Original Article

Hyperemesis gravidarum and early new-born outcomes

Mostafa A. Hamdy

Department of Obstetrics and Gynecology, Faculty of Medicine, Suez Canal University, Egypt

ABSTRACT

Background: Hyperemesis gravidarum (HG) represents a more severe degree of nausea and vomiting of pregnancy and is potentially lethal if not treated well. HG is defined as persisting nausea and vomiting leading to dehydration, weight loss and nutritional deficiencies and was reported to be associated with poor perinatal outcome.
Aim: To evaluate the effect of HG on the perinatal outcome.
Patients and Methods: The study was conducted at Suez Canal University Hospitals, Ismailia at outpatient clinic from October 2015 to January 2017. 132 patients were selected with evidence of HG, the study group, and 137 women with no evidence of HG were the control group. Preterm birth, low birth weight, Apgar score <7 at 5 minutes of birth and perinatal mortality were the studied outcome measures.
Results: The Apgar score at 5 minutes of birth was the only outcome showed significant difference between the both groups (P value <0.001) while other mentioned perinatal outcomes were of insignificant difference. Also such significant difference in the Apgar score was more related to the maternal weight gain.
Conclusion: Apgar score at 5 minutes of birth could be affected by HG if associated with poor maternal weight gain.

Key Words: Hyperemesis gravidarum, nausea and vomiting in pregnancy, pregnancy outcome.

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Corresponding Author: Mustafa A. Hamdy, Department of Obstetrics and Gynecology, Faculty of Medicine, Suez Canal University, Egypt, **Tel.:** 01006896445, **E-mail:** drmustafa_ahmed@yahoo.com

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INTRODUCTION

Nausea and vomiting of pregnancy (NVP) is one of the commonest problems in pregnancy, affecting 50%–90% of women. Hyperemesis gravidarum (HG) is a severe form of (NVP), defined as persistent vomiting that may lead to weight loss more than 5% of pre-pregnancy weight, electrolyte imbalance and appearance of ketonuria, and occurs in about 0.3 -2% of pregnancies[1].

Every year, a significant number of women have one or more hospital admissions for HG (as many as 14 hospitalizations/1000 births). Therefore, early recognition and management of HG could have a profound effect on women's health and quality of life during pregnancy, as well as a financial impact on the health care system[2].

The underlying mechanisms for HG remain unknown, although previous research has suggested genetic factors to be involved[3]. It is not yet clear whether maternal genes or environmental factors are the main contributing factors. Increased levels of human chorionic gonadotropin (hCG), estrogen and leptin have been found to be associated with HG, as have increased levels of fetal DNA in maternal blood; the latter indicating damage of the fetomaternal barrier[4, 6].

HG has been reported to be associated with low birth weight (LBW), preterm birth (PTB), small-for gestational-age (SGA), perinatal mortality and prolonged stay in hospital for the new-born infant[7- 9]. In contrast, other studies reported that just women with HG gaining less than 7 kg during pregnancy had a risk for PTB, LBW and increase in risk for a 5 minute Apgar score < 7[7].

Conflicting results in previous studies can be explained by heterogeneity of methods, definitions and confounders, so this work aims to evaluate the effect of HG on the perinatal outcome; preterm birth, low birth weight, Apgar score <7 at 5 minutes of birth and perinatal mortality in pregnant women complicated with HG in Ismailia city.

PATIENTS AND METHODS

With approval from the ethics committee of the Faculty of Medicine, Suez Canal University this prospective comparative study was conducted at the Obstetrics and Gynecology outpatient clinic of the Suez

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Canal University Hospitals, Ismailia from October 2015 to January 2017. Our study recruited 269 women by the end of the study divided nearly equal into 2 groups a control group (137 women without HG) and a patient group (132 women with HG). The inclusion criteria were singleton pregnancy, GA less than 16 weeks' gestation and free from chronic illness. The exclusion criteria were multifetal gestation, evidence of chronic illness and those aborted before the 24 weeks' gestation.

Data on pre-pregnant BMI, parity and educational level were obtained. Information about maternal weight gain during pregnancy and smoking in pregnancy were recorded. Information on concomitant diseases such as asthma, diabetes, thyroid disorders, depression, anxiety, other psychological problems, anemia, vitamin B12 deficiency and anorexia were obtained to follow the exclusion criteria.

Maternal age was categorized into 4 groups: younger than 20 years, 20–30 years, 30–34 years and 35 years and older. By parity, women were classified as nullipara and multipara. Smoking before pregnancy was categorized as nonsmokers and smokers. BMI was grouped into 4 categories: < 19 kg/m^2, 19-24.9 kg/m^2, 25.0-29.9 kg/m^2 and ≥ 30.0 kg/m^2. Maternal weight gain during pregnancy was categorized no gain, 1-6.9 kg, 7.0- 14.9 kg, 15.0- 19.9 kg, and ≥ 20.0 kg.

Time-point for hospitalization was divided into three groups: first trimester, second trimester and both first-and-second trimesters.

The main outcome measures were gestational age at delivery, birth weight in kilograms, LBW defined as birth weight < 2500 grams, PTB defined as delivery before completed 37 gestational weeks, SGA defined as birth weight below the 10th percentile for the gestational age, perinatal death defined as death during the perinatal period (lasting from $\geq$ 24th gestational week until the 7th day after birth) and Apgar score <7 at 5 minutes of birth.

Statistical Analysis

Data were statistically described in terms of mean and standard deviation, frequencies (number of cases) and percentages when appropriate. Comparison between both groups was done using Chi-Square test in the cross tabulation of the socio-demographic data and nonparametric correlations between both groups and independent sample (t) test to compare numerical variables between both groups and one-way Anova test to compare numerical variables among the three stages of HG. P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 22 for Microsoft Windows.

RESULTS

150 patients were selected from those women who present or are referred to the hospital for management of the HG, they were the study group. Another 150 women were without evidence of HG were also selected and were considered as the control group for comparison. During the follow up of the ANC, 29 pregnant women were dropped out (didn't come, aborted before 16 weeks' gestation or discovered to have a chronic illness). So that, the net population in the study consisted of 269 pregnant women, 137 pregnant women for the control group and 132 pregnant women pregnant women for the studied group.

The mean age for all the studied population was (26.5± 6.2) years ranged from 18 to 48 years old. Table (1) showed the distribution of the demographic data between the 2 studied groups. Of note that most of our patients were aged 21-30 years (48%& 54.7%), primigravida (68%& 60%), nonsmoker (92%& 96%) for the control and the patient group respectively. The educational levels were comparable between both groups with the highest ratio in the low educational level in both control and patient group (36%& 40%) and showed comparable grade regarding the BMI with the highest ratio in the overweight grade in both control and patient group (36% & 52%) respectively. It means that all the demographic data showed insignificant difference between both groups.

Table 1: Demography

Variables		Control Group N (%)	Studied Group N (%)	P value*
Maternal Age (years)	<20	24 (16)	31 (20.7)	0.164
	21-30	72 (48)	82 (54.7)	
	31-35	36 (24)	27 (18)	
	>36	18 (12)	10 (6.7)	
Parity	PG	102 (68)	90 (60)	0.093
	MG	48 (32)	60 (40)	
Education	NON	30 (20)	30 (20)	0.805
	LOW	54 (36)	60 (40)	
	INTERMEDIATE	36 (24)	36 (24)	
	HIGH	30 (20)	24 (16)	
BMI	<19	24 (16)	12 (8)	0.06
	19-24.9	48 (32)	48 (32)	
	25-29.9	54 (36)	78 (52)	
	>30	24 (16)	12 (8)	
Smoking	YES	12 (8)	6 (4)	0.112
	NO	138 (92)	6 (4)	

*= Chi-square test. BMI= body mass index. PG= Primigravida. MG= Multigravida

Tables (2, 3) showed the pregnancy outcomes between the both groups. Of note that Apgar score <7 at 5 minutes of birth was the only outcome showed significant difference between the both groups (P value<0.001) while other variables; mode of the delivery, GA at delivery, birth weight, SGA, PTB, LBW and PNM were of insignificant difference between the both groups (P value > 0.05).

Table 2: Pregnancy outcome between both groups

Variables		Mean ± Std. Deviation	P value#
GA at Delivery	control	37.6 ± 2.9	0.283
	HG	36.7± 5.4	
Birth Weight	control	3.1± 0.3	0.269
	HG	3.1± 0.2	
Apgar Score	control	9.3± 0.6	<0.001
	HG	7.1± 1.9	

#= independent sample (t) test. GA= Gestational age. Hyperemesis Gravidarum.

Table 3: Pregnancy outcome between both groups.

Variables		Control group		Studied group		Spearman R®	P value•
		Yes (%)	NO (%)	Yes (%)	NO (%)		
Mode of Delivery	VD	96 (70.1)	-	91 (68.9)	-	0.01	0.841
	CS	41 (29.9)	-	41 (31.1)	-	0.01	
SGA		5 (3.6)	132 (96.4)	7 (5.3)	125 (94.7)	-0.04	0.513
PTB		15 (10.9)	122 (89.1)	17 (12.9)	115 (87.1)	-0.03	0. 627
LBW		6 (4.4)	131 (95.6)	4 (3)	128 (97)	0.04	0.560
PNM		0 (0)	137 (100)	2 (1.5)	130 (98.5)	-0.09	0.149

•= Chi-square test. ®= Spearman R. VD= Vaginal Delivery. CS= Cesarean Section. SGA=Small for Gestational age. PTB= Preterm Birth. LBW= Low Birth Weight. PNM= Perinatal Mortality.

Tables (4, 5) showed the effect of the maternal weight gain on the pregnancy outcome. Of note that Apgar score <7 at 5 minutes of birth was the only outcome showed significant difference in relation to the gain in the maternal weight. So that the significant difference in the Apgar score <7 at 5 minutes of birth between the both groups may be related the maternal weight gain more than the HG itself.

Table 4: Effect of maternal weight gain on the pregnancy outcome

	Weight Gain (Kg)				
Variables	0-6.9	7-14.9	15-19.9	Spearman ®	P value•
	N (%)	N (%)	N (%)		
SGA	5 (9.4)	7 (3.4)	0 (0)	0.12	0.123
PTB	4 (7.5)	27 (13.2)	1 (8.3)	0.05	0.484
LBW	2 (3.8)	8 (3.9)	0 (0)	0.02	0.784
PNM	1 (1.9)	1 (.5)	0 (0)	0.065	0.285

•= Chi-square test. ®= Spearman R. VD= Vaginal Delivery. CS= Cesarean Section. SGA=Small for Gestational age. PTB= Preterm Birth. LBW= Low Birth Weight. PNM= Perinatal Mortality.

Table 5: Effect of maternal weight gain on the pregnancy outcome

Variables	Weight Gain (Kg)	Mean ± Std. Deviation	P value#
GA at Delivery	0-6.9	37.8± 0.8	0.392
	7-14.9	37± 4.7	
	15-19.9	36.3± 9.3	
Birth Weight	0-6.9	3.1± 0.3	0.124
	7-14.9	3± 0.3	
	15-19.9	3.2± 0.2	
Apgar Score	0-6.9	7.3± 2.2	0.005
	7-14.9	8.5± 1.5	
	15-19.9	8.5± 0.5	

#= Anova test. GA= Gestational age

In tables (6) we could note the relation of the severity of HG and weight gain during pregnancy. It generally apparent that the more the severe the HG the less the weight gain during pregnancy.

Table 6: Severity of HG and weight gain

		Weight Gain (Kg)				
		0-6.9	7-14.9	15-19.9	Spearman R®	P value•
		N (%)	N (%)	N (%)		
Control		9 (6.6)	116(84.7)	12 (8.8)	0.52	<0.001
HG	Mild	11 (19)	47 (81)	0 (0)		
	Moderate	7 (14.9)	40 (85.1)	0 (0)		
	Severe	26(96.3)	1 (3.7)	0 (0)		

•= Chi-square test. ®= Spearman R. Hyperemesis Gravidarum

In both tables (7 & 8) we could find the correlation of the severity of HG and the perinatal outcome. Of note there is highly significant difference among grades of HG in the incidence of Apgar score <7 at 5 minutes of birth, SGA and PNM. It means the more the severity of HG the more the incidence of such problems.

Table 7: Severity of HG and perinatal outcome

	HG Severity	N	Mean±SD	P value #
Apgar Score	mild	58	7.1±1.7	<0.001
	moderate	47	7.8±1.6	
	severe	27	6.7±2.5	
GA at Delivery	severe	58	37.3±0.8	0.261
	moderate	47	36.7±5.1	
	severe	27	37.9±0.7	
Birth Weight	mild	58	3±0.2	0.736
	moderate	47	3±.0.2	
	severe	27	3±0.3	

#= Anova test. GA= Gestational age. Hyperemesis Gravidarum

Table 8: Severity of HG and perinatal outcome

	Severity of HG				
	Mild	Moderate	Severe	Spearman R®	P value•
	N (%)	N (%)	N (%)		
SGA	1 (1.7)	0 (0)	6 (22.2)	0.15	<0.001
PTB	10 (17.2)	6 (12.8)	1 (11.9)	0.03	0.326
LBW	3 (5.2)	0 (0)	1 (3.7)	0.05	0.508
PNM	0 (0)	0 (0)	2 (0.7)	0.18	<0.001

•= Chi-square test. ®= Spearman R. SGA=Small for Gestational age. PTB= Preterm Birth. LBW= Low Birth Weight. PNM= Perinatal Mortality

DISCUSSION

In this study we investigated the effect of HG on the pregnancy outcome. The net result of this work is that the HG has no effect on the pregnancy outcome in terms of GA at delivery, birth weight, SGA, PTB, LBW and PNM. The only exception was the Apgar score <7 at 5 minutes of birth which showed significant difference between the both groups. Also our study showed that Apgar score <7 at 5 minutes of birth was the only outcome showed significant difference in relation to the maternal weight gain (p value < 0.001). So as we said before the significant difference in the Apgar score at 5 minutes post-delivery between the both studied groups may be related the maternal weight gain more than the HG itself (p value = 0.005). We could explain that as we noted that the more the severity of HG the less the weight gain during the course of pregnancy (p value < 0.001). Also our results showed the more the severe the HG, the less the weight gain, the worse the perinatal outcome in terms of Apgar score <7 at 5 minutes of birth, SGA and PNM (p value < 0.001)

The cohort Norwegian study found that HG requiring hospitalization was not associated with increased risks for PTB, LBW or SGA. Pregnancies complicated with HG had a slightly reduced pregnancy course. There was insignificant difference in birth weight according to maternal HG-status. Time point for hospitalization did not influence birth weight or gestational age. Moreover, HG was associated with lower risk for having Apgar score < 7 1 minute of birth, whereas there was no difference in risks for Apgar < 7 score after 5 minutes. The clinical relevance of these findings is, however, limited[10].

In contrast, to Norwegian study, in the Canadian historical birth cohort study of 156,000 pregnancies, HG was found to be associated with an increased risk of PTB, LBW, SGA and Apgar score < 7, 5 minutes of birth, but only for women with maternal weight gain during pregnancy < 7 kg[6].

On discussing the results of the two previous studies, Norwegian study did not show the effect of the weight gain on the study outcomes that why the Apgar < 7 score after 5 minutes showed insignificant difference as we mentioned in our results. We could also explain it as the earl development of fetal CNS is dependent totally on the nutritional status of the mother, glucose level, which may be affected by the HG status and its severity. We agreed with the Canadian study regarding the results of Apgar score < 7, 5 minutes of birth, but disagreed with the other results and that could be explained by the small sample size of our study in relation to theirs.

Maternal weight gain and body composition have, regardless of maternal HG-status, been thoroughly investigated as possible predictors for gestational age and birth weight[11, 12]. A met analysis of 55 studies, 37 cohort and 18 case–control including 3.5 million women, reported that low total gestational weight gain was associated with increased risks for PTB, LBW and intrauterine growth retardation (IUGR) and lower mean birth weight[11]. That results augmented ours regarding the essential role of maternal weight gain and its effect on the perinatal outcomes, Apgar score at 5 minutes post-delivery. Such conclusion was achieved by other investigators found that the associations between HG and adverse pregnancy outcomes may be explained by poor maternal weight gain rather than the mother suffering from HG[6, 9].

Another study based on Swedish births between 1973 and 1982 found that those women with HG were more likely to give birth before 38 gestational weeks and to deliver children with LBW[12]. The American cohort study among more than 500,000 live births found that where HG was associated with SGA and LBW. The two latter studies reported univariate analyses only[13]. Moreover, an American case–control study found women with HG to gain on average 4.6 kg less during pregnancy, and to deliver babies who weighed on average 291 grams less compared to those born from healthy women[7].

In MoBa women with HG gained on average 2.2 kg less than women without HG, but their babies did not have lower birth weight[14]. However, they were born on average one day earlier. In contrast, a Norwegian institution-based case–control study reported that the 175 women hospitalized with HG gained on average 5.1 kg less than women without HG, their babies to be born 0.5 day earlier and weigh on average 138 grams less[15].

Birth weight was positively correlated to maternal weight in early pregnancy, maternal weight gain during pregnancy and parity, but not HG[15]. This is partly in line with our study, where stepwise regression showed that differences in birth weight between babies born to women with and without HG disappeared when maternal weight gain was adjusted for.

Whereas the 1 minute Apgar score reflects the immediate need for resuscitation, the 5 minute Apgar score has more a prognostic value[16]. Most studies therefore report Apgar score after 5 minutes, since this information is of higher clinical importance[17, 18]. Our study showed that Apgar score <7 at 5 minutes of birth was the only outcome showed significant difference in relation to the gain in the maternal weight. So that the significant difference in the Apgar score <7 at 5 minutes of birth between the both studied groups may

be related the maternal weight gain more than the HG itself. Also we said that the more the severe the HG, the less the less the weight gain, the worse the perinatal outcome.

We could see from our results that the severity of HG could affect the perinatal outcome as we found the correlation of the severity of HG and the perinatal outcome. Of note there is highly significant difference among grades of HG in the incidence of Apgar score, SGA and PNM. It means the more the severity of HG the more the incidence of such problems, and we explain that correlation by more reduction in the maternal weight gain on upgrading the HG grade.

Previous studies reporting on pregnancy outcomes stratified by the severity of HG are also inconsistent. Women classified as having severe HG based on clinical test results have similar outcome to those with milder HG[19, 20]. However, studies based on HG severity defined by hospitalization[21] or maternal weight loss of >5% pre pregnancy weight[22] show a reduction in neonatal birth weight.

Other studies[19-23] comparing pregnancy outcomes to HG severity have used other methods to determine HG severity, including hospitalization[21,23] and weight loss[22] defined as severe HG if one of the following criteria is fulfilled: hematocrit >0.43, serum creatinine between 71 and 133 mmol/L, serum urea >7.1 mmol/L or ketonuria 3+ by ketostix[19] and defined as severe HG if one of ketonuria, increased blood urea nitrogen, hematocrit or abnormal electrolytes is present[20].

Two of these studies[19, 20] have not found an association between severe HG and outcome. However, three studies have found severe HG to be associated with reduced birth weight[21, 22, 24].

LIMITATIONS OF THE STUDY

Our study has a few limitations. One is the hospital-based; cross-sectional nature of the study that did not exclude other confounding factors influencing nausea and vomiting, such as social problems and socioeconomic status of the patient.

CONCLUSION

In The net result of this study is that the HG has no effect on the pregnancy outcome in terms of GA at delivery, birth weight, SGA, PTB, LBW and PNM. The only exception was the Apgar score <7 at 5 minutes of birth which showed significant difference between the both groups. Also our study showed that Apgar score <7 at 5 minutes of birth was the only variable showed significant difference in relation to the maternal weight gain. So that the significant difference in the Apgar score at 5 minutes post-delivery between the both studied groups may be related the maternal weight gain more than the HG itself. Also it's noted that the more the severe the HG the more the reduction in the weight gain during the course of gestation and by the way the more the appearance of the perinatal problems.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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