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MATERNAL-FETAL MEDICINE

Hyperemesis gravidarum affects maternal sanity, thyroid hormones and fetal health: a prospective case control study

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Abstract
Purpose Hyperemesis gravidarum (HG) is a condition of severe nausea or vomiting accompanied by various complications during pregnancy. In the present study, we aimed to demonstrate the effects of HG on mother and fetus health.
Methods Control and case group were arranged from 50 healthy pregnant women and 50 pregnant women with HG. Information about the participant women was gathered with data collection form and Beck's Depression Inventory (BDI) and State Anxiety Inventory (SAI) were administered to the women. Following an abortion or delivery, the data about birth complications and neonatal health were collected. All laboratory results (blood count, thyroid hormones, electrolyte values and biochemical parameters) were gathered from the laboratory information system used in the hospital.
Results It was found that in the case group, mean postpartum weight, serum hemoglobin, hematocrit and thyroid stimulant hormone levels were lower than control group ($p < 0.01$). Conversely, case group women have higher T3 and T4 levels than control group ($p < 0.01$). There was no significant difference between the two groups in terms of intrauterine growth retardation, low birth weight and abortion but it was observed that women with HG had often delivered prematurely. The mean scores of BDI and SAI in the case group were higher than those of control group.
Conclusion These results suggested that HG may have adverse effects on both mother and baby's health. Pregnant women with HG should be provided with training and consultancy services and be closely monitored in terms of anemia and thyroid hormones.

Keywords Pregnancy · Hyperemesis gravidarum · Biochemical effects · Depression · Anxiety

Introduction

Hyperemesis gravidarum (HG) is a condition of severe nausea or vomiting that requires hospitalization due to various complications during pregnancy. Nausea and vomiting are seen by nearly 50–80 % among all of the pregnancies. However, incidence of HG shows regional differences and it was between 0.5 and 2 % [1–3]. Although, the cause of HG is not known exactly, it is thought that hormonal, neurological, metabolic and psychosocial factors play a role in the etiology of HG [4]. It generally appears during the 7th and 12th weeks of the first trimester. It is argued that HG continues throughout the pregnancy in some cases [2].

HG causes fluid, electrolyte and acid–base imbalances as a result of weight loss and dehydration when it is clinically not controlled [5]. These disorders may get worse leading to hepatic and renal failures [6, 7]. On the other hand, Tan et al. [8] showed that HG caused transient biochemical hyperthyroidism. In the absence of treatment, it

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may also result in fetal complications due to malnutrition and dehydration [9]. Generally, these complications are intrauterine growth retardation (IUGR), low birth weight (LBW), congenital anomaly, premature labor and fetal death [7, 10]. Therefore, HG is a pregnancy complication that needs to be treated at an early stage [6, 11]. HG may cause not only physical outcomes but also many psychosocial problems by influencing quality of lives, marriages and partner's adaptation to the pregnancy [12]. It is interesting that there are few studies investigating HG effects on mother and fetus health in the literature and they have conflicting results. Some studies report that women who have depressive personality, conversion and poor social support before pregnancy suffer more from HG [13, 14]. Whereas, other studies report that women with HG suffer more from psychological problems such as anxiety and depression [15–17].

In the present prospective case control study, we aimed to investigate the effects of HG on mother's psychological health, blood parameters, physical characteristics and fetus health.

Materials and method

Groups

In the present study, case group was composed of 50 pregnant women (all volunteers) who were aged between 20 and 35 years, diagnosed with HG, attended to Pregnancy Follow-up Polyclinics of Hitit University Çorum Training and Research Hospital and were recruited with simple random sampling method. In the same way, control group was composed of 50 healthy pregnant women. Sample size was calculated with power analysis (80 % power). Pregnant women who are over 35 years of age or have any systemic diseases such as hypertension, heart diseases, chronic renal disease, thyroid disease, gastrointestinal system diseases, liver diseases and diabetes and molar pregnancy, cervical insufficiency or habitual abortus history and multiple pregnancy were not included in the study because these parameters were thought to affect the study results.

Ethical considerations of the research

Before the study, the ethical suitability of the research was approved by Ethical Council of the Medical Faculty of Bozok University (Protocol number: 29.04.2013/99). The Principles set out by the Declaration of Helsinki and national and local ethical guidelines for research were also followed. The necessary official permission from the hospital management was obtained for the pre-test phase and implementation phase of the research that was performed at the Hitit University Çorum Training and Research Hospital. All patients were informed about the purpose of the study with written documents and were told that the information would not be disclosed and their oral consents were obtained.

Data collection

The data of the study were gathered in two phases. In the first phase; all of the information about participant pregnant women regarding demographic information, obstetric examination findings and laboratory results were gathered using data collection form. Then, Beck's Depression Inventory (Version BDI-1A) and State Anxiety Inventory (Turkish version) were administered to all the subjects. The data of the second phase of the study were gathered when the women attended to the clinic due to an abortion or labor. In this phase, the data about birth complications and neonatal health were recorded. All participants filled the inventories themselves alone in noiseless test room. We performed inventories taking into account the literature for minimizing the bias [18].

Beck depression inventory (BDI)

BDI, developed by Beck (1960), is consisted of 21 statements and is used to objectively measure the degree of depression and physical, emotional, mental and motivational symptoms seen during depression. It was found out that test–retest reliability coefficient was 0.65 and split-half reliability coefficient was 0.78. All of the scores are added and depression score is obtained. The highest score of the inventory is 63 (21 × 3). A higher total score means a higher level or severity of depression. Scores obtained from the inventory can be evaluated as follows:

Score evaluation
0–9 normal
10–15 slight depression
16–23 moderate depression
24–63 severe depression

State anxiety inventory (SAI)

SAI has been developed by Spielberger et al. (1970) using "two-factor anxiety" theory of Spielberger [19]. SAI includes 20 questions addressing how a person feels in a specific situation and at a certain time. It was found out that test–retest reliability coefficient was 0.71 and split-half reliability coefficient was 0.86. "Almost never", "sometimes", "most times" and "almost always" are marked while the scale is answered according to the frequency of

the emotion, thought or behaviors in terms of what the items mean. There are reversed and non-reversed items. While the reversed items that signify positive emotions are scored. In non-reversed items that signify negative emotions, the answers scored with "4" demonstrate high anxiety. In the reversed items, answers scored with "4" demonstrate low anxiety while answers scored with "1" demonstrate high anxiety. State anxiety score is calculated by adding 50 to the difference between total weighted scores of the reversed and non-reversed scores. Higher scores mean higher anxiety levels while lower scores mean low anxiety levels. Scores $\leq$36 mean no anxiety, scores between 37 and 42 mean mild anxiety and scores $\geq$42 demonstrate high anxiety.

Statistical analyses

The data obtained from the study were assessed using SPSS 17.0 (SPSS Inc., Chicago, USA) package program. Mann–Whitney *U* test was used for the comparisons of the demographic and obstetric data, biochemical parameters and mean anxiety and depression scores. Chi-square test and Fisher's Chi-square test were employed in the comparisons of the data about birth complications and fetal health. A value of $p < 0.05$ was considered statistically significant.

Results

In the present study, it was observed that mean maternal age of the case group was 26.76 ± 3.50 years while the control group was 28.34 ± 3.46 years. There was no statistically significant difference between the case group and control group in terms of gestational age, gravida number and parity number as demonstrated in Table 1 ($p > 0.05$). Besides, it was noted that mean weight of the women in the case group after pregnancy was 58.42 ± 3.17 kg, which was lower by 7.42 % as compared to the women in the control group ($p < 0.01$). When the weights of the women in the pre-pregnancy period were compared, the difference between the groups was statistically insignificant ($p > 0.05$, Table 1).

Laboratory findings of the participant women in the case group and control group are shown in Table 2. When the findings were examined, it was found out that mean serum hemoglobin (Hb) level was 10.92 ± 1.32 g/dl and hematocrit (Htc) level was 34.88 ± 1.51 among the women of the case group. When these findings were compared to those of control group, it was noted that Hb level was lower by 26.61 % and Htc level was lower by 14.64 % ($p < 0.01$). No statistically significant difference existed between the two groups in terms of electrolyte (Na^+, K^+ and Cl^-) values and creatinine levels ($p > 0.05$). Although serum urea, AST and ALT levels of the case group were higher than the control group (10.4, 17.2 and 16.3 %, respectively), these differences were not considered important in clinical senses. Besides, mean serum thyroid stimulant hormone (TSH) level of the women of the case group was found to be 0.52 ± 0.56 μIU/ml, which was lower than the control group by 81.23 % ($p < 0.01$). Free T3 levels and free T4 levels of the thyroid hormones were found to be higher in the case group by 41.1 and 38.5 %, respectively. The difference between the groups was found to be statistically significant ($p < 0.01$).

The data concerning birth complications and fetus health of the women in the case and the control group were demonstrated (Fig. 1). According to this data, IUGR and LBW were seen in 10.0 % of the babies of the women in the case group while it was by 2.0 % those of the control

Table 1 Some demographic and obstetric characteristics in case and control groups

Parameters	Groups	
	Control	Case
Maternal age (years)	28.34 ± 3.46	26.76 ± 3.50
Gestational age (weeks)	20.68 ± 3.41	21.66 ± 2.60
Gravida number	1.52 ± 0.81	1.62 ± 0.64
Parity number	0.66 ± 0.87	0.62 ± 0.70
Weight before pregnancy (kg)	60.68 ± 2.73	60.78 ± 2.71
Weight after pregnancy (kg)	63.10 ± 2.57	58.42 ± 3.17*

The data were presented in mean ± SD

* Shows $p < 0.01$

Table 2 Laboratory parameters in case and control groups

Parameters	Groups	
	Control	Case
Hb (g/dl)	14.88 ± 1.22	10.92 ± 1.32*
Htc	40.86 ± 2.36	34.88 ± 1.51*
Na^+ (mmol/l)	135.22 ± 0.76	135.00 ± 0.93
K^+ (mmol/l)	3.80 ± 0.10	3.52 ± 0.26
Cl^- (mmol/l)	104.74 ± 0.60	102.79 ± 0.96
ALT (U/l)	17.08 ± 0.40	20.42 ± 1.31
AST (U/l)	17.40 ± 0.49	21.02 ± 1.25
Urea (mg/dl)	7.52 ± 0.65	8.40 ± 0.49
Creatinine (mg/dl)	0.53 ± 0.10	0.66 ± 0.06
TSH (μIU/ml)	2.77 ± 0.32	0.52 ± 0.56*
T3 (μIU/ml)	3.38 ± 0.49	5.74 ± 1.19*
T4 (μIU/ml)	1.18 ± 0.10	1.92 ± 0.07*

The data were presented in mean ± SD

* Shows $p < 0.01$

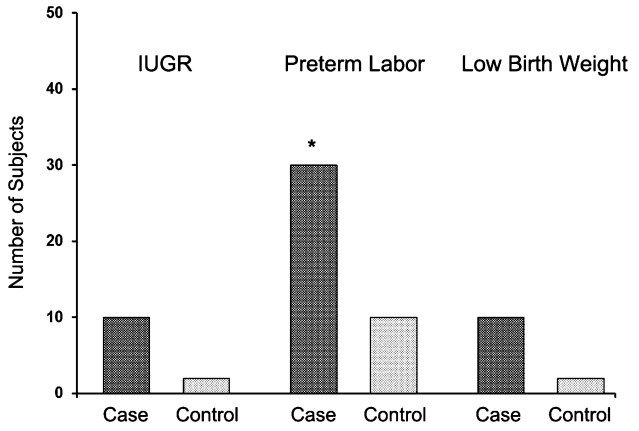

Fig. 1 Distribution of some characteristics of women in terms of birth complications and fetal health. *$p < 0.05$

group. Besides, pregnancy of one woman in the case group resulted in spontaneous abortion while no women in the control group had abortion. In addition, no babies of both the groups presented congenital anomaly. The difference between the two groups was statistically insignificant in terms of abortions, IUGR, LBW ($p > 0.05$), but significant in terms of preterm labor ($p < 0.05$).

We also evaluated the data about psychological status of the participant women. It was seen that mean BDI scores were 25.12 ± 4.16 in the case group and 9.72 ± 2.47 in the control group. Mean SAI scores were found to be 17.82 ± 5.25 in the case group and 10.42 ± 0.95 in the control group. The difference between the two groups was statistically significant when they were compared in terms of both BDI and SAI scores ($p < 0.01$).

Discussion

HG is a complication of severe nausea and vomiting that may lead to dehydration, fluid, electrolyte and acid–base imbalances. Therefore, if it is not controlled properly, it may cause serious complications in mothers and babies and psychosocial problems that influence quality of lives and partner's adaptation negatively. Taking this argument into consideration, we planned our study to investigate the effects of HG on mother's psychological status, blood parameters, physical characteristics and fetus health. According to the findings of the study; women in the case and the control groups showed similar distributions in terms of maternal age, gestational age, gravida number and parity number. This homogeneous distribution in demographic and obstetric characteristics—we thought—increased the reliability of our study.

It was noted that mean weight of the women in the case group after pregnancy was lower by 7.42 % compared to the control group and the difference was statistically significant ($p < 0.01$). According to the literature, HG is an important risk factor that causes dehydration and weight loss during pregnancy [5]. The study of Fejzo et al. [20] indicated that 26.2 % of the women with HG suffered from severe weight loss (>%15) and another study of Fejzo et al. [21] pointed out that nearly all of the recurrent HG cases (98.0 %) underwent weight loss in accordance with the findings of present study.

When the biochemical parameters in the present study were evaluated, it was detected that pregnant women with HG had statistically significant lower TSH and higher serum T4, serum T3 levels as compared to the control group. Increased thyroid activity and TSH suppression among the pregnant women were demonstrated before and this increase was linked by some researchers to the increase in human chorionic gonadotropin (hCG) because of its structural similarity with TSH [22]. On the other hand, some studies suggested that increased thyroid hormone levels were linked to the severity of nausea and vomiting among the women with HG [23, 24]. Biochemical hyperthyroidism that occurred among women with HG in our study supported previous studies and may have developed secondary to the increase in hCG. These findings may give some information about the prognosis of HG in the early period.

Hb and Hct levels in the case group were considerably lower than those of control group. It has previously reported that patients may suffer from nutritional deficiencies (vitamin, iron and mineral deficiencies) depending on the severity of the nausea and vomiting seen in HG [25]. Hb levels seen in our case group (10.9 ± 1.32 g/dl) were also lower than the normal references threshold (11.5 g/dl) and could be considered as anemia. Therefore, it may be concluded that patients with HG may be presented with such clinical problems as anemia and may pose serious risks in nutritional perspectives.

Although it is expected that the pregnant women with HG experience dehydration and electrolyte imbalance due to nausea and vomiting, electrolyte decreases in our study were not statistically significant [26]. Significant increases were seen in urea and creatinine levels but both parameters did not exceed the reference thresholds of these parameters. These findings suggested that dehydration in our case group was not so strong as to break liquid electrolyte balance. Changes in ALT and AST levels were considered within the analytic variability and it was not accepted as clinically significant because these levels did not exceed the reference thresholds.

HG may affect mothers' health negatively through causing malnutrition and dehydration. On the other hand it may lead to such fetal problems as IUGR, LBW, congenital anomaly, premature birth and fetal death and birth

complications [7, 10, 27]. Similar to the literature, our study demonstrated that babies of the women in the case group had more IUGR and LBW and more premature birth complications as compared with the babies in the control group. But only the difference concerning the premature birth was found to be statistically significant between the groups ($p < 0.05$). Besides, no congenital anomaly was seen in both groups. When the studies on this topic were investigated, it was seen that there were different results. In line with our study results, Roseboom et al. [28] reported that adverse pregnancy outcomes were more prevalent among women who had suffered from HG. Similarly, Dodds et al. [7] reported that infants born to women with hyperemesis and with low pregnancy weight gain (<7 kg) were more likely to be of low birth weight, small for gestational age, born before 37 weeks of gestation, and have a 5-min Apgar score of <7. In the same study, it was reported that LBW was 2.8 times higher and premature birth risk was 3.0 times higher among the babies of the pregnant women with HG. In the study of McCarthy et al. [29], it was suggested that serious HG increased premature birth risk. Unlike our study, Vikanes et al. [30] reported that HG did not affect LBW and premature birth rates. But similar to our study, they reported no congenital anomaly among the babies [30]. The difference in the results of the studies may result from the fact that they were conducted with women who had different demographic and obstetric characteristics and lived in different regions.

HG may affect quality of lives and adaption to the pregnancy of the women and thus lead to psychological problems. Main psychological problems experienced by women with HG are anxiety and depression [14–16]. Similar to the literature, our study demonstrated a positive correlation between HG and mean scores of BDI and SAI ($p < 0.01$). In light of this finding, it may be argued that the women with HG experienced more anxiety and depression than healthy pregnant women. When relevant studies are examined, it can be seen that there is an interaction between HG and psychological problems. Similar to our study, some studies reported that HG during pregnancy caused psychosocial problems [15, 16] whereas others point out that psychosocial problems undergone before pregnancy cause HG [13, 14]. Supporting our study results, McCarthy et al. [29] reported that women with HG had significantly higher mean State-Trait Anxiety Inventory, Perceived Stress Scale, Edinburgh Postnatal Depression Scale and limiting response to pregnancy scores compared to women without HG. Similarly, in the study of Şimşek et al. [12] women with HG had higher mean depression and anxiety scores than healthy pregnant women. These emotional changes in women with HG may be related to the increase of thyroid hormones. However, further studies are required to evaluate the underlying causes of emotional changes in HG.

As a result, women who are diagnosed with HG and are followed up at health facilities should be assessed not only physically but also psychosocially with a holistic approach. Pregnant women with HG should be provided with training and consultancy services and be closely monitored in terms of anemia and thyroid hormones. Our results emphasize the need for further studies supported by psychotherapy and more detailed biochemical parameters and assessing the regional variances to gain more information about the effects of HG on mother and baby health.

Conflict of interest There is no conflict of interest in relation to this article.

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