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Risk Factors of Prolonged Hospitalization in Patients with Hyperemesis Gravidarum

Hiperemezis Gravidarum Hastalarında Uzun Süreli Hospitalizasyonun Risk Faktörleri

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ABSTRACT

Purpose: To evaluate the risk factors of prolonged hospitalization in patients with hyperemesis gravidarum (HEG).

Material and Methods: The medical records of 114 patients who were admitted to the Zekai Tahir Burak Women's Health Education and Research Hospital with a diagnosis of HEG in the period January 2013 to June 2014 were analyzed retrospectively. Hospital stay of more than 4 days was considered as prolonged hospitalization. Ninety -three patients with HEG who needed hospitalization less than four days formed the control group and 21 patients with HEG who needed hospitalization equal to or longer than four days formed the study group. The variables regarding age, body mass index, week of pregnancy, number of parity, daily vomiting number, number of days in hospital, need of combined antiemetic use, complete blood count, biochemistry markers, hormone tests, urine analysis were evaluated to assess their relationship with the risk factors for prolonged hospitalization in patients with HEG.

Results: Twenty-one of 114 patients diagnosed with HEG had a prolonged hospital stay, with a mean stay of 5.1 days. Age, body mass index, week of pregnancy, need of using combined antiemetics, complete blood count parameters, liver and kidney function tests were not associated with the duration of hospitalization. Daily vomiting, maternal serum TSH levels and blood urea nitrogen levels were 2.4 ± 1.3 vs 4.2 ± 1.9; p= 0.01, 1.19 ± 0.71 vs 0.82 ± 0.67; p= 0.04, 21.2 ± 6.4 vs 18.1 ± 5.3; p= 0.03; respectively, and these differences were found to be statistically significant among groups. The serum maternal TSH < 0.1 µIU/mL and vomiting ≥ 5 per day were found to be significant indicators for longer hospitalization (OR = 4.05, 95%CI = 1.07-15.3; P <0.05, OR=9.55, 95%CI = 1.81-50.4 P <0.05; respectively).

Conclusion: Number of vomiting per day and maternal serum TSH levels could help physicians to estimate the risk of prolonged hospitalization; however further investigations are needed in large population studies. Identifying the high risk patients is important both for prevention of HEG and beginning appropriate antiemetic treatment to avoid complications to reduce the economic costs.

Key words: Hyperemesis gravidarum, risk factors, pregnancy, hospitalization

ÖZET

Amaç: Hiperemezis gravidarum (HG) hastalarında uzun süreli hospitalizasyonun risk faktörlerinin değerlendirilmesi.

Materyal ve Metod: Zekai Tahir Burak Hastanesinde Ocak 2013 ve Haziran 2014 tarihleri arasında HG tanısıyla hospitalize edilen 114 hastanın medikal kayıtları retrospektif olarak incelendi.. Hastanede kalış süresi 4 gün veya daha fazla olması uzun süren hospitalizasyon olarak tanımlandı. HG tanısını almış ve 4 günden az hastanede yatmış 93 hasta kontrol grubunu ve hastenede kalış süresi 4 gün veya daha fazla olan 21 HG tanılı hasta da çalışma grubunu oluşturdu. Yaş, vücut kitle indeksi, gebelik haftası, parite, günlük kusma sayısı, hastanede kalınan gün sayısı, kombine

antiemetik kullanma ihtiyacı, tam kan sayımı, biyokimyasal markırlar, hormonal testler ve idrar analizi sonuçlarıyla HG'lı hastaların hastanede uzun kalış süreleri arasındaki ilişki değerlendirildi.

Bulgular: HG tanısı almış ve uzamış hospitlizasyonu olan 21 hastanın ortalama hastanede kalış süresi 5,1 gün idi. Yaş, vücut kitle indeksi, gebelik haftası, kombine antiemetik kullanma ihtiyacı, tam kan sayımı, karaciğer ve böbrek testleri uzun süreli hospitalizasyonla ilgili bulunmadı. Günlük kusma sayısı, maternal serum TSH seviyeleri ve kan üre değerleri sırasıyla; 2.4 ± 1.3 vs 4.2 ± 1.9; p= 0.01, 1.19 ± 0.71 vs 0.82 ± 0.67; p= 0.04, 21.2 ± 6.4 vs 18.1 ± 5.3; p= 0.03 bulundu ve aradaki farklar istatistiksel olarak anlamlıydı. Maternal serum TSH seviyesinin 0.1 µIU/mL'in altında olması ve günlük kusma sayısının günde ≥ 5 olması HG' li hastalarda uzun süre hospitalizasyon riskini arttıran faktörler olarak bulunmuştur (OR = 4.05, 95%CI = 1.07-15.3; P <0.05, OR=9.55, 95%CI = 1.81-50.4 P <0.05; sırasıyla).

Sonuç: Günlük kusma sayısı ve maternal serum TSH seviyeleri klinisyenlere uzun hospitalizasyon için riskli olan HG' li hastaları belirlemede yardımcı olabilir ancak bu bulguların daha büyük populasyonları içeren çalışmalarla doğrulanması gerekmektedir. Yüksek riskli hastaların belirlenmesi antiemetik tedaviye erken dönemde başlanabilmesi açısından önemlidir, böylece hem HG bağlı komplikasyonlar hem de ekonomik maliyetler azalacaktır.

Anahtar Kelimeler: Hiperemezis gravidarium, risk faktörleri, gebelik, hospitalizasyon

INTRODUCTION

Nausea and vomiting in pregnancy (NVP) is a common displeasing condition during pregnancy. Most of the NVP cases resolve spontaneously as the pregnancy improves but a small percentage of cases progress to hyperemesis gravidarum (HEG) which result in dehydration and ketonuria and require hospitalization because of the persistent symptoms; compromised nutritional status and electrolyte imbalance[1].

NVP and HEG are associated with many risk factors like low maternal age, nulliparity, placental mass, hCG levels, twin pregnancy, helicobacter pylori infection and female sex of the fetus[2,3]. In a study by Cedergen et al., it was reported that lean body composition had an increased risk of antiemetic drug use and hospitalization because of hyperemesis in early pregnancy compared with normal weight women, while obesity was associated with a reduced risk[1].

In a recent meta-analysis in the USA, 68.8% of pregnancies were complicated with NVP, while the rate of HEG was 1.2%[4]. NVP is the most common indication for admission to the hospital in early pregnancy, and the second most common reason for hospitalization after preterm labor during pregnancy[5,6]. This condition not only affects the mother and the fetus adversely in sociological and physiological means, it also has an economical perspective.

In our study, we aimed to determine if there are risk factors that may help to estimate the length of hospital stay of patients with HEG.

MATERIAL and METHODS

The medical records of 114 patients who were admitted to the Zekai Tahir Burak Women's Health Education and Research Hospital with a diagnosis of HEG[7,8] in the period January 2013 to June 2014 were analyzed retrospectively. Hospital stay of more than 4 days was considered as prolonged hospitalization. Ninety -three patients with HEG who needed hospitalization less than four days formed the control group and 21 patients with HEG who needed hospitalization equal to or longer than four days formed the study group. Ethical approval for the entire study was obtained from the Ethics committee of Zekai Tahir Burak Women's Health Education and Research Hospital. This is a tertiary referral research and education hospital in Ankara, Turkey.

The variables regarding age, body mass index, week of pregnancy, number of parity, daily vomiting number, number of days in hospital, need of combined antiemetic use, complete blood count, biochemistry markers, hormone tests, urine analysis were evaluated to assess their relationship with the risk factors for prolonged hospitalization in patients with HEG. All patients were ordered a treatment regimen of hydration and

antiemetics and the wellbeing of the patients were decided upon the laboratory results on follow-up and the regression of the symptoms. Hospital stay of more than 4 days was considered as prolonged hospitalization.

The mean and standard deviation were calculated for continuous variables. The normality of the variables was analyzed by the Kolmogorov–Smirnov test. Student's t test and the Mann–Whitney U test were used to evaluate associations between the categorical and continuous variables. Chi-square test or Fisher Exact tests were used to compare difference between groups for categorical variables. Multivariable logistic regression of the possible risk factors for prolonged hospitalization was performed in order to eliminate confounding factors using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

In this study 21 of 114 patients diagnosed with HEG had a prolonged hospital stay, with a mean stay of 5.1 days. Age, body mass index, week of pregnancy, need of using combined antiemetics, complete blood count parameters, liver and kidney function tests were not associated with the duration of hospitalization.

Daily vomiting, maternal serum TSH levels and blood urea nitrogen levels were 2.4 ± 1.3 vs 4.2 ± 1.9; p= 0.01, 1.19 ± 0.71 vs 0.82 ± 0.67; p= 0.04, 21.2 ± 6.4 vs 18.1 ± 5.3; p= 0.03; respectively, and these differences were found to be statistically significant among groups (Table 1). The serum maternal TSH < 0.1 µIU/mL and vomiting ≥ 5 per day were found to be significant indicators for longer hospitalization (OR = 4.05, 95%CI = 1.07-15.3; *P* <0.05, OR=9.55, 95%CI = 1.81-50.4 *P* <0.05; respectively) (Table 2).

Table 1. Risk factors associated with prolonged hospital stay in patients with HEG

	Hospitalization< 4 days (n = 93)	**Hospitalization ≥ 4 days (n = 21)**	**p**
Age (years)	26.6 ± 5.2	25.6 ± 4.0	0.32
BMI (kg/m^2)	23.7 ± 4.0	23.6 ± 4.1	0.91
Nulliparity	49 (52.7)	10 (47.6)	0.68
Week of pregnancy	9.6 ± 3.2	9.2 ± 3.3	0.62
Daily vomiting	2.4 ± 1.3	4.2 ± 1.9	0.01
Duration of hospitalization (day)	2.2 ± 0.71	5.1 ± 1.2	<0.01
Need of combined antiemetics *	20 (21.5)	7 (33.3)	0.25
AST [a] (U/L)	20.6 ± 15.8	27.7 ± 36.4	0.39
AST ≥45 U/L	11 (11.8)	3 (14.3)	0.76
ALT (U/L)	21.9 ± 33.7	23.9 ± 26.0	0.77
ALT ≥45 U/L	15 (16.1)	5 (23.8)	0.51
TSH (µIU/mL)	1.19 ± 0.71	0.82 ± 0.67	**0.04**
TSH < 0.1 µIU/mL	8 (8.6)	5 (23.8)	0.05
Free T3 (ng/dL)	3.25 ± 0.79	3.14 ± 0.39	0.35
Free T4 (ng/dL)	1.17 ± 0.46	1.09 ± 0.30	0.36

Blood urea nitrogen (mg/dl)	21.2 ± 6.4	18.1 ± 5.3	0.03
Creatinine (mg/dl)	0.53 ± 0.11	0.54 ± 0.11	0.64
Fasting plasma glucose (mg/dl)	96.7 ± 27.3	95.5 ± 23.5	0.85
Hemoglobin (g/dl)	13.1 ± 1.2	13.2 ± 0.93	0.73
WBC (cells/mm3)	8918 ± 3000	9145 ± 2205	0.69
Platelet (10^5/ mm^3)	1.73 ± 1.39	1.26 ± 1.55	0.17
Neutrophil-Lymphocyte rate	4.57 ± 3.0	4.10 ± 1.49	0.30
Urine ketone (mg/dl)	70.0 ± 53.4	93.8 ± 49.8	0.06

Values are given as mean ± standard deviation or median (minimum-maximum) or number (percentage), p<0.05= statistically significant.

*: Metoklopramid and ondansetron, WBC: white blood cells, HEG: hyperemesis gravidarum

Table 2. Risk factors associated with longer hospitalization in patients with HEG

Characteristics	Adjusted Odds ratio	Confidence Interval
TSH < 0.1 µIU/mL	4.05 a	1.07-15.3
BUN < 13 mg/dL	3.49	0.99-12.3
Urinary ketone ≥ 80 mg/dL	2.38	0.78-7.32
Vomiting ≥ 5 per day	9.55 a	1.81-50.4
Requirement for ≥ 2 antiemetics	0.88	0.21-3.71

TSH: thyroid stimulating hormone, BUN: blood urea nitrogen, [a] indicates p<0.0

DISCUSSION

Nausea and vomiting of pregnancy is the second most common diagnosis of antenatal hospitalization with a rate of 11.4% of indications and the mean hospital stay is 2.7 days[6]. Overall antepartum hospital admission rate with a diagnosis of hyperemesis was reported 0.8% in a large population-based cohort in Canada[3].

In a study by Piwko et al. the economic burden of nausea and vomiting in the USA was analyzed; estimated cost for drug treatment for mild and severe NVP were $40 and $267 respectively[9]. In the same study, the estimated total hospital cost associated with HEG was reported as an average of $12,453 per patient admission[9].

Management of NVP should start with identification of the high risk patients and prevention of HEG. Non-pharmacological approaches should be considered as a first step treatment like dietary recommendations; also the use of vitamin B_6 and ginger is usually effective in preventing the progression[10]. Relieving the symptoms and the support of the patient, treatment of dehydration and electrolyte imbalance and prevention of complications should be managed by physicians.

NVP progresses to HEG in less than 2% of the patients; which is characterized with excessive vomiting, causing to dehydration and electrolyte imbalance and weight loss of more than %5 of prepregnancy weight[11]. Fell et al. found maternal

age, smoking, psychiatric illness, preexisting maternal diseases like hyperthyroid disorders, diabetes mellitus, asthma, gastrointestinal disorders, previous molar pregnancy were risk factors for severe HG[3]. Psychiatric illness, depression, anxiety and development risk of cognitive, behavioral, and emotional dysfunction in pregnancy were more common amongst the patients with HEG[3,12,13]. Severe HEG can result with complications like dehydration, electrolyte imbalance, malnutrition, excessive weight loss, thrombosis, Wernicke's encephalopathy, thrombosis and poor fetal outcomes[2,14].

Previous studies have focused on the risk factors of HEG, maternal and fetal outcome, and risk factors for hospitalization. There is only one study in literature by Tan et al. determining the laboratory indicators for prolonged hospital stay; requesting hematocrit values of 41% or greater were independently associated with prolonged hospital stay[15]. In our study, we identified the risk factors suggested for hyperemesis and we analyzed if they could also have an association with the duration of hospitalization as well as the severity of HEG but the main risk factors determined for NVP like maternal age, nulliparity or BMI did not affect the hospital stay. Vomiting more than 5 times a day increased the risk of prolonged hospitalization 9.55 times while TSH < 0.1 µIU/mL increased the risk 4.05 times. Number of vomiting would be related with both psychological and physical consequences for the mother that may require longer observation. Hyperthyroid disorder; which is also suggested as a risk factor for severe HEG that increases the risk of the need for hospitalization should be assessed in every patient and treated[3].

Severity of hyperemesis would cause longer hospital stay, as well as higher costs for health expenses. The identification of patients with hyperemesis in risk for prolonged hospital stay will be beneficial for planning the treatment to reduce the hospital stay as well as the economic burden to the country.

CONCLUSION

NVP is very common in pregnancy and rarely progresses to severe hyperemesis that require hospitalization. Number of vomiting per day and maternal serum TSH levels could help physicians to estimate the risk of prolonged hospitalization; however further investigations are needed in large population studies. Identifying the high risk patients is important both for prevention of HEG and beginning appropriate antiemetic treatment to avoid complications to reduce the economic costs.

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