PERINATAL JOURNAL

Original Article

Perinatal Journal 2023;31(2):157-163

Seasonal variation of hyperemesis gravidarum prevalence

Yusuf Dal[1], Şebnem Karagün[1], Hatun Çolak[2], Ayhan Coşkun[1]

[1]*Mersin University, Faculty of Medicine, Department of Obstetrics and Gynecology, Perinatology Department, Mersin, Türkiye*
[2]*Mersin University, Faculty of Medicine, Department of Obstetrics and Gynecology, Mersin, Türkiye*

Abstract

Objective: In this study, we aimed to predict the seasonal variation in the prevalence of hyperemesis gravidarum (HEG).

Methods: This study was based on the electronic records of 187 pregnant women diagnosed with HEG according to the inclusion and exclusion criteria between January 2014 and December 2022. The criteria used for the diagnosis of HEG were as follows; symptoms onset in early pregnancy, severe nausea and/or vomiting, decrease in eating and drinking, and limitation in daily activities. Demographic characteristics of the patients, laboratory results, type of follow-up, number of days of hospitalization for hospitalized patients, and year and season characteristics were recorded and compared according to the seasons.

Results: The minimum age of the patients was 18, and the maximum was 42 years. In the comparison of the seasonal distribution of HEG, autumn was significantly different from the other groups (p=0.046). The percentage of HEG did not change significantly according to the seasons (p=0.392). Hospitalization rates in the winter season were statistically significantly lower. We found that the duration of hospitalization was less in winter (p=0.14).

Conclusion: In our study, we determined that the seasons may affect the distribution of HEG and the rates and duration of hospitalization.

Keywords: Hyperemesis gravidarum, climatic changes, season, prevalence

Introduction

Hyperemesis gravidarum (HEG) is characterized by nausea and vomiting, fluid electrolyte and acid-base imbalance, dehydration, weight loss, and ketonuria in the early stages of pregnancy.[1]It is one of the most common reasons for hospital admission in the first trimester of pregnancy. For the definition of HEG, weight loss of more than 3 kilograms (kg) or 5% of weight loss and the occurrence of ketonuria with three or more episodes of vomiting in 24 hours are used.[2] In a study published in 2021, a standardization was made for the definition of HEG. They defined HEG as a condition that begins before 16 weeks of gestation in the early stages of pregnancy, characterized by severe nausea and/or vomiting, impaired eating and drinking, and severe limitation of daily activities. They concluded that it might provide further guidance in predicting disease prognosis.[3]

The etiology and pathophysiology of HEG are still controversial. Studies have shown that HEG has a multifactorial pathophysiological mechanism; factors such as hormonal, immunological, psychological, and genetic predisposition may play a role in its etiology.[4]

Seasonal features and weather changes can affect various medical conditions. It was found that certain weather patterns increase the likelihood of initiating migraine headaches in migraine patients.[5] Some factors have been identified for the etiology of HEG, but seasonal features are not mentioned in its etiology and epidemiology. Seasonal features affect the regions and populations.[6] The role of seasonal changes in HEG is unknown. The-

Correspondence: Yusuf Dal, Mersin University, Faculty of Medicine, Department of Obstetrics and Gynecology, Perinatology Department, Mersin, Türkiye, **e-mail:** dryusufdal@gmail.com , **Received:** April 12, 2023, **Accepted:** July 29, 2023

How to cite this article: Dal Y, Karagün Ş, Çolak H, Coşkun A. Seasonal variation of hyperemesis gravidarum prevalence. Perinatal Journal 2023;31(2)157-163 DOI: 10.59215/prn.23.0312013

ORCID ID: Y Dal 0000-0001-7162-4644; Ş Karagün 0000-0003-2339-1609; H Çolak 0000-0002-0557-1203; A Coşkun 0000-0002-2887-9649.

CETUS Publishing

re is not enough data in the literature on this subject. It is accepted that pregnant women may react differently to extreme heat or cold. Changes in ambient temperature have been associated with various obstetric complications. However, the physiological mechanisms underlying this condition are not fully understood. It is thought that changes in ambient temperature may affect health through systemic inflammatory and oxidative stress responses in the long and short-term.[7] Studies have found that preeclampsia cases occur more at lower temperatures and during dry seasons.[8-10] In a study conducted in Scotland, it was found that birth weight decreased when exposed to high temperatures in the early stages of pregnancy.[11] It was found that increased environmental temperature is associated with higher rates of GDM in approximately 1500 women screened for gestational diabetes mellitus (GDM).[12]

Studies on seasonal and climate changes emphasize the importance of these changes on the health of pregnant women. Maternal and fetal effects of environmental factors in different periods of pregnancy affect maternal and newborn health. In this study, we aimed to predict the seasonal variation in HEG prevalence using the assumption that seasonal characteristics may play a role in the emergence of HEG.

Methods

This study was conducted based on the electronic records of women hospitalized or followed up with HEG between January 2014 and December 2022 at Mersin University Faculty of Medicine, Department of Obstetrics and Gynecology, according to a cross-sectional research design. The study was approved by Mersin University Clinical Research Ethics Committee (Decision no: 2023/38). According to the inclusion and exclusion criteria, pregnant women with a single live pregnancy at 6-13 weeks of gestation were included in the study. The criteria for the diagnosis of HEG were the onset of symptoms in early pregnancy, severe nausea and/or vomiting, decreased eating and drinking normally, and limitation in daily activities.[3] Exclusion criteria were multiple pregnancies, smoking and alcohol use, gastrointestinal problems, psychiatric problems, eating disorders, thyroid disorders, urinary tract infections, and pregnancies with assisted reproductive techniques.

Information about the seasonal characteristics of Mersin province was obtained from the website of the General Directorate of Meteorology of the Republic of Turkey. Seasons; defined as winter, spring, summer and autumn.

Demographic characteristics [age, number of gravida and parity, gestational week at which HEG was diagnosed, body mass index (BMI)], laboratory results (hemoglobin, hematocrit, leukocyte, and platelet count, and ketonuria degree), type of follow-up (hospitalization or outpatient), number of days of hospitalization, year of diagnosis of HEG and seasonal characteristics were recorded from the medical records of the patients. Ketonuria levels were graded as +1, +2, +3, and +4. Hemograms and full urinalysis tests of all pregnant women who applied to our hospital with HEG were requested and recorded. No medication was administered to the patients before the laboratory tests. BMI was calculated based on the current weight at the gestational week at which the patient was diagnosed with HEG. Pre-pregnancy weights of the patients could not be reached because the amount of weight loss was entered as a percentage (less or more than 5%) in all records.

Statistical Package for the Social Sciences (Version 22, SPSS Inc., Chicago, IL, USA) was used to analyze the data. Kolmogorov–Smirnov test, Shapiro–Wilk test, and histograms were used to evaluate the normality of distributions. In the analysis of the data, the mean and standard deviation, median, minimum, and maximum values of the characteristics were used while performing the statistics in the continuous structure, and frequency and percentage values were used while defining the categorical variables. One Way ANOVA and Kruskal Wallis test statistics were used to compare the means of 4 independent groups. If there was a difference between the means in group measurements, pairwise comparisons were evaluated with Post-hoc ANOVA and Mann-Whitney U test with Bonferroni correction. One simple chi-square and chi-square test statistic were used to evaluate the relationship between categorical variables. The statistical significance level was taken as $p<0.05$.

Results

A total of 187 pregnant women who were diagnosed with HEG according to the inclusion and exclusion criteria were included in the study. The minimum age was 18 and the maximum was 42 years. The mean age and deviation were 28.17 ± 5.39, while the median value was 28 (Table 1). The distribution of other descriptive statistics is also given in Table 1.

Table 1. Descriptive statistics distribution.

Parameters	mean ± SD	Median(min-max)
Age (years)	28.17 ± 5.39	28 (18-42)
Gravidity	2.34 ± 1.52	2 (1-10)
Parity	0.9 ± 1.1	1 (0-8)
Gestational week	9.5 ± 2.7	9.1 (4.6-18.2)

Hemoglobin (g/dL)		12.4 ± 1.1	12.4 (8.4-15.6)
Hematocrit (%)		35.9 ± 3.1	36.0 (24.0-43.1)
Leukocytes (×10³/µl)		9.809 ± 2.484	9.600 (4.320-19.690)
Platelet (×10³/µl)		245.070 ± 64.276	233.000 (124.000-568.000)
Ketonuria		2.7 ± 1.0	3 (1-4)
Duration of hospitalization (days)		2.1 ± 2.8	1 (0-18)
BMI (kg/m²)		25.11±3.74	25.20 (17.63-36.00)
		n(%)	
Years	2014	18(9.6%)	
	2015	23(12.3%)	
	2016	24(12.8%)	
	2017	28(15.0%)	
	2018	32(17.1%)	
	2019	28(15.0%)	
	2020	8(4.3%)	
	2021	7(3.7%)	
	2022	19(10.2%)	
Seasons	Spring	52(27.8%)	
	Summer	53(28.3%)	
	Autumn	30(16.0%)	
	Winter	52(27.8%)	
Follow-up status	Outpatient	45(24.1%)	
	Hospitalized	142(75.9%)	

In the comparison of the seasonal distribution of HEG (Table 2); there was a statistically significant difference between seasons (p=0.046). According to the one-sample chi-square test, autumn was significantly different from the other groups in terms of HEG distribution.

In the comparison of demographic, clinical, and laboratory parameters according to the seasons in HEG (Table 3); there was no statistically significant relationship in terms of age, gestational week, number of gravida and parity, BMI, hemoglobin, hematocrit, leukocyte, thrombocyte, and ketonuria values, the total number of pregnant examinations and the percentage of HEG. A statistically significant difference was found in the distribution of the number of hospitalized patients according to the seasons (p=0.032). According to the post-hoc Chi-Square test with Bonferroni correction (p=0.003), hospitalization in winter was statistically significantly less than in other seasons. There was also a difference in the distribution of the length of stay according to the seasons (p=0.023). After the Kruskal Wallis test, it was the spring-winter subgroup that made this difference according to the Mann-Whitney U test with Bonferroni correction (p=0.14).

Table 2. Comparison of seasonal distribution of HEG.

Seasons	Spring(n=52)	Summer(n=53)	Autumn(n=30)	Winter (n=52)	p-value	p-value 1 vs. 2, 1 vs. 3, 1 vs. 4, 2 vs. 3, 2 vs. 4, 3 vs. 4
HEG distribution	27.8%	28.3%	16.0%	278%	**0.046**	0.922, **0.015,** 1.00, **0.012,** 0.922, **0.015**

Significant at the p<0.05 level. One sample chi-square test. Bold p values indicate statistically significant.

Table 3. Comparison of demographic, clinical, and laboratory parameters according to seasons in HEG.

Parameters	Spring (n=52)	Summer (n=53)	Autumn (n=30)	Winter (n=52)	p-value
	mean±SD	mean±SD	mean±SD	mean±SD	
Age (years)	29.08±5.49	27.87±5.02	29.07±6.02	27.06±5.18	0.197*
Gestational week	9.61±2.57	9.42±2.80	9.07±2.33	10.04±2.95	0.440*
BMI(kg/m²)	24.88±4.17	25.56±3.53	25.58±3.62	24.60±3.60	0.500*
Haemoglobin (g/dl)	12.60±1.15	12.33±1.15	12.45±1.20	12.34±1.08	0.613*

Haematocrit (%)	36.26±3.38	35.67±3.07	35.80±3.58	35.85±2.92	0.810*
Leukocyte (×10³/µl)	10.073±2.540	9.709±2.505	9.171±1.994	9.823±2.272	0.425*
Thrombocyte (×10³/µl)	241.404±51.141	232.566±72.577	260.400±54.890	252.635±70.679	0.204*
Total number of pregnant examinations	1972.55±478.87	1808.22±424.25	1662.88±275,17	1806.88±263.04	0.141*
	Median(min-max)	**Median(min-max)**	**Median(min-max)**	**Median(min-max)**	
Gravidity	2 (1-7)	2 (1-8)	2.5 (1-10)	2 (1-5)	0.133**
Parity	0 (0-3)	1 (0-5)	1 (0-8)	1 (0-4)	0.657**
Ketonuria	3 (1-4)	3 (1-4)	2 (1-4)	3 (1-4)	0.364**
Duration of hospitalization (days)	2 (0-15)	2 (0-13)	1 (0-13)	1 (0-18)	**0.023****
	n(%)	n(%)	n(%)	n(%)	
Number of inpatients	44 (84.6%)	43 (81.1%)	23 (76.7%)	32 (61.5%)	**0.032*****
	(%)	**(%)**	**(%)**	**(%)**	
HEG incidence percentage	2.60%	2.90%	1.80(%)	2.80%	0.392****

SD: Standard Deviation is significant at the p<0.05 level. * One Way ANOVA test, ** Kruskal Wallis test, *** chi square test, **** One sample chi square test. Bold p values indicate statistically significant.

Discussion

It is known that HEG is a multifactorial disease, but its etiopathogenesis is still not clear enough. HEG is one of the most common reasons for hospital admissions in the early stages of pregnancy. Therefore, factors that initiate or trigger HEG are important. Seasonal changes can affect societies socially and medically. Considering that seasonal changes may have an effect on HEG like other medical conditions, we examined the effects of seasonal changes on HEG prevalence in this study. We aimed to contribute to the literature as there are not enough studies on this subject. In this study, which investigates the seasonal variation in HEG, we found that the distribution of HEG was less in autumn, but the percentage of HEG did not change between seasons, and in winter, hospitalization rates and length of stay in days were different from other seasons.

There are studies in the literature about the effect of seasonal changes on obstetric populations. In a study investigating the seasonal variation in the prevalence of hypertensive diseases of pregnancy, it was found that this disease was most common in the winter months.[13] In another study, the prevalence of preeclampsia was found to be lowest in summer and highest in winter.[10] During the winter months, each 1 degree Celsius (°C) increase in mean temperature during the week before birth is associated with a 2% reduction in the risk of both preterm birth and preterm birth.[14] In a study investigating the diagnosis of GDM by the seasons, positivity rates were found to be higher in the summer months.[15]

Studies have shown that the thermogenic response in HEG may be different from normal pregnancies, and this may be caused by the increased mobilization of lipid storages. Serum non-esterified fatty acids increased in patients with fasting hyperemesis while the hands were kept in water at 15 °C for 50 seconds, and it was found that this situation was closely associated with weight loss.[16] In the study of Asakura et al., higher temperatures were found around the interscapular region in pregnancies complicated by HEG.[17] In a study investigating the thermoregulatory correlations of nausea, it was concluded that thermoregulatory symptoms may be the cause of the physiological basis of nausea in rats and musk shrews.[18] In the study of Kredel et al., it was concluded that temperature changes did not have a clinically significant effect on the incidence of nausea and vomiting after general anesthesia.[19] In another study, it was found that the weather may have some effect on the occurrence of postoperative nausea and vomiting, but seasonal changes did not have any effect on this symptom.[20] Although these findings are biologically acceptable, they cannot fully explain the relationships between ambient temperatures and HEG. In the study of Akgun et al., it was determined that climate and daily temperature changes did not change the HEG intensity.[21] In another study, no seasonal difference was observed in the distribution of HEG onset.[22] In our study, it was found that the distribution of HEG was significantly less in autumn, but the percentage of HEG did not change according to the seasons.

Seasons also affect the welfare of societies. In the study of Elongi et al., it was concluded that the effect of nutrition due to the decrease in agriculture in low-temperature conditions is an aggravating factor rather than the cause of preeclampsia.[9] Cold seasons affect access to food, but the contribution of nutritional factors to HEG is fully known. It is thought that psychological factors may also play a role in the etiology of HEG and that there may be a strong link between the increased incidence of anxiety and depression and HEG.[23] Physical activities decrease in cold weather and this may lead to anxiety and depression in pregnant women.[24] In their study, Akgun et al. found that hospitalizations due to HEG were higher in the winter months.[21] In our study, it was concluded that HEG increased only in winter compared to autumn and hospitalizations were less.

It is predicted that acute exposure to high or low-temperature changes may cause an increase in oxidative stress and inflammatory markers. Both animal and human studies have shown that this condition is associated with oxidative stress and systemic inflammation.[25,26] The relationship between obstetric pathologies in early pregnancy and inflammation has been investigated in different studies.[27] Although it is thought that there is a relationship between HEG and inflammation, this situation has not been clearly explained. In a study, inflammatory markers increased significantly in HEG patients.[28] In another study, it was concluded that there was no fully significant relationship between inflammation and HEG.[29] These findings do not fully explain the relationship between inflammatory events and HEG, which increases as a result of changes in ambient temperatures.

Ketonuria is the result of metabolic events occurring in HEG and is frequently used in the diagnosis of HEG. The relationship between the severity of HEG and ketonuria severity is not clear. Ketonuria is reported as a criterion in 60% of studies.[30] In one study, it was found that the level of ketonuria was associated with the length of hospital stay,[31] and in another study, it was concluded that ketonuria was not related to the severity of HEG .[32] In our study, the level of ketonuria was not used as a criterion for the severity of HEG, and we found that there was no significant change in the degrees of ketonuria according to the seasons.

The limitations of our study are its retrospective, single-center design, small sample size, and inability to compare pregnant women with HEG in other geographical regions. Conducting the study in a tertiary center and selecting higher-risk pregnancies to be included in the study are the strengths of the study. Another strength of our study is that a single diagnostic criterion was used for the diagnosis of HEG and the patients had not taken any medication before.

Conclusion

In conclusion, we found that seasonal characteristics may affect the distribution of HEG and the rate and duration of hospitalization in our study. This suggested the existence of seasonal risk factors such as food intake and transportation, and physical activity, which may be preventable. However, it is difficult to generalize these potential results because HEG mechanisms are complex and multifactorial, as environmental factors, seasons, and lifestyles can vary greatly between regions and populations. There are limited studies in the literature on the extent to which there may be a relationship between seasonal characteristics and HEG, and these issues deserve further research, especially with the onset of climate change. However, it may be useful to conduct large-scale prospective studies including other possible risk factors to confirm these results.

Conflict of Interest: There is no conflict of interest between the authors.

Funding: The authors have not disclosed any funding.

Data availability: Data availability is supplied up on request.

Ethical approval: All procedures performed in the current study involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments in 2000.

Consent to participate: Written informed consent was obtained from all participants.

References

1. Niebyl JR. Clinical practice. Nausea and vomiting in pregnancy. N Engl J Med. 2010;363(16):1544-50. [PubMed] [CrossRef]
2. Poursharif B, Korst LM, Macgibbon KW, Fejzo MS, Romero R, Goodwin TM. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. Contraception. 2007;76(6):451-5. [PubMed] [CrossRef]
3. Jansen LAW, Koot MH, Van't Hooft J, Dean CR, Bossuyt PMM, Ganzevoort W, et al. The windsor

definition for hyperemesis gravidarum: A multistakeholder international consensus definition. Eur J Obstet Gynecol Reprod Biol. 2021;266:15-22. [PubMed] [CrossRef]

4. Fell DB, Dodds L, Joseph KS, Allen VM, Butler B. Risk factors for hyperemesis gravidarum requiring hospital admission during pregnancy. Obstet Gynecol. 2006;107(2 Pt 1):277-84 [PubMed] [CrossRef]

5. Cooke LJ, Rose MS, Becker WJ. Chinook winds and migraine headache. Neurology. 2000;54(2):302-7 [PubMed] [CrossRef]

6. Goggins WB, Woo J, Ho S, Chan EY, Chau PH. Weather, season, and daily stroke admissions in Hong Kong. Int J Biometeorol. 2012;56(5):865-72 [PubMed] [CrossRef]

7. Cai J, Meng X, Wang C, Chen R, Zhou J, Xu X, et al. The cold effects on circulatory inflammation, thrombosis and vasoconstriction in type 2 diabetic patients. Sci Total Environ. 2016;568:271-7 [PubMed] [CrossRef]

8. Hounton SH, Sombie I, Townend J, Ouedraogo T, Meda N, Graham WJ. The tip of the iceberg: evidence of seasonality in institutional maternal mortality and implications for health resources management in Burkina Faso. Scand J Public Health. 2008;36(3):310-7 [PubMed] [CrossRef]

9. Elongi JP, Tandu B, Spitz B, Verdonck F. [Influence of the seasonal variation on the prevalence of pre-eclampsia in Kinshasa]. Gynecol Obstet Fertil. 2011;39(3):132-5 [PubMed] [CrossRef]

10. Immink A, Scherjon S, Wolterbeek R, Steyn DW. Seasonal influence on the admittance of pre-eclampsia patients in Tygerberg Hospital. Acta Obstet Gynecol Scand. 2008;87(1):36-42 [PubMed] [CrossRef]

11. Lawlor DA, Leon DA, Davey Smith G. The association of ambient outdoor temperature throughout pregnancy and offspring birthweight: findings from the Aberdeen Children of the 1950s cohort. Bjog. 2005;112(5):647-57 [PubMed] [CrossRef]

12. Retnakaran R, Ye C, Kramer CK, Hanley AJ, Connelly PW, Sermer M, et al. Impact of daily incremental change in environmental temperature on beta cell function and the risk of gestational diabetes in pregnant women. Diabetologia. 2018;61(12):2633-42 [PubMed] [CrossRef]

13. Taşın C, Bektaş K. Seasonal change of the prevalence of hypertensive disorders of pregnancy. Perinatal Journal. 2019;27(2):101-4--4 [CrossRef]

14. Ha S, Liu D, Zhu Y, Sherman S, Mendola P. Acute associations between outdoor temperature and premature rupture of membranes. Epidemiology (Cambridge, Mass). 2018;29(2):175 [PubMed] [CrossRef]

15. Cauldwell M, van-de-L'Isle Y, Watt Coote I, Steer PJ. Seasonal and SARS-CoV-2 pandemic changes in the incidence of gestational diabetes. Bjog. 2021;128(11):1881-7 [PubMed] [CrossRef]

16. Watanabe S, Asakura H, Power GG, Araki T. Alterations of thermoregulation in women with hyperemesis gravidarum. Arch Gynecol Obstet. 2003;267(4):221-6 [PubMed] [CrossRef]

17. Asakura H, Nakai A, Araki T. Correlations between interscapular deep temperature and plasma free fatty acid levels in pregnant women with hyperemesis gravidarum. Arch Gynecol Obstet. 2003;268(1):35-40 [PubMed] [CrossRef]

18. Ngampramuan S, Cerri M, Del Vecchio F, Corrigan JJ, Kamphee A, Dragic AS, et al. Thermoregulatory correlates of nausea in rats and musk shrews. Oncotarget. 2014;5(6):1565-75 [PubMed] [CrossRef]

19. Kredel M, Goepfert C, Bassi D, Roewer N, Apfel CC. The influence of the weather and the phase of the moon on post-operative nausea and vomiting. Acta Anaesthesiol Scand. 2006;50(4):488-94 [PubMed] [CrossRef]

20. Eberhart L, Jakobi G, Winterhalter M, Georgieff M. Einfluss von Umweltfaktoren auf das Auftreten von Übelkeit und Erbrechen in der postoperativen Phase. AINS-Anästhesiologie· Intensivmedizin· Notfallmedizin· Schmerztherapie. 2000;35(10):635-40 [PubMed] [CrossRef]

21. Akgun N, Misirligil S, Yegin GF, Keskin HL, Yavuz AF. Do Meteorological Variations and Climate Changes Affect Hyperemesis Gravidarum? Z Geburtshilfe Neonatol. 2022;226(5):304-10 [PubMed] [CrossRef]

22. Matsuo K, Ushioda N, Nagamatsu M, Kimura T. Hyperemesis gravidarum in Eastern Asian population. Gynecol Obstet Invest. 2007;64(4):213-6 [PubMed] [CrossRef]

23. Mitchell-Jones N, Lawson K, Bobdiwala S, Farren JA, Tobias A, Bourne T, et al. Association between hyperemesis gravidarum and psychological symptoms, psychosocial outcomes and infant bonding: a two-point prospective case-control multicentre survey study in an inner city setting. BMJ Open. 2020;10(10):e039715 [PubMed] [CrossRef]

24. Tucker P, Gilliland J. The effect of season and weather on physical activity: a systematic review. Public Health. 2007;121(12):909-22 [PubMed] [CrossRef]

25. Quindry J, Miller L, McGinnis G, Kliszczewiscz B, Slivka D, Dumke C, et al. Environmental temperature and exercise-induced blood oxidative stress. Int J Sport Nutr Exerc Metab. 2013;23(2):128-36 [PubMed] [CrossRef]

26. Cheng CH, Yang FF, Liao SA, Miao YT, Ye CX, Wang AL, et al. High temperature induces apoptosis and oxidative stress in pufferfish (Takifugu obscurus) blood cells. J Therm Biol. 2015;53:172-9 [PubMed] [CrossRef]

27. Dogru S, Atci AA, Akkus F, Erdogan AC, Acar A. Predictability of Hematological Parameters in the Diagnosis of Cesarean Scar Pregnancy. Journal of Laboratory Physicians. 2023 [CrossRef]

28. Soysal C, Işıkalan MM, Bıyık İ, Erten Ö, İnce O. The relationship between inflammation markers and ketonuria in hyperemesis gravidarum. J Obstet Gynaecol Res. 2021;47(9):3078-83 [PubMed] [CrossRef]

29. Dal Y, Akkuş F, Karagün Ş, Çolak H, Coşkun A. Are serum delta neutrophil index and other inflammatory marker levels different in hyperemesis gravidarum? J Obstet Gynaecol Res. 2023;49(3):828-34 [PubMed] [CrossRef]

30. Koot MH, Boelig RC, Van't Hooft J, Limpens J, Roseboom TJ, Painter RC, et al. Variation in hyperemesis gravidarum definition and outcome reporting in randomised clinical trials: a systematic review. Bjog. 2018;125(12):1514-21 [PubMed] [CrossRef]

31. Derbent AU, Yanik FF, Simavli S, Atasoy L, Urün E, Kuşçu UE, et al. First trimester maternal serum PAPP-A and free β-HCG levels in hyperemesis gravidarum. Prenat Diagn. 2011;31(5):450-3 [PubMed] [CrossRef]

32. Koot MH, Grooten IJ, Post J, Bais JMJ, Ris-Stalpers C, Naaktgeboren CA, et al. Ketonuria is not associated with hyperemesis gravidarum disease severity. Eur J Obstet Gynecol Reprod Biol. 2020;254:315-20 [PubMed] [CrossRef]