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Examination of Placental Dysfunction and Neonatal Outcomes in Hospitalized Patients who have Hyperemesis Gravidarum Diagnosis

Hiperemezis Gravidarum Tanılı Hastanede Yatan Hastalarda Plasental Disfonksiyon ve Neonatal Sonuçların İncelenmesi

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Abstract

Aim: Evidence on the effect of hyperemesis gravidarum (HG) on pregnancy outcomes is still unclear. In this study, placenta-related dysfunctions and neonatal outcomes in patients who were hospitalized with HG were retrospectively analyzed.

Material and Method: This study was conducted retrospectively among women who had singleton deliveries in our hospital between January 2015 and January 2020. As the case group, women with singleton pregnancies who were hospitalized due to HG and delivered were included. The control group consisted of women with singleton pregnancies who delivered without hospitalization due to HG. Through the hospitalization files of the patients who were hospitalized due to HG and not hospitalized due to HG, neonatal outcomes such as placental dysfunction, including gestational diabetes, gestational hypertension, preeclampsia, or stillbirth, and low birth weight, small for gestational age (SGA), preterm birth (PTB), the necessity for neonatal intensive care, 5-min Apgar scores, were examined.

Results: The mean gestational age was determined as 37.7±1.5 weeks in the HG group and 37.8±1.4 weeks in the control group. The mean week of gestation upon hospitalization for HG was 10.6±3.6 weeks. There was no significant difference between the groups regarding preeclampsia, PTB, postpartum hemorrhage, birth weight, GDM, or neonatal intensive care unit requirement. It was found that SGA babies with abnormal birth weights were seen more frequently in the deliveries of patients hospitalized for HG (P=0.022). The 5-min Apgar scores were higher in the deliveries of patients hospitalized for HG than in the control group (P=0.004).

Conclusion: It was concluded that hospitalizations due to HG do not pose a risk of placental dysfunction. Of the neonatal outcomes, SGA was more common in the infants of mothers with HG. Contrary to the expectations herein, the 5-min Apgar scores were higher in hospitalized patients for HG.

Keywords: Hyperemesis gravidarum, Placental dysfunction, Neonatal outcomes

Öz

Amaç: Hiperemezis gravidarumun (HG) gebelik sonuçları üzerindeki etkisine ilişkin kanıtlar hala belirsizdir. Bu çalışmada HG ile hastaneye yatırılan hastalarda plasenta ile ilişkili disfonksiyonlar ve neonatal sonuçlar retrospektif olarak incelenmiştir.

Gereç ve Yöntem: Bu çalışma Ocak 2015-Ocak 2020 tarihleri arasında hastanemizde tekil doğum yapan kadınlar arasında retrospektif olarak yapılmıştır. Olgu grubu olarak HG nedeniyle hastaneye yatırılıp doğum yapmış tekil gebeliği olan kadınlar alınmıştır. Kontrol grubu, HG nedeniyle hastaneye yatmadan doğum yapan tekil gebe kadınlardan oluşturuldu. HG nedeniyle hastaneye yatırılan ve HG nedeniyle hastaneye yatırılmayan hastaların yatış dosyaları aracılığıyla, gestasyonel diyabet, gestasyonel hipertansiyon, preeklampsi veya ölü doğum dahil olmak üzere plasenta disfonksiyonu ve gebelik yaşına göre küçük düşük doğum ağırlığı (SGA) gibi yenidoğan sonuçları), erken doğum (PTB), yenidoğan yoğun bakım gerekliliği, 5 dk Apgar skorları incelendi.

Bulgular: Ortalama gebelik yaşı HG grubunda 37,7±1,5 hafta, kontrol grubunda 37,8±1,4 hafta olarak belirlendi. HG nedeniyle hastaneye yatışın ardından ortalama gebelik haftası 10.6±3.6 haftaydı. Gruplar arasında preeklampsi, PTB, doğum sonu kanama, doğum ağırlığı, GDM, yenidoğan yoğun bakım gereksinimi açısından anlamlı fark yoktu. HG nedeniyle hastaneye yatırılan hastaların doğumlarında anormal doğum ağırlığına sahip SGA bebeklerin daha sık görüldüğü saptandı (P=0,022). HG nedeniyle hastaneye yatırılan hastaların doğumlarında 5 dk Apgar skorları kontrol grubuna göre daha yüksekti (P=0.004).

Sonuç: HG nedeniyle hastaneye yatışların plasental disfonksiyon riski oluşturmadığı sonucuna varıldı. Yenidoğan sonuçlarından SGA, HG'li annelerin bebeklerinde daha yaygındı. Buradaki beklentinin aksine HG nedeniyle hastanede yatan hastalarda 5 dk Apgar skoru daha yüksekti.

Anahtar Kelimeler: Hiperemezis gravidarum, Plasenta disfonksiyonu, Neonatal sonuçlar

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INTRODUCTION

Nausea, as well as vomiting during pregnancy, are conditions that are commonly seen and have adverse physical, metabolic, psychological, and social effects on a pregnant woman.[1,2] Hyperemesis gravidarum (HG), also known as morning sickness, usually occurs between the 6th and the 16th week of pregnancy, in the first trimester of pregnancy, and occurs at any time of the day. The increase in human chorionic gonadotropin (hCG) begins within the first four weeks following the last menstrual period (LMP) and peaks at the ninth week of pregnancy, and symptoms increase in parallel.[3] The prevalence of nausea is between 50% and 90%, while it was reported as 50% for vomiting and retching.[4,5] The degree and onset of nausea are related to the hCG level. Of pregnant women with emesis, 60% recover spontaneously at the end of the first trimester, and 91% recover by the 20th week of pregnancy.[6]

'Persistent and excessive vomiting starting before the 22nd week of gestation' was defined as the International Classification of Diseases (ICD)-9 and ICD-10 in accordance with the International Statistical Classification of Disease and Related Health Problems. HG is clinically classified as mild or severe according to associated metabolic disorders, including carbohydrate restriction-induced weight loss, dehydration, ketonuria, and electrolyte imbalance. These symptoms worsen in 0.3% to 1.5% of pregnant women, so pregnant women are treated after hospitalization.[7,8] In the etiology of hyperemesis, conditions with high hCG levels, such as thyroid hormones, estrogen, leptin, fetal-maternal barrier damage, helicobacter pylori infections, multiple pregnancies, and molar pregnancies, are listed as causes.[9,10]

The relationship between placental functions and HG is not fully understood. A suggestion has been made that an increase in hCG levels in women with hyperemesis impairs trophoblast invasion and also changes placental location. Results such as abnormal placenta, preeclampsia, postpartum hemorrhage, small for gestational age (SGA), and stillbirth were found to be associated with high hCG plasma levels, especially during the second trimester.[11,12]

An American cohort study reported that the babies of women who had HG had a birth weight that was significantly lower and was more likely to have SGA.[13] A recent meta-analysis conducted on 13 case-control, 10 cohort, and one cross-sectional study on the outcomes of HG and pregnancy found that pregnant women who had undergone HG had a 30% increased risk of preterm birth (PTB) and a 40% increased risk of SGA.[14]

In the literature, limited studies could be found on placental functions and neonatal outcomes in HG patients. The placental dysfunctions and neonatal outcomes of patients hospitalized with HG were examined in the present study in order to make a regional contribution to the literature on this subject.

MATERIAL AND METHOD

This study was conducted retrospectively among women who had singleton deliveries between January 2015 and January 2020 after obtaining ethical committee approval at our university hospital. Pregnant women hospitalized due to HG and went on to deliver accepted as the case group. The control group consisted of pregnant women who delivered without hospitalization due to HG.

In both groups, the patient's medical history, aspects of pregnancy [LMP, obstetric history (delivery type, gravida, parity, stillbirth, miscarriage)], blood pressure, and proteinuria were studied. Through the hospitalization files at the time of delivery of the patients who were hospitalized due to HG and not hospitalized due to HG, neonatal outcomes including placental dysfunction (gestational hypertension, gestational diabetes (GDM), preeclampsia, stillbirth) and low birth weight (LBW), SGA, fetal growth restriction (FGR), PTB, neonatal intensive care unit (NICU) requirement, and 5-min Apgar scores were examined.

In pregnancy, the classification of hypertensive disorders is done according to the definitions of the International Society for the Study of Hypertension in Pregnancy (ISSHP).[15] The definition of gestational hypertension is having a systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg, occurring twice for a woman without hypertension before the 20th week of pregnancy. The definition of proteinuria in patients who have gestational hypertension is a dipstick reading of 2+ in randomly taken urine samples. A preeclampsia diagnosis is made if proteinuria is present in women with gestational hypertension[16] and eclampsia is defined if one or more convulsions are present[17] >140/90 mm

Fetal loss before the 20 gestational weeks and/or weighing up to 500 g is considered as a miscarriage. The definition of SGA is a birth weight at the gestational age that is less than the 10th percentile of the US National Reference for Fetal Growth[18] LBW is defined as a birth weight below 2500 g, FGR is defined as less than the 10th percentile, estimated fetal weight is determined for the gestational age, and an abdominal circumference is below the 10th percentile.[19-20] Apgar scores are measured at the 5th and 10th min post-birth.[21] The outcome reported for the Apgar score is the postpartum 5-min score. Births before 37 weeks of gestation are considered preterm births.[22] The gestational age at birth is calculated as the number of days from the first day of LMP until the date of admittance to the delivery or operating room. The American College of Obstetricians and Gynecologists defined postpartum hemorrhage as cumulative blood loss that is ≥1000 mL or bleeding, in addition to symptoms of hypovolemia, within the first 24 h after delivery, regardless of the method of delivery used.[23]

HG exposure assessment: Severe HG requiring hospitalization included women with weight loss >5%[24] compared to their weight pre-pregnancy. Women with severe hyperemesis were defined by a maternal caloric deficit, electrolyte disturbance, and ketonuria.

Inclusion criteria: Patients who were hospitalized between the 4th and 21st week of gestation due to HG and gave birth at the same hospital and those with singleton pregnancies were included.

Exclusion criteria: Multiple pregnancies, molar pregnancies, pregnant women with hyperthyroidism were not included in the study. Chronic hypertensive patients and those diagnosed with type 1 or 2 diabetes before pregnancy, as well as those who smoked cigarettes while pregnant, were excluded.

Statistical Analysis

All the data collected for statistical analysis were analyzed using IBM SPSS Statistics for Windows 23.0 (IBM Corp., Armonk, NY, USA). The descriptive characteristics of the relevant variables were calculated. The continuous and categorical variables were presented as the mean±standard deviation, median, or number (%). Evaluation of whether the data had normal distribution was conducted with the Kolmogorov-Smirnov test. A comparison of the normally distributed data was conducted with the student t-test, while the non-normally distributed data was conducted with the Mann-Whitney U test. The chi-square or the Fisher exact test was used to evaluate the categorical data. Statistical significance was accepted as $P < 0.05$.

RESULTS

The group that was hospitalized for HG and the group that was not hospitalized for HG consisted of 61 patients (a total of 122). The age, gravida, parity, number of abortions, and gestational week were similar in both groups. Mean gestational age of 37. 7±1.5 weeks was determined in the HG group and (37.8±1.4 weeks) in the control group. No significant differences were observed between the groups regarding preeclampsia, birth weight, GDM, and neonatal intensive care requirement. The mean week of gestation upon hospitalization for HG was 10.6±3.6.

While the median value of the 5-min Apgar scores was 8 (min 3, max 9) for the HG hospitalized deliveries, it was 7 (min 4, max 9) in the control group (P=0.004).

When the abnormal birth weights were compared in the groups with and without HG hospitalization, there was no difference in LGA and FGR infants; however, it was found that SGA babies were more common in the deliveries of patients hospitalized for HG (P=0.022) (**Table**). No significant differences were observed between the groups regarding the frequency of preterm delivery and postpartum hemorrhage. There was no difference in the vaginal and cesarean delivery rates.

Table. Outcomes of patients with hyperemesis

	HG (n=61)	Control (n=61)	P-value
Age, years	29.7±5.6	28.3±5.3	0.178
Gravida	3 (1, 8)	3(1, 6)	0.549
Parity	1 (0, 3)	1 (0, 5)	0.258
Abort	0 (0, 5)	0 (0, 5)	0.386
Gestational week	37.7±1.5	37.8±1.4	0.711
Preeclampsia	5 (8.2)	4 (6.6)	0.729
Birth weight, g	3201.1±523.7	3143.4±516.5	0.541
GDM	8 (13.1)	7 (11.5)	0.783
Neonatal intensive care	8 (13.1)	6 (9.8)	0.570
5-min Apgar	8 (3, 9)	7 (4, 9)	0.004
Abnormal birth weight			
SGA	8 (13.1)	2 (3.3)	0.022
LGA	4 (6.6)	0 (0.0)	
FGR	4 (6.6)	2 (3.3)	
Delivery complications			
No complication	42 (68.9)	49 (80.3)	0.120
Preterm birth	18 (29.5)	10 (16.4)	
Postpartum hemorrhage	1 (1.6)	0 (0.0)	
Delivery type			
Vaginal	17 (27.9)	23 (37.7)	0.247
Cesarean	44 (72.1)	38 (62.3)	

Data are presented as the mean±standard deviation, median (minimum, maximum), and number (%). SGA: Small For Gestational Age LGA: Large For Gestational Age, FGR: Fetal Growth Restriction, GDM: Gestational Diabetes, HG: Hyperemesis Gravidarum
Significant P-values are indicated in bold.

DISCUSSION

In this study, it was found that HG did not cause a significantly decreased birth weight but increased the birth weights of infants diagnosed with SGA. Contrary to expectations, when the patients with and without HG hospitalization were compared, the 5-min Apgar scores were also higher in the infants hospitalized for HG. No relation between hospitalization for HG and gestational hypertension, preeclampsia, and other forms of placental dysfunction was found. The main finding of the current research was that HG that required hospitalization increased the birth weights of SGA infants. Bolin et al. found that a higher risk of prematurity and preeclampsia is seen when hyperemesis occurs during the second trimester.[24,25] It was determined that women hospitalized for HG were more commonly observed to have given birth prior to 38 weeks of gestation and gave birth to a child with LBW. Among more than 500,000 live births, the aforementioned American cohort study found that HG was related to SGA and LBW.[13] In a study conducted among 1.2 million singleton births, it was stated that HG increased the risk of PTB by 18%; however, no association was found with the risk of SGA or LBW.[26,27] Studies researching the relationship between HG and PTB have thus far been conflicting. In some studies, HG has been reported as a risk factor for PTB,[28,29] while others have reported that there is no effect[30] or the diagnosis of HG may protect against PTB due to high progesterone levels.[31] In the present study, however, no correlation was found between PTB and HG.

In a Canadian study, women with HG in singleton pregnancies had a 3-fold increased risk of PTB and LBW with a pregnancy weight gain of >7 kg and a five-fold increase in the risk of a 5-min Apgar score <7.[32] In the present study, no increased risk of PTB and LBW was observed in deliveries by patients who were hospitalized for HG, while there was an increase in SGA infant births in deliveries by patients who were hospitalized for HG. While the 1-min Apgar score indicated a necessity for instant resuscitation, the 5-min Apgar score has high clinical importance for the neonatal.[33] Therefore, the 5-min Apgar scores were examined. In this study, contrary to expectations, the 5-min Apgar scores were significantly higher than the control group in deliveries by patients hospitalized for HG. This finding was considered unreliable since changes in the Apgar scores are multifactorial and depend on monitoring during labor.

Although benign nausea and vomiting early in pregnancy are associated closely with temporarily elevated hCG levels, a suggestion was put forth that persistently elevated hCG levels in women with hyperemesis disrupt the regular trophoblast migration stimulation and, as a result, alter placentation.[34,35] In conclusion, abnormal placentation can cause placental dysfunction, which manifests clinically as gestational hypertension or preeclampsia, as well as miscarriage, stillbirth, and FGR.[36,37] While the risk of preeclampsia was increased by 1.6 times in pregnant women with HG in early studies,[26] studies conducted later did not show an increased risk.[30,38,39] The results that were obtained herein were unable to prove that severe HG causes an increased risk of placental dysfunction. No significant differences were observed between the groups regarding birth complications, and no difference was observed between postpartum hemorrhage and the delivery types.

Limitations of this study: The study design was retrospective, it included a relatively small number of patients, and the treatments and duration of these treatments received by the patients were excluded from use in the study.

CONCLUSION

HG is a disease associated with hospitalization, drug use, and lower quality of life. However, the findings of the current research suggested that HG has no significant effect on placental dysfunction disorders. Of the neonatal outcomes, SGA was more common in the infants of mothers with HG. However, due to the many different results in the literature and the limitations of this study, there is a need for studies that also examine prospective, broad-based, and long-term results.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission Necmettin Erbakan University Non-interventional Clinical Researches Ethics Committee (Date:18.12.2020, Decision No: 2020/29-46) .

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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