RESEARCH ARTICLE

Hyperemesis gravidarum and risks of placental dysfunction disorders

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Abstract

Objective: To investigate the association between hospitalisation of cases affected during the first and second trimester of pregnancy with the increased intrapartum complication attributed to placental dysfunction disorders. Additionally to highlight the distinct maternal factors and foetal morbidity patterns for improving the obstetrical outcome.

Methods: An observational study was carried out in Al-Yarmouk Hospital, Baghdad, Iraq from the 1st December 2019 to end December, 2020, recruiting 250 singleton pregnancy of gestational age >10 to >21 completed weeks until delivery. Patients were grouped into two; taking gestational age on admission as a divider; group1 < 10 weeks and group 2 > 12 weeks till completed 21weeks. Participants had at least one hospitalisation for this diagnosis. After a detailed history and examination and recording associated maternal morbidities, including hypertension, hyperthyroidism and diabetes; furthermore, we excluded intrapartum complications as Prematurity, abnormality in foetal weight including stillbirth and preeclampsia risk.

Results: None of the demographic criteria nor maternal morbidity factors were significant on analyses. Conversely, all intrapartum complications were significantly higher in both recruited groups.

Conclusion: The strong relationship between hyperemesis gravidarum and placental dysfunction related complications highlight admitted HG cases as a higher risk group; being liable for severe foetomaternal morbidities, demanding more surveillance for a better outcome.

Keywords: Hyperemesis gravidarum, Placental abruption, Preeclampsia, Small for gestational age, Stillbirth.
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Introduction

Hyperemesis gravidarum (HG), defined as intractable and excessive vomiting during pregnancy, leads to fluid, electrolyte imbalance, nutrition deficiency, acid-base imbalance, weight loss, and need for hospitalization.[1] It is one of the commonest reasons for admission to the hospital; pregnancy nausea, and vomiting occurs in about 85% pregnant women. In contrast to the severe uncontrollable form, 0.3-3% necessitating hospitalisation and adequate rehydration.[2]

The Royal College of Obstetricians and Gynaecologists (RCOG) created essential criteria for diagnosing HG includes; hospitalisation, losing weight greater than 5%, and dehydration.[3] HG is most prevalent during the first trimester of pregnancy, typically between 4-10 weeks of gestation and resolves by 20-weeks gestation.[4] There is a diversity in the incidence and reported symptoms severity attributed to a lack of globally accepted definitions, ranging from mild dizziness and dry retching to intractable vomiting.[3,4]

Unfortunately, in 10% of affected women the symptoms continue throughout pregnancy[5] thereby increasing foetal and maternal morbidity, as nutritional deficiencies, Wernicke's encephalopathy, placental abruption, and preeclampsia. Foetal complications are common; small for gestational age (SGA), prematurity and early neonatal morbidities. Studies addressing pregnancy complications and neonatal outcome for affected women are conflicting, although previous studies denied the correlation between HG and intrapartum complications such as preeclampsia, Diabetes Mellitus and hypertension. Current evidence suggested the opposite. Earlier detection is vital for reducing foetal and maternal morbidity.[6,7] Proposed theories for HG are many; immunological factors, genetic factors, and psychological factors. Evidence has supported HG's higher risk in hydatidiform mole, multiple pregnancies implying its association to the highest pregnancy hormone levels, specially human chorionic gonadotropin (HCG), progesterone and oestrogen.[8] Defective placentation was accredited for increased number of pregnancy complications and was linked to HG pathophysiology. Higher β HCG levels in the circulation present during early pregnancy as HG and later on as FGR, preeclampsia (PE) and early neonatal complications.

In this study, we aimed to define the maternal criteria and associated co-morbidities linked with frequent hospitalisation of HG cases and highlight intrapartum complication.

Patients and Methods

An observational-descriptive study was carried out in Al-

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Yarmouk Hospital, Baghdad from the 1st of December 2019 to the end of December 2020 and was approved by the Ethical Committee of the AL-Yarmouk Teaching Hospital. A total of 250 pregnant patients, >10 weeks gestational age, singleton pregnancy until delivery at >21 completed weeks of pregnancy were enrolled after obtaining written and verbal approval. The common cause of hospital admission was dehydration requiring fluid replacement. Enrolled patients had at least one hospital admission for the diagnosis of HG and they were at the end of the first trimester around 8-10 weeks. A detail history was recorded and physical examination was performed. History included age, parity, height, weight for calculation of body mass index (BMI) and gestational age. The gestational age was confirmed by early date ultrasound along with the first day of the last menstrual cycle. Inclusion criteria were defined as, Antepartum complications including hyperemesis gravidarum, gestational diabetes, chronic hypertension, preeclampsia and history of hyperthyroidism. Intrapartum complications like placental abruption, stillbirth, and small for gestational age, were retrieved from patient's hospital records. The exclusion criteria were the hospital admission at 21 weeks gestational age or more with severe nausea and vomiting because it could be related to another cause rather than hyperemesis gravidarum.

The Study's principal parameter was hospital admission for hyperemesis gravidarum, recording information from the patient register about admission dates and the reason.

The enrolled women were divided into two groups; group 1 included patients admitted for the first time with hyperemesis gravidarum before 12 weeks pregnancy, defined as first trimester hyperemesis gravidarum, and group 2 included patients admitted for the first time at gestational age 12 weeks to complete 21 weeks, defined as second trimester hyperemesis gravidarum. The studied parameters of the outcomes were SGA, preterm labour, placental abruption, stillbirth, and preeclampsia (PE). The NICE guidelines.[9] define PE as the onset of blood pressure 140/90 mmHg or greater and associated with proteinuria of more than 0.3 gram per 24 hours and stillbirth as the death of a foetus at 20 weeks gestational age or more. Small for gestational age is considered when the weight is under the 10th percentile for the gestational age.

Data were analysed by the statistical package of SPSS-25 (Statistical Packages for Social Sciences- version 25). The data was presented in simple frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significant differences of 2 different means (quantitative data) were tested using Students-test for the difference between two independent means or Paired t-test for a difference of a paired observations (or two dependent means), or ANOVA test for difference among more than two independent means.

Pearson Chi-square test evaluated the significant difference between various percentages (qualitative data) applying the Fisher Exact test wherever applicable. Statistical significance was considered meaningful whenever the P-value was < 0.05.

Results

We enrolled 250 pregnant hospitalised women for the first time due to hyperemesis gravidarum during their first

Table-1: The demographic characteristics of patients enrolled in the Study divided by their gestational age during the first or second trimester of pregnancy with hyperemesis gravidarum. No statistical differences were observed.

		Total		Hyperemesis gravidarum First Trim (<12W)		Second Trim (12-21W)		P-value
		No	%	No	%	No	%	
Age (years)	20---24	33	13.2	17	16.0	16	11.1	0.136
	25---29	51	20.4	24	22.6	27	18.8	
	30---34	134	53.6	57	53.8	77	53.5	
	=>35y	32	12.8	8	7.5	24	16.7	
	Mean±SD (Range)	30.5±4.8 (20-42)		29.8±4.7 (20-41)		31.0±4.9 (20-42)		
Parity	Para 1	77	30.8	26	24.5	51	35.4	0.182
	Para 2-3	151	60.4	70	66.0	81	56.3	
	Para 4&more	22	8.8	10	9.4	12	8.3	
	Mean±SD (Range)	2.2±1.0 (1-5)		2.3±1.0 (1-5)		2.1±1.0 (1-5)		
BMI (Kg/m^2)	Lean (<18.5)	8	3.2	4	3.8	4	2.8	0.750
	Normal (18.5-24.9)	98	39.2	39	36.8	59	41.0	
	Overweight (25-29.9)	74	29.6	30	28.3	44	30.6	
	Obese (=>35)	70	28.0	33	31.1	37	A25.7	
	Mean±SD (Range)	26.5±4.8 (18.0-35.4)		26.8±5.0 (18.1-35.4)		26.3±4.7 (18.0-35.2)		

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table-2: The associated clinical co-morbidities of patients enrolled in the Study admitted to the hospital with hyperemesis gravidarum.

		Total		Hyperemesis gravidarum First Trim (<12W)		Second Trim (12-21W)		P-value
		No	%	No	%	No	%	
Hyperthyroidism	Yes	8	3.2	4	3.8	4	2.8	0.658
	No	242	96.8	102	96.2	140	97.2	
Pre-gestational diabetes	Yes	45	18.0	15	14.2	30	20.8	0.174
	No	205	82.0	91	85.8	114	79.2	
Chronic hypertension	Yes	32	12.8	16	15.1	16	11.1	0.352
	No	218	87.2	90	84.9	128	88.9	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table-3: The association between the hyperemesis gravidarum and risk of intrapartum complication in both recruited groups, all correlation were statistically significant.

		Total		Hyperemesis gravidarum 1st Trim (<12W)		2nd Trim (12-21W)		P-value
		No	%	No	%	No	%	
Risk of Pre-eclampsia	Yes	108	43.2	18	17.0	90	62.5	0.0001*
	No	142	56.8	88	83.0	54	37.5	
Risk at delivery	Stillbirth	30	12.0	7	6.6	23	16.0	0.0001*
	SGA	49	19.6	8	7.5	41	28.5	
	Placenta abruption	47	18.8	13	12.3	34	23.6	
	No	124	49.6	78	73.6	46	31.9	
Gestational age	Term	120	48.0	79	74.5	41	28.5	0.0001*
	Pre-term	130	52.0	27	25.5	103	71.5	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.
SGA: Small for Gestational Age.

or second trimester taken as group one and two, respectively.

Table 1 shows the demographic criteria of the two groups divided by their gestational age. A trend of higher age, increasing parity, and higher BMI was reported in the second group compared to the first. Still, they failed to score significant statistical differences.

Table-2 Illustrates the associated clinical co-morbidities of the admitted patients regarding the presence of hyperthyroidism, pre-gestational diabetes and chronic hypertension. No meaningful differences were reported between the two groups,

Table-3 shows the significant relation between hyperemesis gravidarum versus poor intrapartum outcomes in terms of small for gestational age, preterm labour, placental abruption, stillbirth, and preeclampsia observed to be significantly higher in both recruited groups.

Discussion

Hyperemesis gravidarum is a debilitating pregnancy ailment; characterized by severe nausea, vomiting, malnutrition, and dehydration with weight loss. Hospitalisation is often needed to correct electrolyte imbalance and vitamins deficiencies.[10-12]

The analysis confirmed that none of the demographic criteria nor the medical co-morbidities collected were impactful to the HG incidence. Nevertheless, the intrapartum outcome and complication all were statistically meaningful.

The demographic criteria of the study participants, showed no significant difference regarding HG, which contradicted Kim et al.'s study.[13]

Among multiparous women, low BMI before conception and female sex of the unborn foetus were leading factors. Kim et al investigators recruited 1.5 million Korean women in 2 years and assessed the pre-pregnancy risk factors for causing HG. Ethnicity was an essential factor in the study, raising the internal bias issue. Our Iraqi populace has a large diversity of multiple ethnic groups that could explain the difference in the conclusion.[13]

There was a high association of low birth weight (LBW) with HG in our study. Similar results were acquired by Clive J. Petry who compared three cohort group of women in the three trimesters of pregnancy.[14] The odds

ratio were 3.5 (1.2, 10.8), $p = 0.03$. for both the first and second. Furthermore, he raised an interesting point that only those who vomit suffer from reduced foetal weight (FW), compared to those who only suffer from nausea.

Amanda Regodón Wallin et al.[15] were of the opinion that first trimester HG was not a significant cause for SGA nor LBW. Conversely, they reported significantly higher LBW and SGA risks among the second trimester (LBW: aRR 1.17; SGA: aRR 1.16). Contradicting our result, they showed significantly lower rates for preterm birth (aRR 0.75). The effect of second-trimester on LBW in their study, was due to rapid foetal growth during this period. Their study linked HG during the 3rd trimester as a risk factor for LBW, a parameter not included in the current study.

The discrepancy in preterm labour risk can be accredited to the difference in socioeconomic class of enrolled cases. The study was conducted in the rural area of Nepal.

The higher risks of the poor neonatal outcome seen in the current study were in line with Naoko Kozuki et al.'s[16] study showing an increased frequency of term-SGA, preterm-SGA births. Moreover, preterm-SGA infants suffered the highest neonatal and infant mortality and morbidity risks.

The Norwegian Study[17] supports our results among HG women as they experienced higher odds of rising blood pressure and pregnancy-associated hypertension and even preeclampsia. The abnormal placentation seen early in pregnancy was accredited for many on-going complications. The defective placentation will be associated with higher HCG levels presented as a severe form of HG. As the pregnancy progresses, more serious complications develop as preeclampsia, foetal growth restriction (FGR), small for date foetuses, preterm labour and even intrapartum stillbirth.[17,18]

The strengths of our study are: The sample size is adequate which gave a wide range of data diversity to overcome sampling bias. Moreover, we have conducted a well-classified assessment of the demographic and medical co-morbidities known for this common underestimated problem. We followed patients from the first and second trimester until delivery to get a better insight of HG and its impact on the intrapartum complications.

Conclusion

HG adversely impacts the health and wellbeing of pregnant women. However, the detrimental impact of HG on the foetomaternal outcome is underestimated. Maternal malnutrition seems to be linked with SGA outcomes making them vulnerable to increased morbidity and mortality. There is an urgent need to interfere with effective interventions as vigorous surveillance is advised with planned delivery in specialized centres to improve the outcome for the high-risk pregnancies.

Limitations

The sample size for this study was not calculated. This should be considered as it can be an important reason for reducing the power of the study.

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Conflict of Interest: None.

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