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MATERNAL-FETAL MEDICINE

Outcomes of pregnancies complicated by hyperemesis gravidarum

Oguzhan Kuru · Serhat Sen · Ozgur Akbayır · B. Pinar Cilesiz Goksedef · Mehmet Özsürmeli · Erkut Attar · Halil Saygılı

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Abstract
Objectives To evaluate maternal and fetal outcomes among women with hyperemesis gravidarum (HG).
Methods In a university hospital and a research and training hospital, a retrospective cohort study was conducted among women with singleton deliveries between 2003 and 2011. Maternal outcomes evaluated included gestational diabetes, pregnancy-induced hypertension, cesarean delivery. Neonatal outcomes also determined were 5-min Apgar score of less than 7, low birth weight, small for gestational age (SGA), preterm delivery, fetal sex, and stillbirth.
Results There were no statistical differences in the mean of age, parity, the number of artificial pregnancy, and smoking between two groups. Infants from HG pregnancies manifested similar birth weight (3,121.5 ± 595.4 vs. 3,164 ± 664.5 g) and gestational age (38.1 ± 2.3 vs. 38.1 ± 2.6 weeks), relative to infants from the control group ($p = 0.67$ and 0.91, respectively). In addition, no statistical significant differences were found in the rates of SGA birth, preterm birth, gestational diabetes, pregnancy-induced hypertension, and adverse fetal outcome between two groups ($p > 0.05$). Cesarean delivery rates were similar in two groups (31.9% in hyperemesis group vs. 27% in control group, $p = 0.49$). Comparing the gender of the newborn baby and Apgar scores less than 7 at 5 min, there were no statistically significant differences between two groups ($p = 0.16$ and 0.42, respectively).
Conclusion Hyperemesis gravidarum is not associated with adverse pregnancy outcomes.

Keywords Hyperemesis gravidarum · Pregnancy · Fetal outcome · Maternal outcome

O. Kuru (✉)
Department of Obstetrics and Gynecology, Kanuni Sultan Süleyman Research and Training Hospital, Seyidömer Mah. Köprülüzade Sok. No:5/4, Fatih, 34098 Istanbul, Turkey
e-mail: drokuru@yahoo.com

S. Sen
Department of Obstetrics and Gynecology, Süleymaniye Research and Training Hospital, Istanbul, Turkey

O. Akbayır
Kanuni Sultan Süleyman Research and Training Hospital, Istanbul, Turkey

B. P. C. Goksedef
Department of Obstetrics and Gynecology, Haseki Research and Training Hospital, Istanbul, Turkey

M. Özsürmeli · E. Attar · H. Saygılı
Department of Obstetrics and Gynecology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey

Introduction

Nausea and vomiting in pregnancy is the most common pregnancy complication, affecting more than half of all women during the first trimester of pregnancy [1]. Hyperemesis gravidarum (HG), usually differentiated from the more common nausea and vomiting experienced during pregnancy with the requirement of hospitalization, occurs in 0.3–2% of pregnancies [2, 3]. Although a number of etiologies have been suggested, the exact cause of HG remain unknown [4, 5].

Hyperemesis is often associated with maternal weight loss, nutritional deficiencies, fluid and electrolyte imbalances, so that concerns about possible adverse fetal and maternal outcomes are raised [6, 7]. Reported pregnancy outcomes in HG are somewhat conflicting. The majority of studies have concluded that there are no adverse affects of

HG on fetal outcome including gestational age, birth weight, incidence of prematurity, and Apgar scoring [8–10]. But some studies have reported lower birth weight associated with HG [11, 12].

In this study, we aimed to evaluate the relationship between HG and pregnancy outcomes in Turkish population. In addition, we described the characteristics of women who suffer from HG as well as the neonatal outcomes of their newborns.

Methods

Patient selection and exclusion criteria

The limit of viability was considered to be around 24 weeks. So, we used all data on singleton deliveries after 24 weeks of gestation or more and a birth weight above 500 g. We defined hyperemetic pregnancies as those with one or more antepartum hospitalizations for emesis, the first of which had to have occurred before 24 weeks of gestation. Singleton pregnancies with no symptoms of hyperemesis and delivered after 24 weeks of gestation or more and a birth weight above 500 g were selected for control group. All the babies were born in Istanbul Medical Faculty Hospital and Istanbul Kanuni Sultan Süleyman Research and Training Hospital which were all tertiary, referral centers in Istanbul, Turkey.

To act as controls, we matched 89 women who joined all the routine antenatal visits and delivered in our centers, who were not known to have HG. Controls were matched with study women taking into account age, parity, artificial pregnancy and smoking.

Exclusion criteria were: multiple or molar gestations, presence of pre-gestational diabetes, pre-gestational hypertension, and other causes of nausea such as appendicitis and pyelonephritis.

Data collection

The case files which were recorded in Istanbul University Istanbul Medical Faculty Hospital and Kanuni Sultan Süleyman Research and Training Hospital, between 2003 and 2010 were detected.

Demographic data of age (mean ± standard deviation), parital status (primiparous, multiparous), artificial pregnancy, smoking; fetal outcomes of birth weight (mean ± SD), small for gestational age (SGA, defined as the bottom tenth percentile for weight according to week of gestation and gender), preterm delivery (defined as birth before 37 weeks of gestation), fetal sex, Apgar score, stillbirth; maternal outcomes of mode of delivery (cesarean sectio, vaginal), gestational diabetes and pregnancy-induced hypertension were all obtained from the patients' medical records.

Routine antenatal care protocols and hospitalization criteria

Antenatal care was designed according to updated National Institute for Health and Clinical Excellence (NICE) guidelines. In both of the clinics, antenatal care was started before the eighth week of gestation. To be detailed, all pregnant women were screened for chromosomal anomalies by the first trimester and triple screening tests, and uterine and umbilical artery Dopplers performed for detecting the uteroplacental insufficiencies according to gestational age. Pregnancy-induced hypertension was routinely screened at every antenatal visit by checking blood pressure. Pregnancy-induced hypertension was diagnosed with blood pressure ≥140/90 mmHg on two occasions at least 4 h apart. Gestational diabetes was screened using clinical risk factors or 50 g 1-h oral glucose test between 24 and 28 weeks of gestation. Those screened positive underwent the 100 g 3-h oral glucose tolerance test with diagnosis for gestational diabetes according to the American Diabetes Association (ADA) criteria [13].

Decision making of hospitalization was depended on clinical evaluation and biochemical work-up. Accordingly in clinical evaluation, weight loss, oral medical therapy failure, lack of oral nutrition, clinical symptoms of dehydration were included. Biochemical parameters were: ketonuria above ≥+2, electrolyte imbalance (hyponatremia, hypokalemia), and azotemia. Loss of >5% of pre-pregnant weight was defined as weight loss. Persistent dehydration, electrolyte loss, oliguria, intractable nausea and vomiting despite the oral therapy were determined as oral medical therapy failure. Thirst, loss of appetite, dry skin, dark colored urine, fatigue, headache, decreased sweating and urination were included as clinical signs of dehydration.

Main outcomes

Fetal outcomes of birth weight (mean ± SD), SGA, gestational week at birth (mean ± SD), preterm birth, fetal sex, Apgar score, stillbirth; maternal outcomes of mode of delivery (cesarean section, vaginal), gestational diabetes, and pregnancy-induced hypertension were assigned as the main outcomes.

Ethics

Ethics Committee approval was obtained for this study.

Statistical analysis

Descriptive analysis was performed using SPSS 15.0 (SPSS, Chicago, IL, USA). Differences of the demographic data and obstetric outcomes were assessed with Student's *t* test to compare the normally distributed data. Chi-square

Table 1 Demographic characteristics of women with and without hyperemesis gravidarum

	Hyperemesis [$n = 72$ (%)]	Control [$n = 89$ (%)]	p value
Age (years) (mean ± SD)	27.9 ± 4.8	26.9 ± 5.2	0.19
Parity			0.10
Primiparous	37 (51.4)	57 (64)	
Multiparous	35 (48.6)	32 (36)	
Artificial pregnancy	2 (2.8)	1 (1.1)	0.44
Smoking	3 (4.2)	6 (6.7)	0.47

SD standard deviation

and Mann–Whitney *U* tests were used for categorized variables. $p < 0.05$ was considered as statistically significant.

Results

One hundred and sixty-one patients were analyzed for this study. Seventy-two of the patients had HG, 89 of the patients were assigned as control group. Table 1 summarized the demographic characteristics of women with and without HG. There were no statistical differences in the mean of age, parity, the number of artificial pregnancy and smoking between two groups ($p > 0.05$).

Pregnancy outcomes of women with and without HG are shown in Table 2. Infants from HG pregnancies manifested similar birth weight (3,121.5 ± 595.4 vs. 3,164 ± 664.5 g) and gestational age (38.1 ± 2.3 vs. 38.1 ± 2.6 weeks), relative to infants from the control group ($p = 0.67$ and 0.91, respectively). In addition, no statistically significant differences were detected in the rates of SGA birth, preterm birth, gestational diabetes, pregnancy-induced hypertension, and adverse fetal outcome between two groups ($p > 0.05$). Cesarean delivery rates were similar in two groups (31.9% in hyperemesis group vs. 27% in control group, $p = 0.49$). Comparing the gender of the newborn baby and Apgar scores less than 7 at 5 min, there were no statistically significant differences between two groups ($p = 0.16$ and 0.42, respectively).

Discussion

Reported pregnancy outcomes in HG are controversial. Kallen et al. and Bailit et al. [14, 15] reported pregnancies complicated by HG result in a decrease in birth weight, an increased rate of being SGA, fetal death in singleton pregnancies, and shorter gestation. Also, Veenendaal et al. [16] reported that HG is associated with a higher female/male ratio of offspring and a higher incidence of low birth weight, SGA and premature babies. But Bashiri et al. and Hallak et al. [10, 17] reported that pregnancies affected by HG have similar fetal outcomes. In our study, it was found that there were no significant negative results associated with HG compared to the control group in any of the outcomes we evaluated.

Although most studies have shown a reduction of mean birth weight with HG, we did not find any difference of mean birth weight in HG compared with control group [14, 18]. To be mentioned, the major risk factors of intrauterine growth restriction (IUGR) which may cause SGA that are chromosomal anomalies and uteroplacental insufficiency were already scanned in our study and no pathologic results were found in both groups. Conflicting data exist in the literature with regard to the relationship between HG and SGA. Roseboom et al. showed an association between being SGA and HG, but this is not supported by Dodds et al. In Dodds et al. study, HG were stratified into those with one or two admissions compared to those with three or more admissions and by maternal pregnancy weight gain (<7 vs. ≥7 kg). The risks of having a low birth weight infant and an infant SGA were higher in women with hyperemesis and who had weight gain less than 7 kg than in

Table 2 Pregnancy outcomes of women with and without hyperemesis gravidarum

	Hyperemesis [$n = 72$ (%)]	Control [$n = 89$ (%)]	p value
Birth weight (g) (mean ± SD)	3,121.5 ± 595.4	3,164 ± 664.5	0.67
SGA	5 (6.9)	12 (13.5)	0.16
GW at birth (weeks) (mean ± SD)	38.1 ± 2.3	38.1 ± 2.6	0.91
Preterm birth	8 (11.1)	12 (13.5)	0.65
Fetal sex			0.16
Female	44 (61.1)	45 (50.6)	
Male	28 (38.9)	44 (49.4)	
Gestational diabetes	4 (5.6)	3 (3.4)	0.49
Pregnancy-induced hypertension	2 (2.8)	9 (10.1)	0.67
Mode of delivery			0.49
C/S	23 (31.9)	24 (27.0)	
NSD	49 (68.1)	65 (73.0)	
Apgar score			0.42
<7	1 (1.4)	3 (3.4)	
≥7	71 (98.6)	86 (96.6)	
Stillbirth	0 (0)	1 (1.1)	0.36
Adverse fetal outcome	12 (16.7)	20 (22.5)	0.35

Adverse fetal outcome: prematurity (<37 weeks) and/or SGA and/or stillbirth

SD Standard deviation, *SGA* Small for gestational age, *GW* Gestational weight, *C/S* Cesarean delivery, *NSD* Normal spontan delivery

women without hyperemesis. Conversely, there was no difference in the rates of low birth weight and SGA among women with hyperemesis and weight gain of 7 kg or more compared with control group [19, 20]. The lack of our data on weight gain restricted us from analyzing the relationship between pregnancy weight gain and pregnancy outcomes among women with HG.

Preterm delivery rate and the mean gestational week of the birth were also similar to controls in our study. But Roseboom et al. [19] showed increased prematurity in HG. Interestingly in the study of Tan et al. [21], average gestation was marginally longer and preterm delivery rate was slightly lower in HG pregnancies compared to controls. It has also been shown that provided HG-affected women have adequate weight gain in later pregnancy, pregnancy outcome is similar to back-ground population [20].

The incidence of Apgar score <7 at 5 min in our study was low and no different from controls. Although Bailit [15] showed a higher fetal death rate in HG, stillbirth rate was similar to controls in our study.

Complicated pregnancy rates were similar in two groups. The rate of pregnancy-induced hypertension in HG was similar to controls in our study and this finding is consistent with the study of Tan et al., but is contrast to the finding by Roseboom et al. [19, 21]. This is largely explained by maternal characteristics. In our study, gestational diabetes rate in HG was no different to control like the findings of previous studies in the literature [17, 20].

Mode of delivery was no different from controls in contrast to Dodds et al. [20], which showed a higher cesarean delivery rate amongst HG.

Although large case control studies from Swedish and Danish birth registries showed a significant increase in the sex ratio of female to male, we did not find any gender difference between HG and control patients [22, 23].

As a secondary outcome, we analyzed demographic data of HG patients. Women who suffered from HG had no statistical differences in the mean of age, parity, the number of artificial pregnancy, and smoking. These findings are contrast to the findings of Vikanes et al., Depue et al., and Roseboom et al. [19, 24, 25] which showed HG patients were slightly younger, more often primiparous, substance abusers, had more often conceived through assisted reproductive techniques and more often had pre-existing hypertension and diabetes mellitus.

Our study has some limitations. Our study group with 72 HG patients is relatively small. The lack of psychiatry consultation and *Helicobacter pylori* investigation were other handicaps. In our cohort, there were no severe HG complications like encephalopathy. In addition, the absence of information on weight gain in the medical records prevented us from evaluating whether the effects of hyperemesis are mediated through reduced weight gain.

In conclusion, HG is not associated with adverse pregnancy outcomes. But comprehensive studies are needed to define long term effects of HG.

Conflict of interest We declare that we have no conflict of interest.

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