring, and timely delivery remain key strategies for improving maternal and perinatal outcomes.

Keywords: Early-onset preeclampsia, late-onset preeclampsia, preeclampsia.

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INTRODUCTION

Preeclampsia is defined as new-onset hypertension and proteinuria or end-organ dysfunction after the 20th week of pregnancy.[1] Preeclampsia occurs in 2–3% of pregnancies.[2] The occurrence of generalized tonic-clonic seizures in a preeclamptic woman, in the absence of other neurological conditions that could cause convulsions, is defined as eclampsia. Each year, more than 4 million women worldwide develop preeclampsia, and eclamptic convulsions occur in about 100,000 of these cases.[3]

Regarding the pathophysiology of preeclampsia, maternal, fetal, and placental factors are involved.[4] Abnormalities in the development of placental vascularization have been identified weeks to months before the onset of the disease, particularly in early pregnancy.[5,6] These abnormalities lead to placental hypoperfusion, hypoxia, and ischemia. Hypoperfusion and ischemia trigger the release of antiangiogenic factors (such as soluble fms-like tyrosine kinase-1 [sFlt-1] and soluble endoglin [sEng]) into the maternal circulation, which can cause widespread endothelial dysfunction. This results in hypertension, proteinuria, and other clinical manifestations of preeclampsia.[7] Although the severity of the disease is primarily influenced by maternal and pregnancy-specific factors, paternal and environmental factors may also play a role.[8]

Preeclampsia is a condition that can cause significant morbidity and mortality for both the mother and the fetus. Despite the marked reduction in maternal mortality in developed countries, it remains one of the leading causes of pregnancy-related deaths.[9] The most effective treatment for improving maternal and fetal prognosis is still the timely termination of pregnancy.

Uteroplacental insufficiency due to vasospasm may endanger fetal life, while cardiovascular, renal, pulmonary, and cerebral complications that develop during eclamptic seizures can threaten maternal life.

In many women, these findings become more prominent, especially after the 34th gestational week (late-onset preeclampsia). Late-onset preeclampsia (LO-PE) (≥34 weeks) is more common than early-onset preeclampsia (EO-PE) (<34 weeks).[10] Approximately 10% of women develop preeclampsia before 34 gestational weeks (EO-PE). Our study aims to compare fetal and maternal outcomes in cases of EO-PE and LO-PE. The study included all cases diagnosed with superimposed preeclampsia, preeclampsia with or without severe features, eclampsia, and HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome.

Women with preeclampsia are at increased risk for life-threatening complications such as placental abruption, acute renal failure, cerebral hemorrhage, hepatic failure or rupture, pulmonary edema, disseminated intravascular coagulation, and eclampsia. Globally, 10–15% of maternal deaths are attributed to preeclampsia.[11] In the United States, preeclampsia is one of the leading causes of maternal mortality.[12–14] Maternal death due to preeclampsia occurs in approximately 1 out of every 10,000 live births.[15,16]

Due to the increased risk of fetal growth restriction and preterm birth in affected pregnancies, fetal and neonatal morbidity and mortality are elevated.[17]

Risk factors:[8] History of preeclampsia in previous pregnancies, nulliparity, family history of preeclampsia, existing medical problems (diabetes, chronic hypertension, antiphospholipid antibodies, body mass index ≥26, chronic kidney disease), multiple pregnancies, advanced maternal age.

The diagnostic criteria according to international guidelines:[18–21]

• Preeclampsia Without Severe Features: Systolic blood pressure detected for the first time after the twentieth week of gestation ≥140 mmHg, diastolic blood pressure ≥90 mmHg, and proteinuria defined as a dipstick result of ≥1+ on a spot urine sample or a protein excretion of ≥300 mg/day in a 24-hour urine collection.

• Preeclampsia With Severe Features: Systolic blood pressure≥160 mmHg and diastolic blood pressure ≥110 mmHg, detected for the first time after the twentieth week of gestation and/or proteinuria, elevated serum creatinine, thrombocytopenia, microangiopathic hemolysis, elevated ALT or AST, persistent headache or other cerebral or visual symptoms, persistent epigastric pain, pulmonary edema, or oliguria.

• Eclampsia: Defined as the occurrence of grand mal seizures in a woman in the absence of other neurological conditions that may cause seizures.

• HELLP Syndrome: Hemolysis, elevation in liver function tests, and thrombocytopenia.

• Chronic Hypertension: Defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg before the 20th week of pregnancy or lasting longer than the 12th postpartum week.

• Superimposed Preeclampsia: Defined as new-onset proteinuria and/or end-organ damage in a chronically hypertensive woman after the 20th week of pregnancy. The aggravation of hypertension may also characterize the condition during the second half of pregnancy, particularly when acute and resistant, or by the emergence of clinical features indicating severe disease.

• Gestational Hypertension: Defined as hypertension occurring after the 20th week of pregnancy, without signs and symptoms of preeclampsia and proteinuria. Hypertension is expected to resolve by the 12th postpartum week.

Post-diagnostic laboratory/imaging evaluations should include:

1. Complete blood count
2. Serum creatinine
3. Serum AST (aspartate aminotransferase) and ALT (alanine aminotransferase) levels
4. Obstetric ultrasound (estimated fetal weight, amniotic fluid volume)
5. Fetal evaluation (fetal biophysical profile or non-stress test)

MATERIAL AND METHODS

This study was carried out by retrospectively examining the files of 193 pregnant women diagnosed with preeclampsia who gave birth in a single tertiary center between January 2013 and January 2014 to compare their maternal and perinatal outcomes, with the approval of the ethics committee. The study was conducted in accordance

with the principles of the Declaration of Helsinki. Approval was obtained from the İstanbul Kartal Research Hospital (approval No: 89513307/1009/416-24, date: 10.02.2015). Informed consent was obtained from all participants.

Pregnant women with a single live fetus diagnosed with preeclampsia were included in the study. The results were compared before and after 34 weeks (EO-PE and LO-PE). Cases of preeclampsia with or without severe features, superimposed preeclampsia, eclampsia, and HELLP syndrome were included in both groups. Multiple pregnancies and in-utero fetal loss were excluded from the study.

Blood pressure measurements for diagnosis were recorded when the patient was found to have elevated values at least twice, at an interval of 6 hours, while resting.

Each patient was evaluated according to demographic and clinical characteristics, including maternal age, parity, gestational age at diagnosis, and type of hypertensive disorder (preeclampsia with or without severe features, eclampsia, HELLP syndrome, or superimposed preeclampsia). Obstetric outcomes, including mode of delivery, indications for cesarean delivery, and administration of magnesium sulfate therapy, were recorded. The presence of concomitant medical conditions (chronic hypertension, diabetes mellitus, pulmonary disease, thyroid disorders, cardiac disease, deep vein thrombosis, gastritis/gastroesophageal reflux, renal disease, or cholelithiasis) was also documented.

Laboratory investigations included hemoglobin concentration, platelet count, liver function tests (AST, ALT), renal function markers (uric acid, BUN, creatinine), and proteinuria assessment (proteinuria assessed by dipstick testing in spot urine samples and quantified by 24-hour urinary protein excretion), along with albumin and total protein levels.

Fetal and maternal complications were analyzed, including fetal growth restriction, oligohydramnios, and maternal morbidities such as blood transfusion requirement, eclampsia, HELLP syndrome, placental abruption, pulmonary embolism, and uterine rupture. Neonatal outcomes were assessed by birth weight, 1- and 5-minute Apgar scores, need for neonatal intensive care unit (NICU) admission, and umbilical cord blood pH values.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 16.0). Categorical parameters were presented with frequency and percentage tables. Normality testing was performed to determine whether parametric or non-parametric tests would be used in comparison tests (for parameters where mean values were analyzed). The Kolmogorov-Smirnov test (Shapiro-Wilk when the sample size was below 50) was used for normality testing.

If the p-value obtained in the Kolmogorov-Smirnov test was greater than 0.05 in all subgroups, the distribution was considered normal, indicating no excessive deviation from normality. In cases where the normality assumption was not met, non-parametric tests (Mann-Whitney-U, Kruskal-Wallis, etc.) were used as an alternative to parametric tests (t-test, analysis of variance, etc.).

In the normality test, two independent sample t-tests were used to compare normally distributed dependent variables according to independent variables with two subgroups. The Mann-Whitney-U test was used to compare dependent variables without normal distribution according to independent variables with two subgroups. The Chi-square test was used to compare categorical variables. The significance level was determined as $p<0.05$.

RESULTS

The mean maternal age of the EO-PE group (30.36±7.54) and the LO-PE group (30.34±6.47) did not differ significantly.

<36.1% of the EO-PE group were primiparous and 63.9% were multiparous. >35.7% of the LO-PE group were primiparous and 64.3% were multiparous. There was no statistically significant difference in parity between the two groups.

In the EO-PE group, among those with comorbidities, 5.6% had hypertension, 2.8% hyperlipidemia and lung disease, 5.6% hyperlipidemia and diabetes, 2.8% goiter and kidney disease, 2.8% hyperlipidemia and goiter, 2.8% diabetes, and 2.8% deep vein thrombosis. In the LO-PE group, among those with comorbidities, 5.1% had hypertension, 1.9% hyperlipidemia and diabetes, 0.6% goiter and kidney disease, 1.3% hyperlipidemia and goiter, 0.6% hyperlipidemia and kidney disease, 0.6% diabetes and lung disease, 0.6% hyperlipidemia and diabetes and lung disease, 1.3% diabetes and goiter, 8.3% diabetes, 1.9% cardiac disease, 4.5% goiter, 1.3% lung disease, and 0.6% renal disease.

<83.3% of the EO-PE group did not have preeclampsia in their previous pregnancy, and 16.7% had preeclampsia. >89.8% of the LO-PE group did not have preeclampsia in their previous pregnancy, and 10.2% had preeclampsia. There was no statistically significant difference in the history of preeclampsia between the two groups.

Among all women included in the study, 40.4% had preeclampsia without severe features, 49.7% had preeclampsia with severe features, 2.1% had eclampsia, 5.2% had HELLP syndrome, and 2.6% had superimposed preeclampsia. In the EO-PE group, 5.6% had preeclampsia without severe features, 72.2% had preeclampsia with severe features, 5.6% had eclampsia, and 16.7% had HELLP syndrome. In the LO-PE group, 48.4% had preeclampsia without severe features, 44.6% had preeclampsia with severe features, 1.3% had eclampsia, 2.5% had HELLP syndrome, and 3.2% had superimposed preeclampsia.

As shown in Table 1, uric acid and creatinine levels did not differ significantly between the two groups. Proteinuria assessed by dipstick testing of spot urine samples and quantified as total protein excretion (mg/day) in 24-hour urine collections, blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) levels were significantly elevated in EO-PE. In contrast, the 1st and 5th minute Apgar scores, umbilical cord blood pH, and birth weight were significantly higher in LO-PE. No significant differences were found between EO-PE and LO-PE for maternal hemoglobin levels, platelet counts, albumin concentrations, and total protein levels.

According to Table 2, comorbidity rates did not differ significantly between the EO-PE (27.8%) and LO-PE (29.9%) groups. Magnesium sulfate use was significantly higher in the EO-PE group (30.6%) compared to the LO-PE group (7%).

Table 1: Comparison of parameters EO-PE and LO-PE- Mann-Whitney U Test results

Parameters	EO-PE			LO-PE			U	p
	n		SD	n		SD		
Uric acid	36	5.59	1.73	157	5.25	1.35	2661.00	0.584
Spot urine protein excretion- dipstick	36	**2.39**	1.20	156	1.67	1.21	1914.00	**0.002**
24 hours urine protein excretion (miligrams/24 hours)	17	**3973.4**	3961.5	46	2302.1	3765.3	248.00	**0.027**
Blood creatinine	36	0.64	0.18	157	0.65	0.37	2542.50	0.348
BUN	36	**12.19**	5.14	157	9.60	5.08	1850.00	**0.001**
ALT	36	**25.33**	29.59	157	18.22	23.80	2072.00	**0.012**
AST	36	**33.78**	33.49	157	28.36	40.05	2184.00	**0.033**
LDH	36	**527.00**	249.34	156	449.88	314.50	2140.00	**0.026**
Apgar score1	36	5.67	2.65	157	**8.46**	0.94	896.00	**0.000**
Apgar score5	36	7.78	2.10	157	**9.64**	0.66	1032.00	**0.000**
Cord blood-pH	36	7.27	0.10	157	**7.36**	0.15	1182.00	**0.000**

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; EO-PE: Early-onset preeclampsia; LDH: Lactate dehydrogenase; LO-PE: Late-onset preeclampsia; n: Number; p: p-value; SD: Standard deviation; U: Mann–Whitney U Test.

Table 2: Chi-Square Analysis Results of Comparison of EO-PE and LO-PE according to their comorbidity status

Gestational age	Additional medical conditions				Total	χ^2	p
	No		Yes				
	n	%	n	%			
EO-PE	26	72.2	10	27.8	36	0.066	0.798
LO-PE	110	70.1	47	29.9	157		
Total	136	70.5	57	29.5	193		

EO-PE: Early-onset preeclampsia; LO-PE: Late-onset preeclampsia; n: Number; p: p-value; %: Percentage; χ^2: Chi-Square Test.

In the EO-PE group, 5.6% delivered vaginally and 94.4% by cesarean section, whereas in the LO-PE group, 25.5% delivered vaginally and 74.5% by cesarean section. The rate of cesarean delivery was significantly higher in EO-PE compared to LO-PE.

According to Table 3, fetal growth restriction was significantly more frequent in the EO-PE group (80.6%) compared with the LO-PE group (36.3%).

According to Table 4, there was no significant difference between the two groups in terms of oligohydramnios.

According to Table 5, all neonates in the EO-PE group required NICU admission, whereas only 23.6% of the LO-PE group did ($p<0.001$). Maternal complications were more diverse and frequent in EO-PE, including blood transfusion (2.8%), eclampsia crisis (2.8%), placental abruption (5.6%), eclampsia (2.8%), HELLP syndrome (11.1%), pulmonary embolism (2.8%), and uterine rupture (2.8%). In the LO-PE group, complications included blood transfusion (3.2%), placental abruption (0.6%), eclampsia (1.3%), and HELLP syndrome (1.9%).

DISCUSSION

This study analyzed demographic and clinical variables in women with preeclampsia, focusing on whether maternal and neonatal outcomes varied significantly when 34 weeks of gestation was applied as the dividing line between early- and late-onset disease. Overall, our findings suggest that 34 weeks represents a critical threshold for maternal well-being, whereas for the fetus, each additional week of gestation is associated with a more favorable prognosis.

Particularly in cases of severe preeclampsia and HELLP syndrome, elevations in AST, ALT, and LDH levels are well recognized. In our study, these parameters were found to be significantly different between early- and late-onset preeclampsia,

Table 3: Chi-Square Analysis Results of Comparison EO-PE and LO-PE According to Fetal Growth Retardation Status

Gestational age	No		Yes		Total	χ^2	p
	n	%	n	%			
EO-PE	7	19.4	29	80.6	36	23.211	**0.000**
LO-PE	100	63.7	57	36.3	157		
Total	107	55.4	86	44.6	193		

EO-PE: Early-onset preeclampsia; LO-PE: Late-onset preeclampsia; n: Number; p: p-value; %: Percentage; χ^2: Chi-Square Test.

Table 4: Chi-Square analysis results of comparison of EO-PE and LO-PE according to oligohydramniosis status

Gestational age	Oligohidramniosis				Total	χ^2	p
	No		Yes				
	n	%	n	%			
EO-PE	19	52.8	17	47.2	36	2.297	0.130
LO-PE	104	66.2	53	33.8	157		
Total	123	63.7	70	36.3	193		

EO-PE: Early-onset preeclampsia; LO-PE: Late-onset preeclampsia; n: Number; p: p-value; %: Percentage; χ^2: Chi-Square Test.

Table 5: Chi-Square analysis results of comparison of EO-PE and LO-PE according to the NICU admission

Gestational age	No		Yes		Total	χ^2	p
	n	%	n	%			
EO-PE	0	0.0	36	100.0	36	72.748	**0.000**
LO-PE	120	76.4	37	23.6	157		
Total	120	62.2	73	37.8	193		

NICU: Neonatal intensive care unit; EO-PE: Early-onset preeclampsia; LO-PE: Late-onset preeclampsia; n: Number; p: p-value; %: Percentage; χ^2: Chi-Square Test.

with higher values observed in the early-onset group. These results suggest that early-onset preeclampsia (EO-PE) is associated with a more severe clinical course than late-onset preeclampsia (LO-PE).

The frequency of magnesium sulfate use for the prevention of eclampsia was markedly higher among patients with EO-PE, consistent with its association with more severe disease.

The rate of admission to neonatal intensive care units was greater among newborns from the EO-PE group. This is an expected finding, given that EO-PE is generally associated with a more severe disease course, a higher incidence of fetal growth restriction causing fetal stress, and preterm delivery performed due to maternal or fetal indications.

The increased frequency of cesarean delivery in the EO-PE group may be explained by multiple factors, including the lower birth weight of premature neonates—prompting cesarean section to reduce the risk of birth trauma–and the frequent absence of sufficient cervical ripening in cases requiring urgent delivery.[22]

Neonatal birth weight and the 1st and 5th minute Apgar scores were also lower in the EO-PE group. Cord blood samples obtained from the umbilical vein demonstrated that infants of mothers with EO-PE were more acidotic at birth.

One of the earliest responses to impaired fetal nutrition is the development of oligohydramnios. Prolonged and more severe nutritional compromise may subsequently lead to fetal growth restriction (FGR). In our study, no significant difference was observed between EO-PE and LO-PE in terms of oligohydramnios; however, FGR was found to be more frequent in the early-onset group.

In EO-PE, both the earlier onset of the disease and its more severe course contributed to oligohydramnios and FGR. In LO-PE, the later onset and the relatively short interval between disease onset

and delivery likely limited the duration of fetal exposure to stress. As a result, although amniotic fluid volume was affected, it did not progress to FGR.

The presence or absence of additional medical conditions did not appear to make a significant difference. This may be explained by the relatively young mean age of the study population, the generally low prevalence of chronic diseases, and the likelihood that any existing chronic conditions in these patients were well controlled under medical follow-up.

Greater disease severity is associated with an increased risk of additional complications.[23] Accordingly, in the EO-PE group—where the disease follows a more severe course—the probability of developing further complications is understandably higher. Conditions such as anemia requiring blood transfusion, placental abruption, eclampsia, and HELLP syndrome were observed more frequently in the EO-PE group.

An increase in serum uric acid has been suggested as a potential marker for predicting preeclampsia. In our study, higher uric acid levels were associated with increased proteinuria, hypoalbuminemia, and elevated creatinine, reflecting renal involvement. However, previous reports suggest that hyperuricemia alone may not be a reliable predictor.[23,24]

Our findings demonstrated that greater protein loss in spot urine or 24-hour collections was linked to higher BUN, creatinine, AST, and ALT values, in addition to reductions in serum albumin, total protein, Apgar scores at both 1 and 5 minutes, and infant birth weight. This supports the concept that the magnitude of proteinuria may be indicative of preeclampsia severity.

A 2014 U.S. study of 670,120 singleton deliveries reported severe maternal morbidity in 15.5% of EO-PE and 12% of LO-PE, with higher rates of cardiovascular, renal, hepatic, and transfusion-related complications in EO-PE.[10] Consistent with this, our study also found increased blood transfusion requirements, elevated liver enzymes, and hypoproteinemia in EO-PE. However, no maternal deaths were observed, likely due to the smaller sample size. Elevated liver function tests and hypoproteinemia were more frequently observed in the EO-PE group.

A 2009 Korean study of 212 patients, using 32 weeks as the cutoff, reported higher rates of severe preeclampsia, elevated liver enzymes, pulmonary edema, fetal death, lower Apgar scores, and increased perinatal mortality in EO-PE.[25] Similarly, in our study using 34 weeks as the cutoff, no differences were observed regarding maternal age, parity, or preeclampsia history, but EO-PE was associated with greater proteinuria, more severe disease, and lower Apgar scores.

A 2013 U.S. study of 456,668 pregnancies reported a preeclampsia prevalence of 3.1%, with EO-PE at 0.38% and LO-PE at 2.72%. EO-PE was associated with African-American ethnicity, chronic hypertension, and congenital anomalies, while LO-PE was more common in younger, nulliparous, and diabetic women.[26] Perinatal death or severe neonatal morbidity occurred in 16.4% of EO-PE versus 2% of LO-PE. In our study, maternal age and parity did not differ between groups. Although comprehensive data on neonatal morbidity were unavailable, neonates born to mothers with EO-PE had significantly lower birth weights and Apgar scores, as well as more acidotic umbilical cord blood gases.

In a study conducted in Türkiye in 2014, preeclamptic patients were divided into early- and late-onset groups using 34 weeks as the cutoff, and maternal-fetal morbidity and mortality were compared, incorporating uterine artery Doppler values as well.[27] Similar to our findings, perinatal outcomes were reported to be worse in the early-onset group. Additionally, impaired uterine artery Doppler values were identified in EO-PE, supporting the conclusion that abnormal placentation is the primary etiological factor in EO-PE.

CONCLUSION

The impact of preeclampsia on maternal and perinatal health is profound, contributing to increased morbidity and mortality. Even in regions where maternal mortality has significantly declined, such as developed countries, preeclampsia continues to be recognized as one of the predominant causes of pregnancy-associated fatal outcomes.

In assessing the severity of preeclampsia, maternal clinical findings and biochemical markers are typically prioritized. Nevertheless, the etiological mechanisms of early-onset and late-onset forms are fundamentally distinct. The pathogenesis of EO-PE is largely driven by abnormal placentation, whereas LO-PE tends to be influenced predominantly by maternal factors.

To conclude, replacing the traditional categorization of preeclampsia based on the presence or absence of severe features with the division into EO-PE and LO-PE appears more suitable for outcome prediction. While early-onset disease carries a higher risk of maternal complications, prolongation of pregnancy has been shown to positively influence neonatal survival and health.

Statement

Ethics Committee Approval: The study was approved by İstanbul Kartal Research Hospital Ethics Committee granted approval for this study (date: 10.02.2015, number: 89513307/1009/416-24).

Informed Consent: Informed consent was obtained from all participants.

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ORIGINAL ARTICLE

The impact of hyperemesis gravidarum on maternal anxiety and depression: A case-control study

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ABSTRACT

Objective: This study aimed to investigate the psychological and biochemical differences between pregnant women diagnosed with hyperemesis gravidarum (HG) and healthy pregnant controls.

Material and Methods: A prospective case-control study was conducted between December 2024 and June 2025 at Sirnak State Hospital. A total of 100 pregnant women under 16 weeks of gestation were included, with 50 diagnosed with HG and 50 healthy controls. Sociodemographic characteristics, routine laboratory parameters (Hb, AST, TSH, etc.), and psychological symptoms were assessed. Psychological evaluation was performed using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Participants with known systemic or psychiatric disorders were excluded.

Results: There were no significant differences between the groups in terms of age, BMI, gravidity, or parity ($p>0.05$). HG patients had significantly lower hemoglobin and TSH levels and higher AST values ($p<0.05$). Depression and anxiety scores were also significantly higher in the HG group compared to controls ($p=0.000$ for both). These findings indicate both physiological and psychological alterations in HG cases.

Conclusion: HG is associated with significant increases in anxiety and depression levels, as well as biochemical disturbances, particularly in hemoglobin, AST, and TSH values. These results suggest that HG may not only be a physical condition but also involve notable psychological distress. Multidisciplinary care, including psychiatric support, should be considered in HG management.

Keywords: Anxiety disorders, depressive disorder, hyperemesis gravidarum, pregnancy complications.

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INTRODUCTION

Pregnancy is a complex period marked by profound physiological changes and significant psychosocial adjustments. Nausea and vomiting of pregnancy (emesis gravidarum) occur in approximately 50–70% of pregnancies.[1] These symptoms are commonly referred to as morning sickness. Symptoms typically begin in the 4th–5th gestational week, peak between weeks 8–12, and resolve by weeks 16–20, although some cases persist throughout gestation. Hyperemesis gravidarum (HG), a more severe and clinically significant variant, affects 1–2% of pregnancies.[2,3] It can cause serious maternal and fetal complications.

Clinically, HG is characterised by persistent, pregnancy-related nausea and vomiting with systemic manifestations such as dehydration, electrolyte disturbances (e.g., hypokalemia, hyponatremia), ketonuria, weight loss exceeding 5%, and occasionally renal or hepatic dysfunction.[4,5] The condition's aetiology is multifactorial, involving hormonal, genetic, environmental, and psychological influences.

Risk factors include high body mass index, young maternal age, multiple or molar pregnancy, primigravidity, previous HG history, comorbidities (e.g., migraine, reflux, gastritis), heightened taste and smell sensitivity, and lack of periconceptional multivitamin use.[2] A family history—especially maternal or sibling HG—substantially increases risk. Female fetal sex is positively associated with HG, whereas smoking and advanced maternal age appear protective.[6] Ethnic differences are notable, with higher prevalence in developed Western and urban populations and lower rates in Africa, Alaska, and Japan.[7]

The pathophysiology remains incompletely understood, though β-hCG is a leading candidate given its temporal correlation with symptom peaks. Other hormones—including estrogen, progesterone, thyroid hormones, leptin, ghrelin, and nesfatin-1—may impair gastrointestinal motility and stimulate central nausea pathways. Gastrointestinal dysmotility, such as reduced lower oesophageal sphincter tone and delayed gastric emptying, is a key mechanism. Helicobacter pylori infection has also been implicated, though causal links remain unclear.

The psychological dimension of HG has gained increasing attention. Studies demonstrate significantly higher rates of depression, anxiety, and personality disorders in women with HG compared to healthy pregnancies.[8–10] Whether these psychiatric symptoms are a cause, a consequence, or both remains unresolved. Eating disorders may exacerbate HG via nutritional deficits, hormonal dysregulation, and pre-existing vomiting behaviours.[11,12]

Although the existing literature extensively addresses the clinical and hormonal aspects of HG, its psychological component remains underexplored. In particular, the bidirectional relationship between HG and mental health disorders lacks a clear definition, limiting the development of integrated care models. This study addresses this gap by systematically examining HG's psychological impact, combining clinical, psychiatric, and behavioural data. Findings aim to inform multidisciplinary approaches, enhance patient outcomes, and shift clinical management toward a comprehensive biopsychosocial framework.

MATERIAL AND METHODS

This prospective case-control study was conducted on pregnant women who visited the Gynaecology and Obstetrics Outpatient Clinic and Emergency Department of Sirnak State Hospital between December 2024 and June 2025. The study included patients who were 18 years of age or older, literate, had no known systemic diseases, were not taking any medications other than vitamins and iron, and had a singleton live pregnancy of less than 16 weeks. Gestational age was determined using the crown-rump length (CRL) measured in the sagittal plane via transabdominal or transvaginal ultrasound.

The 100 patients included in the study were divided into two groups: 50 cases diagnosed with HG and 50 healthy control subjects without nausea and vomiting complaints. The control group consisted of healthy pregnant women who attended routine antenatal visits at the obstetrics outpatient clinic of Sirnak State Hospital between December 2024 and June 2025 and who did not meet any of the exclusion criteria.

Exclusion criteria included being under 18 years of age, illiteracy, known systemic disease or regular medication use, active infection, gestation greater than 16 weeks, absence of fetal heartbeat, multiple pregnancy, and refusal to participate in the study.

Demographic and obstetric information (height, weight, age, gravida, parity, number of abortions), smoking status, marital status, history of nausea and vomiting in previous pregnancies, and hospitalisation status were recorded for all participants. BDI and BAI were also administered. Patients were provided with a suitable and calm environment to fill out the forms on their own; detailed information about the study was provided, and informed consent was obtained. Participation was voluntary, and the confidentiality of personal data was ensured. The study was approved by Sirnak University Ethics Committee (No: E-74546226-050.04-134910, Date: 02.06.2025) and conducted in accordance with the principles of the Declaration of Helsinki.

The educational and employment statuses of the patients included in the study were assessed as homogeneous between the groups.

The patients' routine laboratory tests performed in the first trimester were evaluated, and the following parameters were examined: sodium (Na; 136–145 mEq/L), potassium (K; 3.1–5.1 mEq/L), haemoglobin (Hb; 10.8–15.1 g/dL), haematocrit (Htc; 32.7–45%), aspartate aminotransferase (AST; 0–35 U/L), alanine aminotransferase (ALT; 0–45 U/L), thyroid-stimulating hormone (TSH; 0.57–5.6 μIU/mL), and the presence of ketones in urine (graded from 0 to +3).

The diagnosis of hyperemesis gravidarum was based on the patient's inability to tolerate food and drink, a weight loss of at least 5%, signs of dehydration on physical examination, and the presence of pathological values in laboratory tests.

Statistical Analysis

Statistical analyses were performed using the SPSS for Windows version 26.0 program. Continuous variables were reported as mean±standard deviation (SD). Categorical variables were reported as numbers and percentages. The variables showed a normal distribution ($p>0.05$), so an unpaired t-test and Pearson's chi-square test were

used to compare the continuous and categorical variables between the groups. A value of p<0.05 was considered statistically significant.

RESULTS

A total of 100 participants, equally divided into patient and control groups (n=50 each), were evaluated for sociodemographic characteristics, laboratory findings, and psychiatric symptomatology. No statistically significant differences were found between the groups in terms of age (patients: 28.9±4.9 years; controls: 27.5±4.4 years, p=0.144), gravidity (median 2 vs. 2, p=0.285), parity (median 1 vs. 1, p=0.648), body mass index (25.2±3.1 vs. 25.2±3.3 kg/m², p=0.755), or gestational age (median 11 vs. 11 weeks, p=0.651), indicating demographic comparability between groups (Table 1).

Regarding laboratory parameters, hemoglobin levels were significantly lower in the patient group compared to controls (11.06±2.21 vs. 12.26±1.24 g/dL, p=0.021). Although hematocrit values were slightly reduced in patients (35.9±3.1% vs. 36.9±3.1%), the difference did not reach statistical significance (p=0.073). Aspartate aminotransferase (AST) levels were significantly higher in the patient group (29.8±3.3 vs. 21.7±1.1 U/L, p=0.005), whereas alanine aminotransferase (ALT) levels showed a non-significant trend toward elevation in patients (27.1±2.7 vs. 20.2±1.7 U/L, p=0.100). No meaningful differences were detected in sodium (136.6±2.6 vs. 133.8±19.0 mmol/L, p=0.702) or potassium levels (4.0±0.5 vs. 4.7±0.9 mmol/L, p=0.933). By contrast, thyroid-stimulating hormone (TSH) concentrations were markedly lower in patients (0.97±0.81 μIU/mL) compared to controls (1.64±0.92 μIU/mL, p=0.000), highlighting significant endocrine alterations (Table 2).

Psychological assessment revealed striking differences between the groups. Median Beck Depression Inventory (BDI) scores were significantly higher in patients than in controls (19.92 vs. 8.76, p=0.000). Similarly, Beck Anxiety Inventory (BAI) scores were elevated in patients (18.16 vs. 11.06, p=0.000), indicating a substantial psychological burden associated with the clinical condition (Table 3).

In summary, although the two groups were demographically comparable, patients displayed significant hematological (reduced Hb), hepatic (elevated AST, trend in ALT), endocrine (lower TSH), and psychological (higher BDI and BAI) abnormalities, suggesting that these parameters may be closely related to the pathophysiology of the disorder.

Table 1: Sociodemographic characteristics of patient and control groups

Variable	Control group	Patient group	p
Age (mean±SD)	27.46±4.35	28.90±4.90	0.144
Gravida (median)	2.00	2.00	0.285
Parity (median)	1.00	1.00	0.648
BMI (kg/m²), (mean±SD)	25.23±3.28	25.23±3.10	0.755
GA (weeks) (median)	11.00	11.00	0.651

BMI: Body Mass Index; GA: Gestational age.

Table 2: Laboratory parameters of patient and control groups

Variable	Control group (Mean±SD)	Patient group (Mean±SD)	p
HB (g/dL)	12.26±1.24	11.06±2.21	0.021
HTC (%)	36.87±3.10	35.93±3.09	0.073
AST (U/L)	21.72±1.13	29.80±3.27	0.005
ALT (U/L)	20.20±1.65	27.14±2.74	0.100
K (mmol/L)	4.68±0.95	3.98±0.51	0.933
Na (mmol/L)	133.77±18.96	136.59±2.56	0.702
TSH (μIU/mL)	1.64±0.92	0.97±0.81	0.000

HB: Hemoglobin; HTC: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; K: Potassium; Na: Sodium; TSH: Thyroid stimulating hormone.

Table 3: Depression and anxiety scores of patient and control groups

Variable	Control group (Median)	Patient group (Median)	p
Beck depression score	8.76	19.92	0.000
Beck anxiety score	11.06	18.16	0.000

DISCUSSION

Nausea and vomiting of pregnancy (NVP) are common symptoms affecting up to 70% of pregnant women, typically emerging around the 4th or 5th gestational week, peaking between the 8th and 12th weeks, and generally subsiding by the 16th to 20h week. However, in approximately 1–2% of cases, symptoms progress to HG, a severe form of NVP that can lead to significant maternal morbidity and even hospitalization.[2,3] Diagnostic criteria for HG remain variable, with clinical judgment guided by signs of dehydration, electrolyte imbalances, ketonuria, significant weight loss, and, in severe cases, hepatic or renal dysfunction. HG is increasingly recognized as a multifactorial condition involving both biological and psychosocial contributors.

Our study adds to the growing body of literature supporting the role of psychological distress in the pathophysiology of HG. We observed significantly higher levels of anxiety and depression in patients diagnosed with HG compared to healthy pregnant controls, as measured by BAI and BDI. These findings mirror previous studies showing elevated psychometric scores among HG patients.[13] For instance, a study by Simşek et al.[13] evaluating 41 HG patients and 45 healthy controls using the same instruments demonstrated similar results, reinforcing the association between severe NVP and increased psychological burden.

In addition to psychometric assessments, our study also identified notable laboratory differences between groups. Specifically, patients with HG had significantly lower hemoglobin levels and elevated AST values, as well as reduced TSH concentrations compared to the control group. These findings suggest that HG is not only associated with psychological alterations but also reflects systemic physiological stress. In contrast, some studies, such as the one by Özen et al.,[14] did not report significant laboratory discrepancies except for serum potassium levels. Our results expand on those findings by highlighting a broader range of physiological abnormalities in HG patients, possibly mediated by malnutrition, dehydration, and endocrine disruption.

Consistent with our findings, previous literature suggests that HG may be more prevalent among women with underlying personality traits or psychiatric vulnerabilities, including histrionic, depressive, or anxious dispositions. Several studies have proposed that HG may be a psychosomatic response to familial or environmental stressors, with some women demonstrating improvement upon removal from triggering home environments.[15] Simpson et al.[16] also noted that women with HG exhibited higher levels of depressive, hypochondriacal, and hysterical personality traits during pregnancy, although these symptoms did not persist postpartum.

Notably, our inclusion criteria excluded participants with a prior history of psychiatric illness, which minimizes the confounding influence of preexisting mental health disorders. This methodological decision supports the interpretation that elevated anxiety and depression levels observed in our HG group likely emerged as a consequence of the clinical condition itself rather than as a predisposing factor. This view aligns with the conclusions of Tan et al.,[9] who suggested that psychological symptoms in HG may be reactive rather than etiologic.

However, the causal relationship between HG and psychiatric symptoms remains contentious. Some prospective studies, such as that by Annagür et al.,[10] have reported that a significant proportion of HG patients experienced psychiatric symptoms before pregnancy, suggesting a bidirectional or predisposing model. Conversely, Bozzo et al.[17] found no significant difference in the incidence of NVP between women with and without pre-pregnancy depression who were receiving antidepressant treatment, further complicating the etiological narrative.

Our findings support the theory that anxiety and depression may be consequences of the distressing physical symptoms of HG, including persistent nausea, weight loss, fatigue, and functional impairment. The observed alterations in TSH levels among HG patients may also hint at an underlying neuroendocrine mechanism contributing to mood dysregulation during pregnancy. Although thyroid function abnormalities are not universally reported in HG, our data suggest they may be more prevalent than previously recognized and potentially relevant to the psychological state of affected women.

Despite the consistent association between HG and psychological symptoms, the literature still lacks a unified model explaining their interplay. Poursharif et al.[18] highlighted that psychological distress can persist beyond the resolution of HG symptoms, suggesting longer-term impacts on mental health. However, as our study did not include postpartum follow-up, we were unable to assess the longitudinal course of psychiatric symptoms in HG patients. Future studies with extended follow-up periods are warranted to explore whether the emotional sequelae of HG resolve with the improvement of physical symptoms or represent a more persistent psychiatric risk.

Our findings underscore the need for a multidisciplinary approach to managing HG. Beyond standard medical interventions targeting dehydration and metabolic disturbances, the routine assessment of psychological well-being should be considered in HG care protocols. Women presenting with HG symptoms should be screened not only with laboratory workups but also with validated tools such as the BDI and BAI to identify those in need of psychological support. Early identification and intervention may prevent the worsening of psychiatric symptoms and improve overall maternal outcomes.

In conclusion, our study contributes to the existing evidence that HG is associated with both physiological disruptions and significant psychological distress. The correlation between higher anxiety and depression scores and altered lab parameters suggests that HG is a multifaceted condition requiring integrated obstetric and mental health management. While the direction of causality remains unclear, the clinical implications are evident: addressing the mental health of pregnant women with HG is essential for comprehensive and compassionate care.

Study Limitations

The present study has certain limitations. The relatively small sample size, single-centre design, and lack of longitudinal follow-up may limit the generalizability of the findings and preclude conclusions about the persistence of psychological symptoms beyond pregnancy. Future multi-centre studies with larger cohorts and extended follow-up periods are warranted to validate and expand upon these results.

CONCLUSION

This study highlights the multifactorial nature of hyperemesis gravidarum (HG), demonstrating its association with both physiological disturbances and significant psychological distress. Patients with HG exhibited markedly higher anxiety and depression scores compared to healthy pregnant controls, along with notable laboratory abnormalities such as reduced hemoglobin and TSH levels and elevated AST values. While the causal direction between HG and psychiatric symptoms remains debated, the exclusion of participants with preexisting psychiatric conditions supports the interpretation that these symptoms may develop as a consequence of HG.

From a clinical perspective, these findings underscore the importance of a multidisciplinary management approach that addresses both physical and psychological aspects of care. Routine psychological screening—using validated tools such as the BDI and BAI—should be integrated into the clinical evaluation of women presenting with HG, alongside standard obstetric and laboratory assessments. Early identification and appropriate psychiatric support have the potential to improve maternal well-being, enhance treatment adherence, and optimize pregnancy outcomes. Future longitudinal and multi-centre studies are warranted to determine the persistence of psychological symptoms postpartum and to refine comprehensive care protocols for HG.

Statement

Ethics Committee Approval: The Sirnak University Clinical Research Ethics Committee granted approval for this study (date: 02.06.2025, number: E-74546226-050.04-134910).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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ORIGINAL ARTICLE

The effects of vaginitis on genital hygiene: A comparative descriptive cross-sectional study

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ABSTRACT

Objective: This study aimed to determine the genital hygiene behaviors of women with and without vaginitis, as well as the factors influencing these behaviors.

Material and Methods: This comparative descriptive cross-sectional study was conducted between October 2023 and February 2024 with a total of 188 women–94 diagnosed with vaginitis and 94 without a diagnosis of vaginitis—who attended the Gynecology Outpatient Clinic. Data were collected through face-to-face interviews using the Descriptive Information Form and the Genital Hygiene Behavior Scale. Ethics committee approval, institutional authorization, and written consent from all participants were obtained.

Results: The numbers of pregnancies, deliveries, miscarriages, and curettages were higher in women with vaginitis compared to those without vaginitis ($p<0.05$). Women without vaginitis had significantly greater knowledge about genital tract infections ($p<0.05$). Women with vaginitis scored significantly lower on the menstrual hygiene subscale of the Genital Hygiene Behavior Scale compared to those without vaginitis ($p<0.05$). In the multivariate analysis, age, duration of menstruation, and frequency of sexual intercourse were identified as determinant factors for genital hygiene behaviors in women with vaginitis.

Conclusion: This study shows that women, both with and without vaginitis, exhibit high genital hygiene behaviors. However, significant differences were observed between the two groups, with women without vaginitis demonstrating better hygiene practices.

Keywords: Genital hygiene, vaginitis, women.

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INTRODUCTION

The age period of 15–49, considered the reproductive years for women, is a time when reproductive issues and health problems are most prominent.[1] Vaginitis is one of the most common health issues among women, caused by the colonization of microorganisms from the external environment in the reproductive organs or the spread of an existing infection.[1] The estimated prevalence ranges from 5% to 70% in both developed and developing countries.[2–6] This widespread health issue represents a significant burden on both individual and societal health.[7]

Vaginitis, characterized by dysfunction of the vaginal flora, commonly presents with increased discharge and itching caused by vaginal irritation from the discharge.[7] Many factors contribute to the development of genital infections, including lack of education, low socioeconomic status, a high number of children, inadequate perineal and menstrual hygiene, not washing hands before and after using the toilet, vaginal douching, wearing inappropriate underwear, infrequent changes of vaginal tampons, unsafe sexual practices, polygamy, smoking, alcohol use, and performing abortions or curettages under unhealthy conditions.[8–10] However, the primary cause of infection is inadequate genital hygiene.[11] Therefore, genital hygiene is an important element in preserving women's reproductive health.[12]

Ensuring genital hygiene is one of the most important steps in preventing genital infections. Genital hygiene practices encompass all behaviors related to the removal of waste products from urine, stool, and menstruation.[13] Proper and thorough personal and genital hygiene is essential to protect the genital area from infections.[10] Inadequate and poor genital hygiene behaviors are known to increase the risk of infection.[8,9] Therefore, genital hygiene behaviors are the most important method for preventing vaginal infections and avoiding more serious consequences (such as cervicitis, endometritis, and PID) that may result from these infections.[11]

Accordingly, since lack of genital hygiene is recognized as one of the primary causes of vaginitis, this study was designed to determine the genital hygiene behaviors of women with and without vaginitis, as well as the factors influencing them.

- Is there a significant difference in genital hygiene behaviors between women with and without vaginitis?
- What are the factors influencing genital hygiene behaviors of women with and without vaginitis?
- How are the genital hygiene behaviors of women with and without vaginitis?

MATERIAL AND METHODS

This comparative descriptive cross-sectional study was conducted between October 2023 and February 2024 with women who applied to the Gynecology Outpatient Clinic of a public hospital. A sample size calculation was performed based on a known population size, which was determined to be 1,268 women. The sample size was calculated considering a 95% confidence interval and a 5% margin of error. Accordingly, a total of 188 women were included in the study, consisting of 94 women diagnosed with vaginitis and 94 healthy women without vaginitis. The participants were aged between 18 and 49, spoke and understood Turkish, had no communication barriers, and were willing to participate in the study.

The data were collected by the researchers through face-to-face interviews. In the study, the data were obtained using the Descriptive Information Form and the Genital Hygiene Behaviors Scale (GHBS).

Descriptive Information Form

Through a review of the relevant literature, the researchers developed a set of 33 questions covering women's sociodemographic characteristics (such as age, education level, employment status, income level, chronic diseases, smoking and alcohol use, etc.), obstetric features (number of pregnancies, number of abortions and miscarriages, number of births, delivery type), menstrual and gynecological characteristics (menstrual duration, frequency, daily pad usage, history of gynecological examinations, reproductive tract infection history, frequency of sexual intercourse, use of contraception, etc.), and genital hygiene behaviors (genital area hygiene, bathing habits, vaginal douching, etc.).[11,13–15]

Genital Hygiene Behaviors Scale (GHBS)

The scale was developed by Karahan in 2017 and consists of three sub-dimensions and 23 items. The sub-dimensions of the scale are "General Hygiene Habits" (items 1–12), "Menstrual Hygiene" (items 13–20), and "Awareness of Abnormal Findings" (items 21–23). The scale is a five-point Likert scale with a minimum score of 23 and a maximum score of 115. High scores indicate positive genital hygiene behavior. The Cronbach's alpha value of the scale was determined as 0.80.[12] In this study, the Cronbach's alpha value of the scale was calculated as 0.88.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were used. The normal distribution of the data was assessed using the Shapiro–Wilk test. To compare independent groups, Student's t-test and Mann–Whitney U test were applied, and the Chi-square test was used for analyzing categorical data. Linear regression analysis was employed to identify factors that may influence women's genital hygiene behaviors. In this study, $p<0.05$ was considered statistically significant.

Ethical Consideration

Ethics committee approval (10.25.2023/142) and institutional study authorization (251137893) were obtained from the ethics committee of the hospital where the study was conducted, in accordance with the Declaration of Helsinki. Women who agreed to participate in the study were provided with information about the study's purpose, and their written and verbal informed consent was obtained.

RESULTS

It was determined that the ages of women with and without vaginitis were similar. No statistically significant differences were

Table 1: Individual and obstetric characteristics of participants

Characteristics	Group with vaginitis (n=94)		Group without vaginitis (n=94)		t	p
	Mean±SD		Mean±SD			
Age	33.07±7.19		32.35±5.88		0.755	0.451
Number of pregnancies*	2..66±1.23		1.62±0.96		**6.485**	**0.000**
Number of miscarriages*	1.99±0.46		1.78±0.32		**3.282**	**0.001**
Number of curettage*	1.90±0.29		1.73±0.44		**3.092**	**0.002**
Number of births*	2.09±0.95		1.60±0.87		**2.312**	**0.023**
	n	%	n	%	χ^2	p
Education level						
<8 years	31	33.0	34	36.2	0.282	0.645
>8+ years	63	67.0	60	63.8		
Marital status						
Married	73	77.7	66	70.2	1.356	0.244*
Single	21	22.3	28	29.8		
Employment status						
Working	43	45.7	61	64.9	2.345	0.619
Not working	51	55.3	33	35.1		
Income level						
Income less than expenditure	23	24.5	18	19.2		
Income matches expenditure	46	47.5	49	51.1	0.781	0.677
Income more than expenditure	25	26.0	27	28.7		
Chronic disease status						
Yes	17	18.1	17	17.0	0.037	0.848*
No	77	81.9	78	83.0		
Smoking status						
Yes	41	43.6	33	35.1	1.426	0.232
No	53	56.4	61	64.9		
Alcohol use status						
Yes	30	31.9	25	26.6	0.643	0.423
No	64	68.1	69	73.4		
Mode of delivery**						
Vaginal delivery	36	58.1	13	44.8	0.911	0.340*
Caesarean section	26	41.9	16	55.2		

SD: Standard deviation; t: Student's t-Test; χ^2: Chi-Square analysis; *: Yates Corrected Chi-Square; **: Only women with a history of pregnancy were included.

found between women with and without vaginitis in terms of education level, marital status, income level, employment status, chronic disease status, smoking, and alcohol use (p>0.05). When evaluating the obstetric characteristics of the participants, it was found that the number of pregnancies, deliveries, miscarriages, and curettages was significantly higher in women with vaginitis compared to those without vaginitis (p<0.05) (Table 1).

In the study, there was no significant difference between women with and without vaginitis in terms of mean menstrual duration and frequency of sexual intercourse; however, there was a statistically significant difference between the two groups in terms of gynecological examination, history of continuous discharge in husband/partner, and knowledge of genital infection (p<0.05). Women with vaginitis were more likely to undergo gynecological examination and to have

Table 2: Participant's menstrual and genital hygiene characteristics

Characteristics	Group with vaginitis (n=94)		Group without vaginitis (n=94)		t	p
	Mean±SD		Mean±SD			
Duration of menstruation (days)	5.79±1.60		5.78±1.38		0.049	0.961
Frequency of sexual intercourse (per week)	1.70±1.09		1.71±1.01		-0.069	0.945
	n	%	n	%	χ^2	p
Gynecological examination status						
Yes	83	88.3	70	74.5	6.052	**0.014**
No	11	11.7	24	25.5		
Use of family planning methods						
Effective method	46	48.9	37	39.4	1.797	0.186
Inefficient method	48	51.1	57	60.6		
Spousal discharge						
Yes	11	11.7	2	2.1	7.322	**0.021***
No	83	88.3	92	97.9		
Daily pad use status						
Yes	38	40.4	38	38.3	0.089	0.765
No	56	59.6	58	61.7		
Knowledge of genital infection						
Yes	60	63.8	74	78.7	5.137	**0.023**
No	34	36.2	20	21.3		
Knowledge of genital hygiene						
Yes	68	72.3	79	84.0	3.812	0.051*
No	26	27.7	15	16.0		

SD: Standard deviation; t: Student's t-Test; χ^2: Chi-Square analysis; *: Yates Corrected Chi-Square.

a history of continuous discharge in their partners ($p<0.05$). On the other hand, women without vaginitis were more likely to have knowledge of genital infection ($p<0.05$) (Table 2).

The majority of women with vaginitis (42.2%) underwent gynecological examination due to complaints of vaginal discharge, whereas 50% of women without vaginitis presented for routine examination. In addition, it was determined that women with vaginitis (51%) and without vaginitis (53.2%) mostly used the withdrawal method among family planning methods. Condom use rates were low (vaginitis group: 23.4%, non-vaginitis group: 26.6%). The most preferred products for cleaning the genital area in the toilet in both groups were water (vaginitis group: 51%, non-vaginitis group: 66%) and toilet paper (vaginitis group: 30.9%, non-vaginitis group: 21.3%) (Table 2).

When the Genital Hygiene Behavior Scale and sub-dimension scores of women with and without vaginitis were examined, no significant difference was found between the mean scores of all sub-dimensions and total scores of the scale except for the menstrual hygiene sub-dimension. It was determined that women without vaginitis had significantly higher scores in the menstrual hygiene sub-dimension ($p<0.05$). It was also determined that women in both groups had high genital hygiene behaviors according to the highest score (Max=115) that could be obtained from the scale (Table 3).

In the multivariate analysis, age, duration of menstruation, and frequency of sexual intercourse among women with vaginitis were identified as factors affecting their genital hygiene behaviors. These factors explained 30% of the variance in the Genital Hygiene Behavior Scale score ($R^2=0.296$). It was found that as the age of women with vaginitis increased, their genital hygiene behaviors were positively influenced, while longer menstruation duration and higher frequency of sexual intercourse negatively affected their genital hygiene behaviors (Table 4).

DISCUSSION

This study aimed to identify the differences in genital hygiene behaviors between women with and without vaginitis, as well as the factors influencing these behaviors. Additionally, the general characteristics of genital hygiene practices in both groups were

Table 3: Participant's genital hygiene behavior scale subscale and total score averages

Variable	Group with vaginitis (n=94)	Group without vaginitis (n=94)	t	p
Genital Hygiene Behavior Scale	**Mean±SD**	**Mean±SD**		
Genital hygiene subdimension	50.10±5.05	50.85±4.19	-1.098	0.274
Menstrual hygiene subdimension	33.00±4.69	34.72±4.82	**-2.484**	**0.014**
Abnormal Finding Awareness Subscale	13.08±2.29	12.61±2.56	1.317	0.189
Total	96.19±9.17	98.19±8.45	-1.555	0.122

SD: Standard deviation; t: Student's t- Test.

Table 4: Factors affecting genital hygiene behaviors of women with vaginitis according to linear regression analysis

Variables	B	SE	Beta (β)	t	p	95% CI (OR)	
Constant	92.558	4.128		22.414	0.000	84.411	100.705
Age	0.196	0.100	0.146	1.971	**0.050**	0.000	0.393
Duration of menstruation (days)	-0.706	0.431	-0.119	-1.937	**0.049**	-1.557	0.145
Frequency of sexual intercourse (per week)	-1.347	0.615	-0.160	-2.190	**0.030**	-0.134	1.211

SE: Standard error; CI: Confidence interval; OR: Odd ratios; Dependent variable: Genital Hygiene Behavior Scale, R: 0.419, Adjusted R^2: 0.296, F: 3.080, p=0.05.

examined. The findings provide valuable insights into the role of sociodemographic characteristics, reproductive health history, and individual hygiene habits in the development of vaginitis. In the following discussion, these results are interpreted in light of existing literature to highlight the importance of education, knowledge level, and behavioral factors in the prevention of vaginitis.

Vaginitis is one of the most important reproductive health problems, and its prevalence is increasing with the decrease in the age of unprotected sex.[16] The main cause of vaginitis is the lack of genital hygiene.[11] Similar to the results of this study, it has been reported that as the number of pregnancies, births, abortions, and curettages increases, genital hygiene behaviors decrease and the incidence of vaginitis rises; women with vaginitis undergo more gynecological examinations, and their husbands have a history of discharge.[11,16–18]

The most important factor in preventing vaginitis is maintaining genital hygiene.[11] It is emphasized that using only water for genital hygiene is healthy, and the use of additional products increases the risk of vaginal infections.[13,19] In studies, it has been reported that water and toilet paper are mostly used for genital hygiene.[14,15,19,20] Similarly, women in this study reported that they mostly used water and toilet paper for genital hygiene. This can be considered an important strategy to reduce the risk of vaginitis.

However, in this study, it was determined that women without vaginitis maintained better menstrual hygiene, and their menstrual hygiene behaviors were higher. Similar studies have also found that the risk of vaginal infection increases when menstrual hygiene deteriorates.[21–23] In a descriptive study conducted by Sianou et al.[24] investigating the prevalence of vaginitis in different age groups (prepubertal, pubertal, reproductive-age women, and postmenopausal women), it was found that vaginitis cases were most common in women of reproductive age, especially during the menstrual period. It is believed that encouraging menstrual hygiene practices during menstruation, providing education and counseling on the correct use of menstrual hygiene products, and expanding these educational efforts to raise awareness can contribute to the prevention of vaginal infections.

The levels of genital hygiene behaviors vary from woman to woman. While some studies indicate that women's genital hygiene behaviors are at a high level,[15,21,25] other studies indicate that, particularly in women with genital tract infections, poor genital hygiene behaviors are prevalent, which create a foundation for the frequent recurrence of infections.[11,14,16] In this study, it was determined that women's genital hygiene behaviors were high. Although the high levels of genital hygiene behaviors and awareness of genital infections in both groups may appear surprising, this can be explained by the high educational attainment of the participants, regular access to healthcare services, and the voluntary nature of the study sample, which might have attracted women with greater health awareness.

In one study, it was found that advancing age negatively affected genital hygiene behaviors in women,[26] while in another study, it was determined that genital hygiene behaviors increased as the age of women increased.[25] In this study, while no significant differences were found in terms of age, education level, marital status, or income between the two groups, multivariate analysis revealed that

age, menstrual duration, and frequency of sexual intercourse were significant predictors of hygiene behaviors in women with vaginitis. The positive influence of age may be due to increased health awareness and experience. On the other hand, longer menstrual duration and more frequent sexual activity may create challenges in maintaining consistent hygiene routines, which could reduce overall hygiene scores. Moreover, women without vaginitis had higher menstrual hygiene scores and greater knowledge about genital infections, suggesting that knowledge and preventive practices play a crucial role. These findings suggest that both knowledge and health-seeking behavior are important determinants of effective hygiene practices. Factors such as education level, cultural norms, health literacy, and previous infection experiences may also contribute to the development of hygiene behaviors and should be further explored in future research.

In a study by McLaughlin et al.,[27] it was found that the duration of menstruation and increased frequency of sexual intercourse were associated with higher rates of vaginal infections. In this study, it was determined that as the age of women with vaginitis increased, their genital hygiene behaviors were positively affected, while as the duration of menstruation and frequency of sexual intercourse increased, their genital hygiene behaviors were negatively affected. Multivariate regression analysis revealed that age, menstrual duration, and sexual activity frequency were significant predictors of genital hygiene behaviors, accounting for approximately 30% of the variance. The positive effect of age on hygiene practices may reflect greater health awareness and experience among older women. Conversely, longer menstrual periods and more frequent sexual activity negatively affected hygiene behaviors. This may be due to increased physical burden during menstruation and inconsistent postcoital hygiene practices. Although these three factors were statistically significant, a large portion of the variance remains unexplained, indicating the potential influence of other variables such as education, cultural practices, and access to reproductive health information.

Women's knowledge of genital infections is an important factor in preventing vaginitis.[11] In a study conducted by Nirmalasari Hariadi Putri et al.[28] with 50 female motorcycle taxi drivers, it was found that women with vaginitis had limited knowledge about vaginal infections. In contrast, a cross-sectional study by Erbil et al.[18] with married women found that their knowledge of genital tract infections was high. In this study, similar to the results of Erbil's study, women without vaginitis exhibited a high level of knowledge about genital tract infections.[18] It is believed that the high level of education among both women with and without vaginitis in the study contributed to their increased awareness of genital tract infections.

It is emphasized that the use of barrier contraceptive methods, such as condoms, helps reduce the risk of vaginal infections and contributes to maintaining overall genital hygiene.[29] While methods such as the use of intrauterine devices and withdrawal contribute to the development of vaginitis, condom use has a preventive effect against vaginitis.[27,30] In a descriptive study conducted by Calık et al.[11] with married women, it was found that the withdrawal method was the most commonly used contraceptive, while condom use was reported to be quite low. This study also found that the withdrawal method was the most commonly used, while the rate of condom use was low.

Limitations

The limitations of this study include the reliance on self-reported data from participants, which may introduce recall bias. Additionally, as the study was conducted at a single institution with women who sought care only there, the results cannot be generalized to the wider population.

CONCLUSIONS

The study findings show that both women with and without vaginitis exhibit high genital hygiene behaviors. Significant differences were observed in the genital hygiene behaviors between the two groups, with women without vaginitis demonstrating better hygiene practices. Additionally, it was found that as the age of women with vaginitis increased, their hygiene behaviors improved; however, as the duration of menstruation and frequency of sexual intercourse increased, their hygiene behaviors were negatively affected.

Knowledge about vaginal infections is a critical factor in the prevention of vaginitis. In this context, nurses should organize informative training sessions on vaginal infections and genital hygiene for women of all age groups and their partners. These training sessions will increase the health knowledge of both women and their partners, thereby contributing to the development of proper hygiene behaviors. Furthermore, it is recommended to conduct scientific research on vaginitis and genital hygiene behaviors using a larger sample of individuals from various sociodemographic backgrounds and cultures. Additionally, collaborating with non-governmental organizations and the media to organize awareness campaigns on the prevention of vaginitis and genital hygiene is suggested to reach broader audiences.

Statement

Ethics Committee Approval: The University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 25.10.2023, number: 142).

Informed Consent: Written consent was obtained from all participants. **Conflict of Interest:** The authors have no conflict of interest to declare.

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ORIGINAL ARTICLE

Assessment of patients' perception of emergency in the gynecology and obstetrics emergency clinic: Is it an actual emergency? A retrospective analysis

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ABSTRACT

Objective: Emergency departments are crucial components of healthcare systems, providing rapid and effective medical services. However, unnecessary emergency visits lead to inefficiencies in resource allocation and service delivery. Pregnancy often alters women's health perceptions, increasing emergency department visits. This study aimed to evaluate the urgency of visits to the gynecology and obstetrics emergency department and analyze the impact of pregnancy on emergency service utilization.

Material and Methods: This retrospective, cross-sectional study analyzed the reasons for admission, demographic characteristics, and hospitalization rates of patients who visited the Zeynep Kamil Women and Children Diseases Training and Research Hospital between 2013 and 2023. Data were collected from the hospital automation system, categorized using ICD-10 codes, and statistically analyzed with IBM SPSS Statistics 26.0 software.

Results: A total of 174,790 emergency visits were recorded, with 69.76% involving pregnant patients. Among pregnant patients, 26.04% required hospitalization, whereas the hospitalization rate for non-pregnant patients was 8.23%. The most common reasons for emergency visits included pregnancy-related conditions (O26.8, O26.9) and pregnancy status (Z33, Z32.0). The analysis of emergency visit trends revealed a decline in 2019–2020, followed by an increase after 2021.

Conclusion: The findings suggest that gynecology and obstetrics emergency services are predominantly utilized for pregnancy-related concerns, with some visits being unnecessary. To optimize emergency department efficiency, patient education, improved outpatient services, and enhanced triage systems are recommended. Future multicenter studies should explore patient motivations and long-term health outcomes. The study recommends improving emergency service efficiency through patient education, better outpatient access, and effective triage implementation.

Keywords: Emergency service utilization, gynecology, pregnancy.

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INTRODUCTION

Emergency services constitute a vital element of healthcare systems, designed to deliver prompt and effective medical care in situations necessitating immediate intervention.[1,2] In Türkiye, as in several other countries, the overutilization of emergency services can result in service delivery disruptions and wasteful allocation of healthcare resources. Visits to emergency services, particularly in gynecology and obstetrics, hold significant relevance for the administration of emergency healthcare services. Pregnancy is a significant phase that influences women's health perceptions, leading pregnant women to assess every symptom with greater seriousness.[3] This scenario may elevate the frequency of emergency service visits among pregnant individuals and prompt an inquiry into the actual urgency of these visits. Common obstetric emergencies include preeclampsia, eclampsia, ectopic pregnancy, preterm labor, and postpartum hemorrhage, while frequent gynecologic emergencies consist of ovarian torsion, acute pelvic inflammatory disease, and severe abnormal uterine bleeding. Awareness of these conditions is essential for contextualizing patterns of emergency department utilization.[4]

This study analyzed the reasons for application, demographic characteristics, and hospitalization rates of patients presenting to the gynecology and obstetrics emergency department of a reference hospital. The impact of pregnancy on emergency department utilization was examined, comparing the emergency visit trends of pregnant and non-pregnant patients. The primary objective of the study was to assess data regarding the superfluous utilization of the emergency department and to propose recommendations for enhancing the efficacy of health service delivery. Numerous studies in the literature indicate that most presentations to gynecology and obstetrics emergency departments involve problems manageable in outpatient clinic settings. Nonetheless, insufficient data exist regarding the number of individuals seeking assistance who genuinely necessitate emergency care versus those who require observation or hospitalization. This study investigated hospitalization circumstances among pregnant and non-pregnant patients presenting to the emergency room, evaluating them based on "real emergency" criteria.

The primary research questions of the study are as follows:

- What are the demographic and clinical characteristics of patients presenting to the gynecology and obstetrics emergency department?
- How does pregnancy influence the likelihood of utilizing emergency services and the perception of what constitutes an emergency?
- What proportion of emergency department visits are classified as true emergencies?
- Are there significant differences between patients who require hospitalization and those who do not?
- What strategies can be proposed to improve the efficient use of emergency department resources?

Addressing these questions will yield critical information to enhance the efficiency of health service delivery and reduce unnecessary emergency room visits. The study's results are anticipated to aid in formulating strategies for managing obstetrics and gynecology emergency departments more effectively.

MATERIAL AND METHODS

This research is a retrospective, cross-sectional analysis assessing the demographic features, admission grounds, and urgency of patients presenting to the Gynecology and Obstetrics Emergency Department of Zeynep Kamil Women and Children Diseases Training and Research Hospital. This study was conducted with authorization from the Ethics Committee of Obstetrics and Gynecology, İstanbul, Türkiye (Approval Number: 45, Approval Date: 20.03.2024). In the study, personal data were anonymized to safeguard patient privacy and were examined in accordance with ethical guidelines.

The study analyzed all patients presenting to the emergency department, categorizing them into several groups: pregnant women, hospitalized patients, and inpatient pregnant women. The data were retrospectively examined and processed using the hospital automation system. The study utilized data extracted from the hospital's computerized health records. All patients who presented to the emergency department from 2013 to 2023 were incorporated into the study. Patients with absent or erroneous records were excluded.

The demographic data, pregnancy status, admission diagnosis, therapy administered in the emergency department, and hospitalization need were analyzed. The grounds for patient admissions and their illnesses were categorized using ICD-10 codes. The patients' hospitalization status served as the criterion for urgency evaluation. In this study, a "genuine emergency" was defined as any condition requiring immediate medical intervention, as evidenced by hospital admission, surgical procedure, or vital sign instability.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics 26.0 software. The following statistical methodologies were employed:

- Descriptive statistics: Number of applications, percentage distributions, mean±standard deviation.
- Pairwise comparisons: The Chi-square test and Independent Sample t-test were used to analyze the application behaviors of pregnant and non-pregnant patients.
- Regression analysis: A logistic regression model was developed to examine the factors influencing the necessity for hospitalization.
- Time series analysis: ANOVA and time-series methodologies were utilized to investigate variations in emergency application trends over the years.

Results with a $p<0.05$ were deemed statistically significant.

Ethic Approval

This study was conducted with authorization from the Ethics Committee of Zeynep Kamil Women and Children Diseases Training and Research Hospital (Approval Number: 45, Approval Date: 20.03.2024). In the study, personal data were anonymized to safeguard patient privacy and were examined in accordance with ethical guidelines. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Table 1: Emergency admissions overview (2013–2023)

Category	Number	Rate (%)
Total emergency admissions	174790	
Pregnant admissions	121930	69.76
Hospitalized patients	36098	20.65
Hospitalized pregnant patients	31745	26.04

RESULTS

Table 1 presents the total number of applications to the Gynecology and Obstetrics Emergency Department of our hospital from January 2013 to December 2023, detailing the distribution between pregnant and non-pregnant patients, as well as the classification of these applications based on the necessity for hospitalization or observation. A total of 20.65% of all emergency applications resulted in hospitalization, while 26.04% of pregnancy-related applications required hospital admission. This indicates that the majority of patients presenting to the emergency department were pregnant and that most of those admitted were also pregnant.

Upon examining the emergency application behaviors of pregnant and non-pregnant patients, it was found that pregnant patients made a total of 121,930 applications, with 31,745 resulting in hospitalization. The hospitalization rate was determined to be 26.04%. The total number of applications from non-pregnant patients was 52,860, with 4,353 resulting in hospitalization. The hospitalization rate for this group was 8.23%. The data indicate that pregnant women utilized the emergency department more frequently and had a significantly higher hospitalization rate compared to non-pregnant women. The evaluation, conducted using the diagnosis codes established by the physician during the application, yielded the distribution presented in Table 2.

Additional analyses revealed that the age range of participants was between 18—45 years. The frequency of repeat hospital visits was higher among pregnant women. Surgical interventions were required in approximately 6% of hospitalized cases, and the average duration of hospital stay was 3.2±1.4 days. The most frequent clinical diagnoses included pregnancy-related conditions, urinary tract infections, and abnormal uterine bleeding.

The results indicate that pregnancy-related disorders represent a significant share of the utilization of the Gynecology and Obstetrics Emergency Department, with several patients presenting due to normal pregnancy-related processes. An examination of patient applications to the Gynecology and Obstetrics Emergency Department over the years revealed that the number of emergency visits fluctuated, with notable increases and decreases occurring during specific intervals (Fig. 1). In 2013, there were 15,432 applications, which rose to 24,678 by 2023. A decline occurred particularly between 2019 and 2020; however, applications began to rise again after 2021.

Table 2: Most common diagnoses in emergency, pregnant, and inpatient patients

Emergency diagnoses (n, %)	Count	Pregnant diagnoses (n, %)	Count	Inpatient diagnoses (n, %)	Count
Other specified pregnancy-related conditions (64.73%)	93268	Other specified pregnancy-related conditions (71.78%)	93268	Other specified pregnancy-related conditions (75.07%)	25257
Pregnancy-related condition, unspecified (10.61%)	15290	Pregnancy-related condition, unspecified (11.77%)	15290	Pregnancy-related condition, unspecified (12.42%)	4178
Gynecological examination (6.39%)	9207	Pregnancy, not yet confirmed (7.09%)	9207	Pregnancy status (3.55%)	1195
Post-surgical recovery period (3.96%)	5711	Pregnancy status (4.4%)	5711	Gynecological examination (1.77%)	595
Abnormal uterine and vaginal bleeding (3.67%)	5285	Ectopic pregnancy (3.92%)	5091	Abnormal uterine and vaginal bleeding (2.04%)	686
Pregnancy, not yet confirmed (3.53%)	5091	Threatened abortion (0.36%)	468	Pregnancy, not yet confirmed (2.06%)	692
Pregnancy status (3.48%)	5011	Twin pregnancy (0.33%)	426	Post-surgical recovery period (1.4%)	472
General examinations (1.25%)	1805	Missed miscarriage (0.17%)	220	Ectopic pregnancy (0.54%)	181
Rh incompatibility reaction (1.2%)	1725	Other ectopic pregnancy (0.11%)	143	Other pregnancy-related conditions (0.62%)	207
Acute upper respiratory infection (1.17%)	1685	Pregnancy confirmed (0.09%)	111	Ectopic pregnancy (unspecified) (0.54%)	181

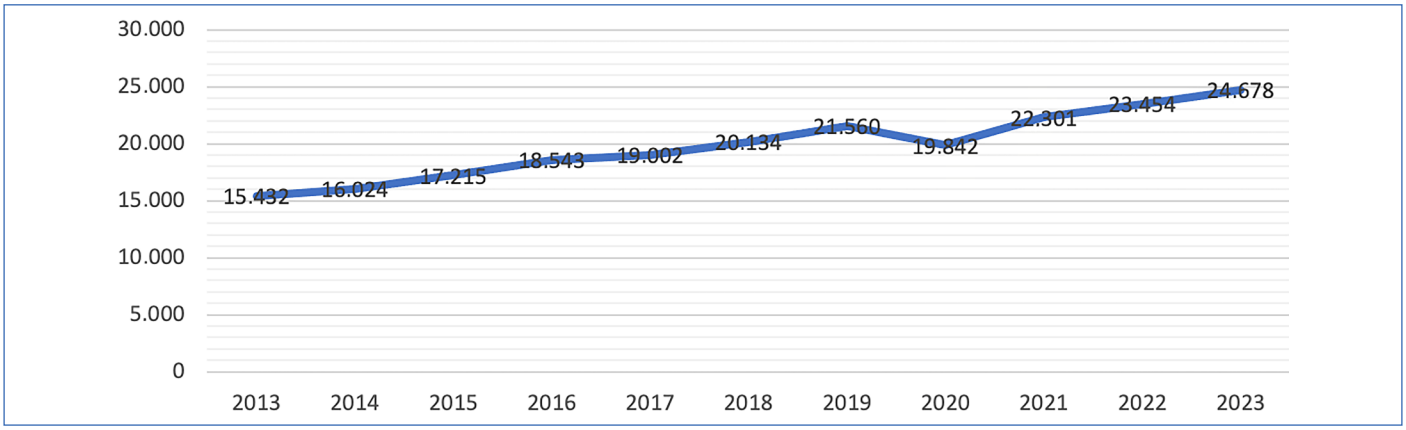

Figure 1: Yearly distribution of emergency department application figures.

DISCUSSION

This study retrospectively assessed the reasons for application, pregnancy status, and hospitalization needs of patients who presented to the Zeynep Kamil Women and Children Diseases Training and Research Hospital. The results indicate that a significant proportion of admissions to the Gynecology and Obstetrics Emergency Department pertain to pregnancy, with many cases associated with typical pregnancy processes.

The acquired statistics indicate that 69.76% of patients presenting to the Gynecology and Obstetrics Emergency Department were pregnant. The elevated frequency of emergency department visits by pregnant patients may be linked to concerns and perceived health risks associated with the pregnancy process. The literature indicates that women utilize health services more frequently during pregnancy and are more likely to assess their symptoms with greater seriousness.[4,5] This scenario may be more pronounced among women experiencing their first pregnancy. Moreover, it is believed that the physiological alterations induced by pregnancy may lead to certain symptoms being perceived as urgent.

The study revealed that 26.04% of pregnant patients presenting to the emergency room were hospitalized, compared to 8.23% of non-pregnant patients. The elevated hospitalization rates among pregnant patients suggest that problems associated with pregnancy heighten the probability of necessitating emergency intervention. The predominant diagnoses were "pregnancy-related conditions" (O26.8, O26.9) and "pregnancy status" (Z33, Z32.0), suggesting that numerous cases were non-urgent or could be addressed in outpatient settings. Comparable research indicates that a substantial fraction of obstetric emergency room visits are not classified as "genuine emergencies".[6,7] In obstetric and gynecologic practice, genuine emergencies such as preeclampsia, postpartum hemorrhage, ovarian torsion, and ruptured ectopic pregnancy require rapid intervention. The relatively low frequency of such severe cases in our cohort underscores that many visits may not represent true emergencies, highlighting the importance of triage and patient education.[8]

The rationale for patients' visits to the emergency department and their urgency was examined using ICD-10 diagnosis codes. Nonetheless, the inadequate or erroneous entry of diagnosis codes in hospital automation systems significantly impacts the accuracy of the acquired data. In the emergency department, physicians may code diagnoses rapidly due to time constraints, which can result in insufficient precision. Furthermore, in certain instances, overarching categories like generic pregnancy-related codes (e.g., O26.8 – Other specified conditions related to pregnancy) may be preferred, complicating the analysis of individual health issues. Inaccurate or insufficient coding may adversely affect the identification of genuine emergency patients, strategic planning for emergency department utilization, and decision-making in healthcare administration.

Consequently, future research should implement supplementary procedures to enhance the precision of diagnosis codes, such as manual file examination or secondary physician assessment to improve data accuracy. Furthermore, enhancing diagnosis coding training for healthcare personnel and refining diagnosis entry procedures in automated systems can augment data reliability. Unnecessary visits to emergency services are recognized to impede healthcare service delivery and result in inefficient resource utilization.[8]

The study's results indicate that patients often utilize gynecology and obstetrics emergency care for conditions that could be effectively managed in outpatient clinics. This scenario can induce superfluous congestion in emergency services, hindering patients in genuine need of immediate intervention from obtaining timely assistance. The presence of non-hospitalized patients seeking merely routine prenatal examinations or reassurance for anxiety-related concerns represents a challenge that requires consideration in health policy planning.

The examined data indicated that the volume of applications to gynecology and obstetrics emergency services varied from 2013 to 2023. The decline noted between 2019 and 2020 can be attributed to the effects of the COVID-19 pandemic. Emergency applications diminished during the pandemic due to individuals' reluctance to seek medical care and the prioritization of healthcare systems on pandemic-related issues.[9] Nonetheless, applications have risen once more after 2021. This pattern may indicate a resurgence in normal healthcare utilization as the impacts of the pandemic diminish.

CONCLUSION

The findings of this study suggest the need to develop initiatives aimed at enhancing the efficiency of gynecology and obstetrics emergency services. Educating patients about the conditions that

genuinely require emergency care may help reduce unnecessary admissions, particularly among pregnant individuals.

Enhancing outpatient clinic services: Improving the accessibility of obstetrics and gynecology outpatient clinics and optimizing appointment procedures can encourage patients to seek care in appropriate settings rather than emergency departments.

Implementing an effective triage system: Establishing and maintaining a structured triage system is essential to accurately assess the urgency of patients presenting to emergency rooms, ensuring that true emergencies receive timely and appropriate medical attention.

Statement

Ethics Committee Approval: The University of Health Sciences, Turkey. Istanbul Zeynep Kamil Women's and Children's Diseases Training and Research Hospital Ethics Committee granted approval for this study (date: 20.03.2024, number: 45).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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ORIGINAL ARTICLE

Evaluation of the relationship between proteinuria levels and perinatal and neonatal outcomes

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ABSTRACT

Objective: To evaluate the relationship between proteinuria levels and maternal and neonatal outcomes.

Material and Methods: This study retrospectively evaluated a total of 2,266 pregnant women who received follow-up care and delivered at our hospital between January 2018 and 2024. Of these, 76 patients who exhibited proteinuria during pregnancy were included in the analysis. We assessed demographic, laboratory, and obstetric data for all participants, including age, smoking status, gravida, blood urea nitrogen (BUN) levels, platelet count, 24-hour proteinuria values, gestational hypertension (GHT), fetal growth restriction (FGR), preeclampsia, preterm birth (PTB), Apgar scores, and birth weight.

Results: The severe group had significantly higher rates of gestational hypertension (GHT), preeclampsia, preterm birth (PTB), and fetal growth restriction (FGR) compared with the other groups ($p<0.001$ for all). Apgar scores at 1 and 5 minutes were lower, and birth weight was significantly reduced in the severe group ($p<0.001$). The rate of NICU admissions was also higher in the severe group ($p<0.001$).

Conclusion: This study shows that severe proteinuria is associated with hypertensive diseases, fetal growth restriction, preterm birth, and neonatal complications. Close monitoring of pregnant women with proteinuria and early intervention may play an important role in reducing possible complications. Evaluation of proteinuria levels together with maternal and fetal risk factors may optimize clinical management to improve pregnancy outcomes.

Keywords: Maternal, perinatal, preeclampsia, proteinuria.

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INTRODUCTION

Urine analysis, one of the most common screening tests performed during pregnancy, is considered a critical tool for the detection of proteinuria. Although proteinuria has historically been considered a marker of preeclampsia, it can also be a nonspecific indicator of renal disease. Various mechanisms may contribute to the development of proteinuria during pregnancy, including increased plasma protein concentration, increased glomerular permeability, decreased tubular protein reabsorption, and renal hemodynamic changes.[1–3] In normal renal function, glomerular filtration rate and protein filtration dynamics are affected by factors such as molecular weight, shape, and electrical charge. Guidelines published by the American College of Obstetricians and Gynecologists (ACOG) in 2013 suggested that proteinuria should not be considered a necessary criterion for the diagnosis of preeclampsia. However, proteinuria remains an important risk marker when evaluated together with hypertensive disorders.[4] Preeclampsia is associated with serious maternal and perinatal complications and includes pathophysiologic processes that lead to systemic inflammation, endothelial dysfunction, and multiorgan damage, along with new-onset gestational hypertension.[5,6] Significant physiological changes that occur during pregnancy affect renal hemodynamic changes, endocrine regulation, and tubular function. Pregnancy-related hyperfiltration and increased renal blood flow alter renal function, while increased renal venous pressure and changes in glomerular permeability, along with the effects of uteroplacental circulation, contribute to proteinuria.[7,8] It has been observed that the risks of preeclampsia, fetal growth restriction, premature birth, and loss of maternal renal function are increased in pregnant women with chronic kidney disease. Proteinuria is an important indicator of glomerular damage and, when present in high amounts and persistently, can cause serious complications such as glomerular sclerosis, tubulointerstitial damage, and end-stage renal failure.[9] Proteinuria is classified into different degrees during pregnancy, and these degrees differ in terms of clinical significance. Physiologic, i.e., transient proteinuria, can be observed during pregnancy due to increased renal blood flow and glomerular filtration rate. This situation typically ranges from 150 to 300 mg per day and is not considered clinically significant or associated with any pathological processes.[10] Determination of proteinuria levels may be important in predicting pregnancy outcomes, regardless of the presence of concomitant preeclampsia. However, some studies suggest that the severity of proteinuria is not directly associated with preeclampsia complications, and scientific debates continue on this issue.[11] In this context, it is important to analyze the associations of different proteinuria levels with maternal and fetal morbidity. This study aimed to evaluate the relationship between proteinuria levels and maternal and neonatal outcomes.

MATERIAL AND METHODS

The present study had a retrospective observational design following the principles of the Helsinki Declaration. Informed consent documents were received from all patients. The study received approval from our hospital's Ethics Committee (Date: 26/03/25, Number: 2025/430). A total of 2266 pregnant women who underwent pregnancy follow-up in the Gynecology and Obstetrics Clinic of our hospital and gave birth in our clinic between January 2018 and January 2024 were retrospectively evaluated. Among these patients, 77 patients with proteinuria during pregnancy were included in the study. The inclusion criteria were proteinuria detected during pregnancy in laboratory examination results and urine protein levels >0.3 g/24 hours on different days. Patients with multiple pregnancies, primary hypertension, nephropathy and diabetes, patients with incomplete follow-up and birth record data, and patients with missing laboratory data were excluded from the study. Demographic and laboratory data of all patients, such as age, smoking, gravida, parity, body mass index (BMI), blood urea nitrogen (BUN), serum creatinine, serum uric acid, aspartate transaminase (AST), alanine transaminase (ALT), platelet count, and 24-hour proteinuria value, were evaluated retrospectively. All patients' data on gestational hypertension (GHT), fetal growth restriction (FGR), gestational diabetes mellitus (GDM), preeclampsia, preterm birth (PTB), preterm pre-labor rupture of membranes (PPROM), 1st and 5th minute Apgar scores, neonatal intensive care unit (NICU) history, and birth weight were evaluated retrospectively. The American Diabetes Association criteria were used to diagnose GDM.[12] GHT was diagnosed in accordance with the most recent bulletin of the ACOG.[13] The Delphi criteria were used to diagnose FGR.[14] Preterm birth (PTB) is defined as a birth (live-born or stillborn≥20+0 weeks of gestation) that occurs at <37+0 weeks of gestation.[15] PPROM is defined as the rupture of fetal membranes before 37 weeks of gestation.[16] Patients were evaluated in three groups according to their proteinuria levels: mild proteinuria (300 mg <24-hour proteinuria <1000 mg), moderate proteinuria (1000 <24-hour proteinuria <3500 mg), and severe proteinuria (24-hour proteinuria >3500 mg).[13,17]

Statistical Analysis

Statistical analysis was performed using the SPSS version 26.0 software package (IBM Inc., Chicago, IL, USA). The normality of the distribution was evaluated with the Kolmogorov–Smirnov and Shapiro–Wilk tests based on whether the data demonstrated normal distribution. Standard deviation (SD) was used to evaluate normally distributed data. Categorical variables were presented using frequency and percentage (%). Chi-square tests were used in the analysis of categorical data. Continuous variables were compared among groups using analysis of variance (ANOVA) and Student's t-test. A logistic regression analysis of proteinuria severity for adverse pregnancy outcomes was performed. The results were evaluated at 95% confidence intervals (CI). P-values of <0.05 were regarded as statistically significant.

RESULTS

The mean BMI of the severe group was significantly higher compared with the other groups (p=0.046). BUN and creatinine levels were significantly lower in the mild group compared with the other groups (p=0.036 and p=0.027, respectively). AST and ALT levels were significantly higher in the severe group compared with the other groups (p=0.021 and p=0.018, respectively) (Table 1).

GHT and preeclampsia rates were significantly higher in the severe group compared with the other groups (p <0.001 and p <0.001, respectively). PTB and FGR rates were significantly higher in the

Table 1: Comparison of demographic and laboratory data between groups

	Mild (n=42) Mean±SD	Moderate (n=22) Mean±SD	Severe (n=13) Mean±SD	p
Age (years)	31.9±4.7	32±4.8	32.0±4.6	0.540
BMI (kg/m^2)	26.2±2.2	26.3±2.5	27.3±3.1	0.046
Smoking, n (%)	3 (7.1%)	2 (9%)	1 (7.6%)	0.120
Gravidity	2.07±1.08	1.99±1.14	1.98±1.12	0.390
Parity	0.91±0.66	0.90±0.75	0.89±0.73	0.760
BUN (mmol/L)	4.28±1.46	5.52±3.66	7.58±4.12	0.036
Creatinine (mmol/L)	52.66±12.18	67.73±38.62	79.26±41.12	0.027
Uric acid (mmol/L)	356.4±99.4	399.8±99.9	471.1±122.2	0.032
AST (U/L)	32.26±26.66	34.72±29.16	52.22±33.18	0.021
ALT (U/L)	20.72±11.82	21.22±12.36	35.18±28.68	0.018
Platelet (n/mL)	230.7±61.33	222.6±58.22	201.2±88.16	0.042

SD: Standard deviation; BMI: Body mass index; BUN: Blood urea nitrogen; AST: Aspartate transaminase; ALT: Alanine transaminase.

Table 2: Comparison of perinatal outcomes between groups

	Mild (n=42) n (%)	Moderate (n=22) n (%)	Severe (n=13) n (%)	p
GHT	7 (16.6)	5 (22.7)	4 (30.7)	<0.001
GDM	4 (9.5)	2 (9)	1 (7.6)	0.140
Preeclampsia	5 (11.9)	5 (22.7)	8 (61.5)	<0.001
PTB	8 (19)	8 (36)	7 (53.8)	<0.001
PPROM	5 (11.9)	3 (13.6)	2 (15.3)	0.160
FGR	4 (9.5)	5 (22.7)	6 (46.1)	<0.001

GHT: Gestational hypertension; GDM: Gestational diabetes mellitus; PTB: Preterm birth; PPROM: Preterm pre-labor rupture of membranes; FGR: Fetal growth restriction.

Table 3: Comparison of neonatal outcomes between groups

	Mild (n=42) Mean±SD	Moderate (n=22) Mean±SD	Severe (n=13) Mean±SD	p
Apgar (1st min)	7.5±0.8	7.2±0.6	6.7±0.7	<0.001
Apgar (5th min)	8.1±0.6	7.3±0.9	6.8±1.1	<0.001
Birth weight (gr)	2970±540	2420±610	1980±590	<0.001
NICU, n (%)	7 (16.6)	8 (36)	9 (69.2)	<0.001

SD: Standard deviation; NICU: Neonatal intensive care unit.

severe group compared with the other groups (p <0.001 and p <0.001, respectively) (Table 2).

Apgar 1st and 5th min scores were significantly lower in the severe group compared with the other groups (p <0.001 and p <0.001, respectively). Birth weight was significantly lower in the severe group compared with the other groups (p <0.001). The NICU rate was significantly higher in the severe group compared with the other groups (p <0.001) (Table 3).

DISCUSSION

Although there are numerous studies on proteinuria in the literature, studies examining the effects of proteinuria levels on perinatal and neonatal outcomes are limited. Our study revealed that the rates of GHT, preeclampsia, FGR, PTB, and NICU admission were higher in pregnant women with severe proteinuria compared with those with mild and moderate proteinuria. These results support previous studies showing that proteinuria is an important marker of maternal and fetal morbidity.

One of the most important findings of our study is that the rates of GHT and preeclampsia are higher in patients with severe proteinuria. This is related to endothelial dysfunction and renal hemodynamic changes associated with proteinuria. Similarly, the study by Dong et al.[18] found that the rate of preeclampsia was increased in pregnant women with severe proteinuria. Morikawa et al.[19] suggested that severe proteinuria was associated with systemic inflammation and oxidative stress and might worsen hypertensive conditions in pregnancy.

In addition, the significantly higher FGR and PTB rates in the severe proteinuria group indicate that proteinuria has adverse effects on fetal development. The study by Jiao et al.[20] also showed that the rate of delivery before the 37th week of gestation was increased in pregnant women with severe proteinuria. It is well known that placental insufficiency, an important feature of preeclampsia, contributes to FGR and preterm birth. The study by Hu et al.[21] also supports the

increased FGR rates in cases of severe proteinuria. These findings indicate that severe proteinuria may be an important clinical marker for impaired placental function.

In our study, newborns born to mothers with severe proteinuria had lower 1st and 5th minute Apgar scores and lower birth weights compared with the mild proteinuria group. The study by Wang et al.[22] also showed that severe proteinuria was an independent risk factor for low Apgar scores. Özkara et al.[23] supported this conclusion by showing that the rate of NICU admission increased as the severity of proteinuria increased. The higher NICU admission rates in the severe proteinuria group emphasize the long-term effects of intrauterine growth retardation and prematurity on newborn health.

In terms of biochemical markers, BMI, AST, and ALT levels were significantly higher in the severe proteinuria group. This suggests that metabolic and hepatic dysfunctions may also play a role in maternal and neonatal complications. Similarly, the study by Alves Ferreira et al.[24] showed that AST and ALT levels were higher in patients with severe proteinuria. In addition, Fishel Bartal et al.[25] found that the rate of proteinuria increased as the BMI value increased, similar to our study. At the same time, the increase in liver enzymes in patients with severe proteinuria is an indicator of hepatic involvement seen in severe preeclampsia and HELLP syndrome.

One of the important advantages of our study is that it has a large sample size covering a wide range of patients. This increases the reliability of the results obtained. In addition, criteria that comply with international standards were used in the diagnosis of obstetric complications such as preeclampsia, GHT, fetal growth retardation, and premature birth, thus supporting the scientific validity of the study.

However, the retrospective nature of the study may lead to the possibility that some clinical variables were recorded incompletely. In addition, because it was conducted in a single center, the generalizability of the results to different patient groups may be limited. The study only examined neonatal outcomes in the early postnatal period, and there are no data on long-term infant health.

Considering all these advantages and disadvantages, our study makes significant contributions to the existing literature. However, larger, multicenter, and long-term prospective studies are needed to evaluate the relationship between proteinuria and pregnancy outcomes in more detail.

CONCLUSION

This study highlights the important association between proteinuria severity and adverse maternal and neonatal outcomes. Severe proteinuria is associated with hypertensive disease, FGR, preterm birth, neonatal complications, low birth weight, and higher rates of NICU admission. These findings suggest that close monitoring of pregnant women with proteinuria and early intervention may play an important role in reducing potential complications. Given the ongoing debate about the predictive value of proteinuria for preeclampsia and adverse perinatal outcomes, further research is needed to develop risk stratification strategies and optimize the management of affected pregnancies. Proteinuria levels should be assessed in conjunction with other maternal and fetal risk factors, and careful monitoring should be provided to improve pregnancy outcomes.

Statement

Ethics Committee Approval: The Buca Seyfi Demirsoy Training and Research Hospital Ethics Committee granted approval for this study (date: 26.03.2025, number: 2025/430).

Informed Consent: Informed consent documents were received from all patients.

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ORIGINAL ARTICLE

Evaluation of respiratory problems in children with esophageal atresia

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ABSTRACT

Objective: Esophageal atresia (EA) is the most common esophageal anomaly associated with respiratory morbidity in childhood. This study aimed to evaluate respiratory problems in children who underwent surgery for esophageal atresia.

Material and Methods: A total of 33 cases with EA were included in the patient group, and 20 cases diagnosed with isolated gastroesophageal reflux disease (GERD) were included in the control group. This case-control study also included observational and analytical evaluations. Respiratory symptoms and findings were recorded. Spirometry was performed to assess lung function, and laboratory tests indicating an allergic condition were examined.

Results: In the patient group with a median age of 4.7 years (IQR: 6.7), 84.8% had recurrent or chronic cough, 51.5% had wheezing, 63.6% had a history of respiratory distress in the past year, 24.2% had recurrent pneumonia, and 63.6% had a history of hospitalization due to respiratory problems at least once. Aspiration pneumonia was present in 27.2% of patients, asthma diagnosed by a physician in 33.3%, and tracheomalacia in 18.1%. Asthma, cough, and wheezing were observed at similar rates in both groups, while aspiration pneumonia and hospitalization due to respiratory problems were more common in the patient group. Pulmonary function test (PFT) abnormalities were significantly more common in the EA group compared with the control group ($p<0.001$).

Conclusion: Respiratory problems in EA are based on structural and functional causes and are quite widespread. We emphasize the importance of conducting research using more detailed respiratory tests in larger patient series to obtain clearer data.

Keywords: Cough, esophageal atresia, pneumonia, pulmonary function tests.

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INTRODUCTION

Esophageal atresia (EA) is the most common congenital structural anomaly of the esophagus. According to the most recent prevalence studies, it is observed in one in every 3500–4500 live births.[1–3] The most common long-term complications include esophageal motility disorder, gastroesophageal reflux disease (GERD), and respiratory system problems.[4–7] The development of neonatal intensive care and surgical conditions has increased survival rates, which in turn has raised the prevalence of long-term complications, especially those related to respiratory problems.[8,9]

According to clinical studies conducted to date, the etiology of respiratory complications is multifactorial.[8,10,11] Prematurity and respiratory system malformations such as tracheomalacia, laryngeal cleft, and lung hypoplasia have been found to pose a risk for respiratory morbidities.[12] Apart from structural disorders in the respiratory tract, the reason for poor respiratory function is not fully understood.[13] It has been stated that long-term respiratory complications may be associated with upper respiratory tract conditions (such as tracheomalacia, aspiration, and difficulty swallowing), the gastrointestinal system, and lower respiratory tract morbidities.[7,13–17]

The goal of this study was to analyze long-term respiratory complications in children who underwent EA repair. The study aimed to determine the frequency of respiratory symptoms, their relationship with identified risk factors, and measurements of spirometric respiratory functions, in addition to assessing supporting factors for asthma, such as total immunoglobulin E (IgE) level, eosinophilia, and house dust mite (*D. farinae*)-specific IgE level.

MATERIAL AND METHODS

This study was conducted in collaboration with the Pediatric Pulmonology, Pediatric Gastroenterology, and Pediatric Surgery clinics at Istanbul Medeniyet University Göztepe Training and Research Hospital. The research process began after parents were provided with detailed information and gave informed consent through the "Informed Consent Form." The study included 33 patients who underwent surgery for EA and were followed up at pediatric pulmonology clinics between September 1, 2018, and April 1, 2019.

A control group of 20 children diagnosed with isolated GERD (according to ESPGHAN/NASPGHAN guidelines), unrelated to EA and other structural abnormalities, was selected to investigate the presence of morbidities that could cause respiratory symptoms and findings in patients diagnosed with EA. The aim was to identify factors other than reflux that could lead to respiratory complications in patients who underwent EA repair.

To evaluate the impact of gastroesophageal reflux (GERD) on respiratory outcomes, the rates of respiratory symptoms and complications were compared between the patient group (EA patients with GER) and the control group (patients with GERD but without EA). The presence of chronic cough, wheezing, episodes of respiratory distress, hospitalization due to respiratory problems, and aspiration pneumonia was recorded and compared between the groups. The baseline variables of the study and control groups, such as age, gender, prematurity, and length of stay in intensive care, are presented in Table 1.

Table 1: Comparison and characteristics of the patient group and control group.

	Patient group (n=33)	Control group (n=20)	p
Age (year), median (IQR)	4.7 (6.7)	10.1 (4.7)	0.030
Gender, n (%)			
Male	17 (51.5)	13 (65)	0.114
Female	16 (48.5)	7 (35)	0.396
Length of NICU stay (day) median (IQR)	30 (44)	5.2 (4.5)	0.009
Birth status, n (%)			
Term	19 (57.6)	15 (75)	0.050
Preterm	14 (42.4)	5 (25)	0.002

IQR: Interquartile range; NICU: Newborn intensive care unit.

Patient Selection

Upon reviewing the records of the Pediatric Surgery Clinic for the past 13 years, 107 patient files were identified. Examination of hospital records revealed that 14 patients had died and 50 patients could not be reached due to insufficient contact information or discontinuation of treatment. Ten patients' family members reported that they were unable to participate in the study for various reasons. Thirty-three patients aged 6 months to 18 years were being followed up at the Pediatric Pulmonology outpatient clinic. Patients with intellectual disability and neuromuscular disease were not included in the study; however, no patients meeting these exclusion criteria were identified.

Interview Forms and Data Collection

Based on previous studies, common respiratory complications and associated morbidities in patients with EA were identified, and an interview form was prepared. The interview form was designed to collect the following information: detailed prenatal, natal, and postnatal histories; type of EA, time, and technique of surgery; surgical and other complications; associated anomalies; history of GERD; allergic diseases previously diagnosed by a physician; and respiratory symptoms and findings. The presence of cough and wheezing was asked about separately in detail. Patients were asked whether they had experienced respiratory distress requiring emergency department visits, bronchodilator or inhalation/systemic steroid use, and, if so, how many times per year on average.

A history of tracheomalacia, inspiratory stridor, and associated metallic cough was assessed according to criteria, and bronchoscopic examination reports were reviewed if available. The number of hospitalizations due to respiratory problems and a history of ≥3pneumonia episodes in the past year was determined. Clinical information was obtained from parental interviews, detailed physical examination of the patient, and medical records.

Spirometry and Early Reversibility Test

Spirometry was performed in the patient and control groups aged six years or older using the Spirolab III Color LCD device. Data were recorded using the WinspiroPRO 6.8 program. Respiratory function tests were performed in accordance with the recommendations of the European Respiratory Society (ERS) and the American Thoracic Society (ATS).[18,19] The forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), and forced expiratory flow ($FEF_{25–75\%}$) were reported. The FEV_1/FVC ratio was documented. Spirometric measurements were evaluated and interpreted according to the guidelines of the aforementioned associations.[20,21]

Regardless of baseline lung function, an early reversibility test with a bronchodilator was performed. A change in FEV_1 of ≥12% was considered a positive result.

Serum Total IgE Level and Eosinophil Percentage

The serum total IgE levels of patients and the control group were analyzed using the *in vitro* immunoturbidimetric method with the Abbott Architect Biochemistry Analyzer. The IgE level determined by the current method was considered high if it exceeded the upper reference limit for the corresponding age group.[22] The eosinophil percentage was considered high if it was >5%.

House Dust Mite (*D. farinae*) Specific IgE Level

The results were obtained by *in vitro* quantitative measurements of serum using a specific IgE kit suitable for IMMULITE 2000 3g Allergy Systems analyzers. A standard classification system was used to interpret quantitative values.[23]

This study was conducted in accordance with the 1964 Helsinki Declaration and subsequent protocols, which set ethical standards for research involving human subjects. Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Istanbul Medeniyet University Göztepe Training and Research Hospital on August 15, 2018 (decision number 2018/0318).

Statistical Analysis

SPSS version 17.0 software was used for statistical analyses. The normality of the variables was examined using histogram graphs and the Shapiro–Wilk test. Descriptive analyses were presented using mean, standard deviation, median, and minimum–maximum values. Pearson Chi-square and Fisher's Exact tests were used for binary parameter comparisons.

When comparing variables that did not follow a normal distribution (non-parametric variables), the Mann–Whitney U test was used for two groups, and the Kruskal–Wallis test was used for more than two groups. The Spearman correlation test was used to analyze the measured data with each other. Results with a $p<0.05$ were considered statistically significant.

RESULTS

Thirty-three patients who underwent EA repair participated in the study. The median age was 4.7 years (IQR:6.7). The male-to-female ratio was 17:16. According to the Gross classification,[24] 66.6% (22/33) of patients were type C, 21.2% (7/33) were type A, 9% (3/33) were type B, and 3% (1/33) were type E. A total of 66.6% of patients (22/33) underwent early primary repair, 12.2% (4/33) underwent delayed primary repair, and 21.1% (7/33) underwent esophageal replacement surgery. Surgical complications included stricture in 54.5% (18/33) of patients, anastomotic leak in 6% (2/33), and recurrence of fistula in 3% (1/33).

Table 2: Respiratory complications, concomitant respiratory comorbidities

	EA patient group	
	n	%
Cough	28/33	84.8
Chronic cough (>4 weeks)	7/28	25
Recurrent cough	21/28	75
Wheezing	17/33	51.5
Respiratory distress episode	21/33	63.6
Hospitalization due to respiratory problems	21/33	63.6
Recurrent pneumonia	8/33	24.2
Doctor-diagnosed		
Asthma	11/33	33.3
Allergic rhinitis	4/33	12.1
Atopic dermatitis	1/33	3
Aspiration pneumonia	9/33	27.2
Tracheomalacia	6/33	18.1
Chest deformity	7/33	21.2

EA: Esophageal atresia.

GERD was diagnosed in 72.7% (24/33) of patients, and 29.1% (7/24) of these patients underwent anti-reflux surgery. Stricture development was observed in 66.6% (16/24) of patients with GERD.

During the postoperative follow-up period, esophagogastroscopy was performed in 75.7% (25/33) of patients, and esophagitis was detected in 20% (5/25) of these patients.

The median number of hospital admissions due to respiratory problems was 1 (IQR:3). The median number of respiratory distress episodes in the past year was 1 (IQR:3). The most common clinical findings in our patients were cough (84.8%), respiratory distress attacks and hospital admissions (63.6%), and wheezing (51.5%) (Table 2).

Table 3 presents the rates of respiratory symptoms and signs by age groups ($p>0.05$).

Fiberoptic bronchoscopic examination was performed in 33.3% (11/33) of patients due to recurrent wheezing and respiratory tract infections. Tracheomalacia was detected in six of the 11 EA patients, and refistulation was detected in one patient.

No significant correlation was found between gestational age, birth weight, postoperative invasive mechanical ventilation (MV)

Table 3: Rates of respiratory symptoms and signs by age groups

	Aged ≤5 Total n=18 n (%)	Aged >5 Total n=15 n (%)	p
Cough	14 (77.7)	14 (93.3)	0.215
Wheezing	10 (58.8)	7 (46.6)	0.492
Recurrent pneumonia	4 (22.2)	4 (26.6)	0.767
Respiratory distress episode (Mean±SD)	2.9±2.3	4.8±5.9	0.515
Hospitalization due to respiratory problems (Mean±SD)	3.36±2.5	4.2±3.3	0.747

SD: Standard deviation.

requirement, and EA type with cough, wheezing, recurrent pneumonia, number of respiratory distress episodes in the past year, or number of hospitalizations due to respiratory problems. Similarly, no significant correlation was found between the length of stay in the neonatal intensive care unit (NICU) and coughing, wheezing, or recurrent pneumonia (Table 4).

Dysphagia was present in 24 patients (72.7%). Among these patients, 87.5% (21/24) had coughing, 54.1% (13/24) had wheezing, 25% (6/24) had recurrent pneumonia, 70.8% (17/24) had a history of respiratory distress, and 62.5% (15/24) had a history of hospitalization due to respiratory problems. Eighteen patients (54.5%) had a history of esophageal stricture. Among these patients, 55.5% (10/18) had a history of cough, 61.1% (11/18) had wheezing, 22.2% (4/18) had recurrent pneumonia, 72.2% (13/18) had a history of respiratory distress, and 55.5% (10/18) had a history of hospitalization due to respiratory problems. When comparing patients with and without dysphagia or stricture, no significant difference was found in the frequency of respiratory symptoms and findings (Table 5).

Overall, 72.7% (24/33) of patients had symptoms and findings consistent with GERD, and 29.1% (7/24) of these patients underwent anti-reflux surgery. Among patients with GERD, 87.5% (21/24) had cough, 54.1% (13/24) had wheezing, 20.8% (5/24) had recurrent pneumonia, 70.8% (17/24) had a history of respiratory distress, and 62.5% (15/24) had a history of hospitalization due to respiratory problems. There was no significant difference in the frequency of respiratory symptoms and findings between patients with and without GERD (Table 5).

The frequency of respiratory symptoms and findings was evaluated between the 24 EA patients diagnosed with GERD and the control group. There was no significant difference in the rates of chronic cough and wheezing complaints between the patient and control groups. However, the hospitalization rate due to respiratory problems was higher in the patient group (62.5%) compared to the control group (25%) (p=0.013). The rate of aspiration pneumonia history was also higher in the patient group (27.2%) than in the control group (5%) (p=0.045) (Table 6).

The rate of asthma diagnosis was 37.5% (9/24) in the patient group and 40% (8/20) in the control group. PFT data were obtained from 15 EA patients and 18 control patients who underwent the test. According to spirometry, the mean FVC (62.3%±17.8 of predicted, mean±SD), FEV_1 (66.5%±19.2 of predicted, mean±SD), and $FEF_{25–75\%}$ value (75.1%±28.3 of predicted, mean±SD) were lower than those in the control group (p<0.001) (Fig. 1). The early reversal test was positive in nine of 15 patients (60%) and six of 17 controls (35%) ($\Delta FEV_1 \geq 12\%$). There was no statistically significant difference between the groups (p=0.065).

When ventilation patterns were compared between the groups, a mixed type was detected in eight (53.3%) patients, a restrictive type in four (26.6%) patients, and an obstructive type in one (6.6%) patient. The number of normal ventilation patterns was significantly higher in the control group (p=0.001) (Fig. 2).

The median total IgE level was higher in the control group than in the patient group (control group median 32.8 IU/L [IQR:43.3], patient group median 5.5 IU/L [IQR:16.7]) (p=0.004). The median eosinophil percentage was also higher in the control group (control group median 3.1% [IQR:2.3], patient group median 2.2% [IQR:2]) (p=0.023).

House dust mite (*D. farinae*)-specific IgE measurements were higher in the control group (control group median 0.35 [IQR:2.76], patient group median 0.1 [IQR:0]) (p=0.030). No significant correlation was found between house dust mite-specific IgE measurements and cough, wheezing, or annual respiratory distress attacks (p=0.946, p=0.763, p=0.083).

Table 4: The relationship between the respiratory symptoms and findings of the patients and gestational age, birth weight, neonatal NICU length of stay, post-operative invasive MV requirement, and EA type

p	Cough	Wheezing	Recurrent pneumonia	The number of episode*	The number of hospitalization**
Gestational age	0.905	0.946	0.746	0.930	0.493
Birth weight	0.698	0.704	0.810	0.841	0.409
Length of stay at NICU	0.546	0.664	0.333	0.621	0.303
Post-operative invasive MV	0.508	0.809	0.212	0.655	0.201
EA type	0.072	0.078	0.242	0.156	0.495

*: The number of respiratory distress episodes in the past year; **: The number of hospitalizations due to respiratory problems; NICU: Newborn intensive care unit; MV: Mechanical ventilation; EA: esophageal atresia.

Table 5: The relationship between the respiratory symptoms and signs and the presence of surgical complications, tracheomalacia, and chest deformity

p	Cough	Wheezing	Recurrent pneumonia	The number of episodes	The number of hospitalizations
Stricture	0.478	0.162	0.767	0.399	0.099
Dysphagia	0.488	0.538	0.868	0.712	0.154
GERD	0.778	0.380	0.456	0.492	0.263
Tracheomalacia	0.943	0.100	0.793	0.283	0.452
Chest deformity	0.208	0.810	0.763	0.270	0.387

GERD: Gastroesophageal reflux disease.

Table 6: The rates of respiratory symptoms and signs between the EA patients with GERD and control groups

	EA patients with GERD (n=24) n (%)	Control group (n=20) n (%)	p
Chronic cough	7 (29.1)	4 (20)	0.669
Wheezing	13 (54.1)	10 (50)	0.532
Respiratory distress episode	17 (70.8)	10 (50)	
Hospitalization due to respiratory problems	15 (62.5)	5 (25)	**0.013**
Aspiration pneumonia	9 (27.2)	1 (5)	0.045

EA: Esophageal atresia; GERD: Gastroesophageal reflux disease.

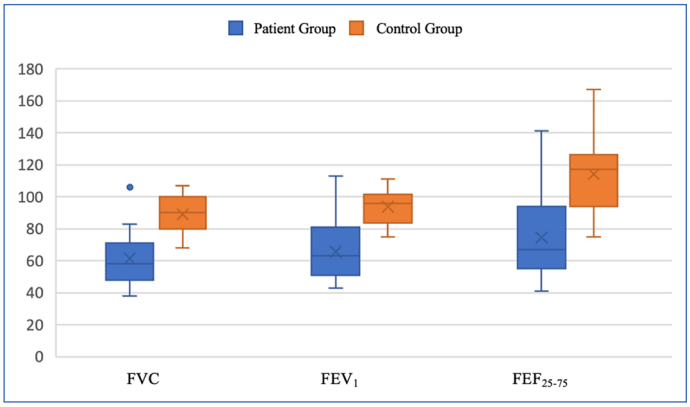

Figure 1: PFT/spirometry results in the graphic of patient and control group (p<0,001).

FVC predicted % patient group 62.3±17.84-control group 89.0±12.39; FEV_1 predicted % patient group 66.57±19.23-control group 93.82±10.88; FEF_{25-75} predicted % patient group 75.1±28.3-control group 114.1±25.7.

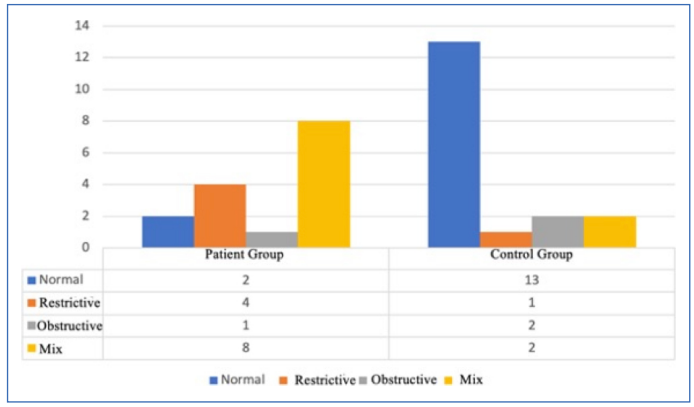

Figure 2: Pulmonary function disorders in the patient and control groups.

DISCUSSION

Respiratory problems in children with EA are structural and functional in nature and are quite widespread. However, we did not observe an increase in respiratory problems among those with esophageal stricture or dysphagia. Children with EA experienced more aspiration pneumonia and were hospitalized more often than the control group. In children with EA and asthma symptoms, we observed that an allergic etiology was not predominant.

In our study, 84.8% of patients had a history of at least one emergency department visit due to recurrent cough, 21.2% due to chronic cough, 51.5% due to wheezing, and 63.6% due to respiratory distress. The median number of emergency department visits per year for respiratory issues was 1 (IQR: 3). Similarly, 24.2% of patients had experienced ≥3 episodes of pneumonia in the past year, 63.6% had a history of hospitalization due to respiratory problems at least once in their lives, and the median number of hospitalizations was 1 (IQR: 3) per year.

Respiratory symptoms and findings were observed at similar rates in patients under and over 5 years of age. No significant correlation was found between gestational age, birth weight, length of stay in the

NICU, postoperative mechanical ventilation requirement, type of EA, presence of surgical complications, tracheomalacia, chest deformity, and respiratory symptoms or findings. Similar results have been reported in most previous studies.[2,8,12,13]

Although the etiology of respiratory complications in EA is not fully understood, it is believed to be multifactorial.[6,7,14,24–28] Surgery-related pathologies and associated structural and functional abnormalities are thought to contribute to the development of short- and long-term respiratory complications.[25,27] Therefore, respiratory complications have been associated with upper airway anomalies, gastrointestinal issues (such as GERD, esophageal motility disorder, and esophageal stricture), dysphagia, aspiration, and lower airway pathologies.[6,7,10,14]

In a meta-analysis, the overall prevalence of chronic cough and wheezing was reported as 14.6% and 34.7%, respectively, based on data from six different studies.[9] In a study conducted by Cartabuke et al.[29] on 43 patients with an average age of 8 years, the prevalence of cough and wheezing was reported as 72.1% and 53.5%, respectively. In our study, 84.8% of patients had recurrent cough, 51.5% had wheezing, and 21.2% had chronic cough. In a study conducted by Chetcuti et al.[17] on 334 patients aged 1–37 years who underwent EA repair, it was found that chronic cough decreased with age, but the frequency of wheezing remained similar. In a retrospective study conducted by Little et al.[25] on 69 patients, it was observed that the frequency of respiratory tract infections decreased with age. In our study, the similarity in respiratory findings such as cough and the number of respiratory tract infections between age groups can be attributed to the fact that the median age of our patient group was lower than that of other studies. Additionally, we did not find any association between respiratory symptoms such as coughing, wheezing, and recurrent pneumonia and conditions like esophageal stricture, dysmotility, GERD, tracheomalacia, and chest deformity.

Asthma diagnosis and respiratory distress attacks are quite common during the follow-up of patients with EA. In a systematic review on respiratory complications conducted by Sistonen et al.,[28] the prevalence of asthma diagnosed by a physician during childhood and adolescence was reported to be between 12% and 29%. In a study by Malmström et al.[30] (mean age 13.8 years), the prevalence of patients diagnosed with asthma by a physician and experiencing wheezing episodes was reported as 22%. However, histopathological features in biopsy samples obtained through bronchoscopic examination were not consistent with asthma, and findings indicative of chronic bronchial inflammation were identified. In our study, we also did not find a relationship between an allergic background and the etiology of asthma in EA cases. This finding supports the notion that asthma-like clinical findings in EA patients do not reflect the histopathological features of asthma, do not develop on an allergic background, and may be related to chronic bronchial inflammation.

Recurrent pneumonia is among the other common respiratory complications in EA patients. According to a meta-analysis conducted by Connor et al.,[9] the prevalence of recurrent pneumonia ranged from 9.5% to 51.5% (with an estimated average prevalence of 24.1%) across different age groups. In two different studies, the incidence of pneumonia decreased with age.[17,25] In a case-control study by Pedersen et al.[13] (mean age 10.2 years), the proportion of patients with a history of three or more episodes of pneumonia was 54.2%. The median age of our patients was also low, similar to the sample in the latter study, indicating that the incidence of pneumonia and wheezing is currently high but may decrease with age.

Hospital admissions due to respiratory problems, like other respiratory symptoms, are also on the rise. In a multicenter study conducted by Sulkowski et al.[31] on 2,887 patients, the rate of hospital admission with a diagnosis of pneumonia within the first two years after surgery was 12.7%. Additionally, 25.7% of these patients were hospitalized three or more times during follow-up. In a study by Chetcuti et al.,[17] the hospitalization rate due to respiratory problems was 73% in children under five years of age and approximately 28% in those over five years of age. In our study, the rates of recurrent pneumonia and hospitalizations were similar in both the under-five and over-five age groups. We did not observe a decrease as seen in other studies.

Perhaps we should take a moment to reflect and emphasize that infection control is a priority issue for patients with EA and that vaccination and awareness are important. In a study by Malmström et al.,[30] 54% of patients had a positive skin prick test; however, this was not significantly associated with bronchial reactivity.

Pedersen and colleagues found no significant association between obstructive dysfunction and sensitivity in their patient group.[13] In our study, the median total IgE level and eosinophil percentage were quite low in the patient group, and no sensitivity to house dust mites (*D. farinae*) was detected. There was no significant correlation between respiratory complications and total IgE levels, eosinophil counts, or sensitivity to house dust mites. Based on this finding, we can reemphasize that non-allergic factors also play a role in the etiopathology of asthma in these patients.

In a case-control study conducted by Pedersen and colleagues, the control group consisted of children diagnosed with GERD. A history of recurrent pneumonia and respiratory symptoms were significantly more common in the control group.[13] The findings of this study were not in accordance with those of Pedersen et al.[32] A higher number of hospital admissions and a greater incidence of aspiration pneumonia were observed in the EA patient group in comparison with the control group. Therefore, we can conclude that it is essential to investigate the presence of comorbid conditions, other than reflux, that may trigger respiratory symptoms and aspiration pneumonia. We believe that studies evaluating swallowing dysfunction may shed light on this issue.

In situations where multiple respiratory events are intertwined, it is natural to expect impaired respiratory function tests.[28,30] In a study by Sistonen and colleagues, obstructive and restrictive disorders were observed equally in 21% of patients, while both ventilation patterns were present in 36%.[28] In a study by Legrand and colleagues, PFTs were performed on 36 children, and obstructive disorders were detected in 50% of cases, while restrictive disorders were detected in 11%. However, no significant association was found between respiratory disorders and accompanying anomalies or esophageal pathologies.[5] In our study, restrictive, obstructive, and mixed respiratory disorders were detected in 26%, 6.67%, and 53.3% of patients, respectively. Although obstructive disorders were predominant in the study by Legrand and colleagues, no association was detected between these disorders and accompanying anomalies

or esophageal pathologies. However, both in Sistonen's study and in ours, restrictive and mixed patterns of dysfunction were predominant. These findings suggest that restrictive issues are not negligible and that factors such as chronic lung parenchymal damage and chest wall deformities may also play a role. This is because the disorder cannot be explained solely by airway narrowing or obstruction by secretions accompanied by asthma. In our study, the respiratory function of EA patients diagnosed with GERD was found to be lower than that of the control group diagnosed with GERD. This suggests that other clinical pathologies related to the primary disease, aside from GERD, may contribute to the etiology of long-term respiratory problems.

More accurate and reliable results can be obtained by including a larger number of patients and utilizing tests such as respiratory muscle strength measurement, IOS (impulse oscillometry system), and Lung Clear Index (LCI) to clarify this issue.

This study has several limitations, including a small sample size, missing data, and variability in the reporting of results. The limitations are attributed to the collection of retrospective data from a single institution and the potential for changes in surgical techniques and perioperative approaches over time. Since our clinic did not have a device such as IOS that could successfully measure lung function in patients under the age of five, PFT could only be performed in patients over the age of six. Finally, it was thought that patients with respiratory complaints were more willing to participate in the study, while those without respiratory complaints were reluctant (families expressed this during telephone interviews). This may have created a bias in the study population.

An important aspect of our study is that it highlights the importance of a multidisciplinary approach and follow-up for many respiratory problems.

CONCLUSION

Respiratory problems in children with EA are structural and functional in nature and are quite widespread. We would like to emphasize the importance of conducting research using more detailed respiratory tests, such as IOS, LCI, and functional assessment of swallowing, in larger patient series to obtain clearer data on this subject.

Statement

Ethics Committee Approval: The Istanbul Medeniyet University Goztepe Training and Research Hospital Ethics Committee granted approval for this study (date: 15.08.2018, number: 2018/0318).

Informed Consent: The research process began after parents were provided with detailed information and gave informed consent via the "Informed Consent Form."

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

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Use of AI for Writing Assistance: We acknowledge that we employed ChatGPT 3.5 and 4 to assist us in refining the clarity of our writing while developing the draft of this case report. We always maintained continuous human oversight(editing and revising) and verified the artificial intelligence-generated output. We never used AI to find, locate, or review the literature or resources, summarize the articles, analyze the selected articles, or synthesize the findings. The authors completed all analyses with higher-level efforts.

Author Contributions: Concept – GP, SG; Design – GP, SG, SÇ, ÇUD; Supervision – GP, SG, SÇ, ÇUD; Resources – GP, SG, SCO; Materials – GP, SG, SÇ, ÇUD; Data Collection and/or Processing – GP, SG; Analysis and/or Interpretation – GP, SG; Literature Search – GP, SG, SCO, ZRO; Writing – GP, SG, SCO, ZRO; Critical Reviews – GP, SG, SCO.

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