

# Prevalence of Hyperemesis Gravidarum and Associated Factors Among Pregnant Women at Jimma University Medical Center, South West Ethiopia: A Cross-Sectional Study

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#### **Abstract**

**Background:** Nausea and vomiting are common symptoms during early pregnancy. Hyperemesis gravidarum represents a severe intractable nausea and vomiting before the 20<sup>th</sup> week of gestation. Although rare, clinical and social impact of hyperemesis gravidarum can be immense, it can cause serious maternal morbidity or even maternal death.

**Objective:** This study has determined the prevalence, associated factors and described management and treatment outcome of hyperemesis gravidarum.

**Methods:** Institution based descriptive cross sectional study design was carried out on 102 pregnant women admitted with hyperemesis gravidarum to Jimma university medical center over one year period. Descriptive statistics was used to summarize data. P-value and  $\chi^2$  test were used to measure associations.

Results: The prevalence of hyperemesis gravidarum among pregnant women presenting to Jimma university medical center before 20 weeks of pregnancy was 4.8%. Majority (81.4%) of these women were admitted in their first trimester and 15.7% of them were readmission cases. Over one fourth (28.4%) of these mothers were treated for more than four days in the hospital. Twenty seven point five percent of women had gastrointestinal diseases, 17.6% had urinary tract infection, and 9.8% had other factors, including diabetes mellitus, hyperthyroidism as aggravators. Social factors (family conflict) was identified in 5 (4.9%) of these cases. Twenty patients (19.6%) had more than one factor. Treatment strategies involved bed rest, fluid & electrolyte replacement, antiemetic therapy, vitamin supplementation and dietary advice. Promethazine was the most prescribed antiemetic drug accounting for 73.5% and only 10.8% were given steroid therapy.

Conclusion and recommendation: In this study, overall hospital prevalence of hyperemesis gravidarum was high. Gastrointestinal diseases and urinary tract infection were frequently identified as associated conditions. Management followed was as per the medical center's guideline. A larger study is needed to establish the difference in prevalence, risk factors and management protocol of hyperemesis gravidarum among different maternity health care settings. In addition, the findings of high readmission rate and prolonged hospitalization require further exploration as to their relation with patient related or medical personnel problems. Exploration of this high prevalence of hyperemesis gravidarum leads to the recommendation that physicians and nurses should pay more attention to these women who were diagnosed with the problem.

Keywords: Hyperemesis gravidarum, Nausea and vomiting in pregnancy, Jimma, Ethiopia

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### Introduction

Nausea and vomiting are common symptoms during early pregnancy affecting as many as 90% of pregnant women. Nausea and vomiting are usually limited to the first trimester and commonly resolve by the 20th week of gestation (generally about 60% of the cases resolve by the end of first trimester and about 90% resolve by 20 weeks of gestation), but 10% of women have symptoms that continue throughout pregnancy [1,2] and in approximately 5% of women, symptoms resolve only after delivery of the baby [1,2,3]. Although the reasons for persistence of nausea and vomiting beyond the first trimester are unclear, several factors associated were allergies, restrictive diet, maternal overweight and lower maternal age [3].

Hyperemesis gravidarum (HEG) is the term used to describe the severe end of the symptom spectrum characterized by severe nausea and vomiting that interferes with nutritional intake and metabolism, causes fluid and electrolyte imbalances, and commonly requires hospital management [1,2,4,5]. HEG complicates between 0.3% and 2 % of all pregnancies [4,6,7,8-12,13,14,15,16] with up to 15% recurrence risk [17]. Although rare, clinical and social impact of HEG can be immense [9]. It is the most common cause of hospitalization in the first half of pregnancy and is second only to preterm labor for pregnancy overall [10,11]. It can cause a potentially life-threatening complication of pregnancy and is potentially lethal if not treated [2,3,17,18]. The socioeconomic impact of the complete spectrum of nausea and vomiting of pregnancy on time lost from either paid employment or household work is substantial. About 8.6 million hours of paid employment and 5.8 million hours of housework are lost each year because of this condition [9]. Estimates of severe nausea and vomiting of pregnancy vary greatly and range from 0.3% in a Swedish registry to as high as 10.8% in a Chinese registry of pregnant women [19,20]. Asian populations tend to have higher incidence rates. For example, a Malaysian study identified that the prevalence of HEG is 3.9% [20,21]. Additionally, a study in an Eastern Asian population observed HEG in 3.6% of the population [22,23]. As mentioned, a study revealed the highest rate of severe nausea and vomiting of pregnancy in Shanghai, China with an incidence of 10.8%. A study assesses the prevalence and risk factors of hyperemesis gravidarum among pregnant women at the Woman's Health Center, Assiut University, Egypt revealed that the prevalence of HEG was 4.5%,, who were admitted to the antenatal inpatient wards at the Woman's Health Center for one year [20]. A study assesses nausea and vomiting of pregnancy on antenatal care (ANC) clients of three hospitals of Addis Ababa showed that the prevalence of nausea and vomiting of pregnancy was 74.5%, with 4.4% being admitted for severe symptoms [32].

The etiology and pathogenesis of HEG is unknown. But it is said to be multifactorial and the result of complex interaction of endocrinologic, psychoneurotic, genetic and environmental factors [2,5-9,11,12,24].

One popular theory is nausea and vomiting of pregnancy is related to trophoblastic activity and gonadotropin production, possibly secondary to elevated serum human chorionic gonadotropin (hCG) levels. It was noted that women with nausea and vomiting of pregnancy had higher concentration of urinary hCG than asymptomatic pregnant women. A relationship to the level of hCG has been postulated because the incidence of HEG is higher in multiple gestation pregnancies as well as in molar disease where hCG levels are markedly elevated [2,6,9,11,12,24].

The theory concerning elevated hCG at the beginning of pregnancy has gained considerable attention as a causing factor for HEG. Consequently, HEG is more prevalent when hCG levels are elevated, such as twin pregnancies and trophoblastic disease. Generally, hCG decreases throughout the second trimester of pregnancy and most patients report an amelioration of HEG [2,5,24,25]. Biological theories (especially endocrinological hypotheses) are currently the dominant paradigm to understanding the origins of HEG. However, psychological theories have also been proposed to explain the etiology of HEG [6,8,11,24].

A number of risk factors associated with HEG have been reported, including nulliparity, low maternal age, multiple gestation, trophoblastic disease, a previous pregnancy complicated by HEG, female sex, psychiatric conditions, and both high and low maternal pre-pregnancy weight [2,11,24-28]. According to the HER Foundation (2006), there are common risk factors for hyperemesis such as women being

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less than 20 years of age, nonsmokers, food aversions before pregnancy, high saturated fat diet, posttraumatic stress disorder, multiple gestation, history of motion sickness, allergies, ulcers, mother or sister with HEG and poor diet [2,3,17,24]. Risk factors vary among different populations and female sex of the off-spring, several previous pregnancies, and a high daily intake of primarily saturated fat before pregnancy are reported to cause a higher risk [2,11,26]. The incidence of HEG increases with multiple gestation, molar pregnancy, trisomy gestation and hydrops fetalis [2,24].

The diagnosis of HEG is also associated with low birth weight, intrauterine growth restriction, preterm delivery, lower 5min Apgar scores and fetal and neonatal death [2,3,17,18]. Moreover, HEG affects a woman's quality of life and daily functioning, and is the most common reason for hospitalization during early pregnancy [10,11,29]. HEG is sufficiently pernicious to produce weight loss, dehydration, acidosis from starvation, alkalosis from loss of hydrochloric acid in vomits and hypokalemia [1,2,4,6,7,10-13,17,18,24,25]. HEG can be responsible for increased health care use hospitalization, time lost from work, and reduced quality of life during pregnancy [9,29,30] Both relatively benign and pernicious complications may be caused by HEG. Weight loss, dehydration, acidosis from malnutrition, alkalosis from vomiting, hypokalemia, muscle weakness, electrocardiographic abnormalities, tetany, and psychological disturbances may be included in the "benign" group. Life threatening complications include esophageal rupture due to severe vomiting, Wernicke's encephalopathy, central pontine myelinolysis, retinal hemorrhage, renal damage, spontaneous pneumomediastinum, intrauterine growth restriction, and fetal death [3,4,5,18,29,31]. HEG can be associated with serious maternal and fetal morbidity such as Wernicke's encephalopathy, fetal growth restriction, and even maternal and fetal death [3,10,18].

There is no universally agreed therapy for HEG [7]. Treatment is generally supportive care and management of symptoms [7,22]. A range of treatment of HEG includes dietary and lifestyle modifications, complementary therapies (i.e. acupuncture), and pharmaceutical therapies including a variety of classes of anti-emetics and corticosteroids, and enteral/parenteral nutrition. The goals of therapy are generally to reduce nausea and vomiting, minimize hospitalization, prevent progression of symptom severity, and improve quality of life [22,23,28].

Information on the prevalence of HEG and associated factors as well as management protocol and treatment outcome of HEG cases is critical for the improvement of quality of care. However, very limited studies have been conducted to determine prevalence of HEG and identify associated factors as well as describe management protocol and treatment outcomes of HEG cases in Ethiopia. Moreover, there is no study in JUMC on this topic. Therefore, the objective of this study is to determine prevalence of HEG and identify its associated factors among pregnant women at JUMC, South west Ethiopia and describe their management protocol and treatment outcomes.

### **Materials and Methods**

The study was conducted from January 1, 2015 to December 31, 2015 in JUMC, a teaching hospital located in Jimma town of Oromia Regional State, Ethiopia. Located 350 km from Addis Ababa the capital city of Ethiopia, JUMC is the only specialized referral hospital in the South-Western region of Ethiopia. The hospital has a predominantly rural catchment population of 15 - 20 million people for tertiary level care. JUMC is also serving as a clinical postgraduate specialty teaching hospital for different specialties including obstetrics and gynecology, pediatrics and child health, internal medicine and general surgery since 2005. Department of obstetrics and gynecology has two wards (gynecology and maternity/labor), one MCH outpatient clinic, one general gynecologic outpatient clinic, one family planning clinic and a referral clinic where cases with gynecology oncology, benign gynecologic diseases, and high risk pregnancy are seen on different days of the week. It has eight senior obstetricians and gynecologists and 43 residents of different years (levels) of study.

Institution based cross sectional descriptive study design was used in carrying out this study. All pregnant mothers with HEG in the gynecologic ward during the study period were consecutively included into the study. HEG cases were followed for treatment outcome until discharge from the hospital.

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A single population proportion formula, [n =  $(Z_{\alpha/2})^2$  p  $(1-p)/d^2$ ], was used to estimate the sample size. The following assumptions had been made: 2% prevalence of HEG among pregnant women [7], 95% confidence interval, 1% margin of error (d = 0.01), and 10% expected non-response rate.

$$n = \frac{(z_{\alpha/2})^2 p(1-p)}{d^2} = \frac{(1.96)^2 0.02(0.98)}{(0.01)^2} = 752.9536 \approx 753$$

Where, n = sample size

P = prevalence of hyperemesis gravidarum (from previous study)  $\alpha$  = type I error (probability of rejecting true null hypothesis)

d = margin of error

 $Z_{\alpha/2}$  = standard value of normal distribution at 1-  $\alpha/2$ 

Since the annual average admission of the patients with obstetric complication at JUMC is less than 10,000 (around 2/week\*52wks = 104), the above sample is corrected using population correction formula as follows:

$$n_c = \frac{n}{1 + \frac{n}{N}} = \frac{753}{1 + \frac{753}{104}} = 91.379 \approx 92$$

Where, n = sample size

N = estimated size of the source population (average for a year)

Adding 10% expected non-response rate ( $10\%*92 = 9.2 \approx 10$ ), the final sample size for this study becomes 102.Consecutive sampling technique was used. All eligible (those satisfying inclusion criteria) pregnant mothers admitted to JUMC with obstetric complications during the study period were included into the study until the required sample size is achieved.

Data were collected by reviewing medical records and interviewing mothers. A pretested structured questionnaire was used to collect data regarding patient socio-demographic characteristics, obstetric history, current admission history, and investigations done for the patients with HEG and management protocol and treatment outcome for each HEG case. Data on HEG cases were collected by four diploma nurses who were trained on how to complete the data collection questionnaire during patient follow-up period. Maternal body mass index (BMI) was objectively measured in terms of body weight and height. Weight was measured using beam balance to the nearest 0.1 kg. The scale was checked and calibrated before weighing for each mother. Height was measured using Stadiometer to the nearest 0.1 cm. Aggregate data on total number of pregnant women presenting to the hospital in the first half of pregnancy, up to 20 weeks of gestation during the study period was obtained by reviewing registration books of the ANC clinic and gynecology ward. The data collection process was supervised by the principal investigator, a resident in the department during the data collection period.

Data was checked for completeness, cleaned and entered into SPSS version 20 on a daily basis. Statistical analysis was done by using SPSS version 20 statistical software package. Data were presented using descriptive statistics in the form of frequencies and percentages for categorical variables and means and standard deviation for quantitative variables.

Before data collection, ethical review committee of the College of health sciences, Jimma University has approved this study. Informed verbal consent was obtained from patients before their participation in the study.

# Results

The age of study participants ranged from 18-38 years with mean of 25 years, with 91.2% of them being in the age group between 20 - 35 years. Majority of the women included in this study were Oromo (76.5%), Muslims (68.6%), partnered (92.2%) and has college/university education (30.4%). Two fifth of the cases are urban residents (61.8) and were house-wives (59.8%) (Table 1).

Characteristics	Category	Frequency	Percentage
		N = 102	100%
Age of the mother	Mean ± SD	25 ± 3.988	
	< 20	4	3.9
	20 - 35	93	91.2
	> 35	5	4.9
Residence	Rural	39	38.2
	Urban	63	61.8
Ethnicity	Oromo	78	76.5
	Amahara	21	20.6
	Others	3	2.9
Religion	Christian	32	31.4
	Muslim	70	68.6
Marital status	Partnered	94	92.2
	Non-partnered	8	7.8
Occupation	House wives	61	59.8
	Employers	31	30.4
	Others	10	9.8
Educational level	Illiterate	18	17.6
	Read & write only	14	13.7
	1-8 <sup>th</sup> grade	22	21.6
	9-12 <sup>th</sup> grade	17	16.7
	College/University	31	30.4
Monthly income	More than minimum wage	34	33.3
	Missing	68	66.7
Personal habit*	Khat chewing	6	5.9
Personal history of HEG	Yes	2	2.0
Family history of HEG	Yes	4	3.9

**Table 1:** Socio-demographic characteristics of women with HEG, 2015, JUMC. \*other habits (smoking, alcohol) were not identified

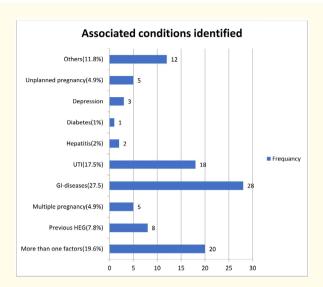
Of the total 2133 pregnant women who presented to JUMC before the  $20^{th}$  week of gestation 102 (4.8%) were diagnosed with HEG and were admitted for management in gynecology ward.

Almost half of women with HEG are gravida-I (47.1%) and have prior history of abortion (46.1%). The pregnancy was unplanned in 16 (15.7%) and twin pregnancy was identified in 5 (4.9%). The mean gestational age in weeks is 9.62 and in 18.6% of HEG was diagnosed after 12 weeks of pregnancy. Twenty-two (21.6%) of the study participants were under weight (BMI < 18.5), whereas there are no women with BMI>25. Asto weight loss during the index pregnancy, 27 (26.5%) have lost more than 5% of their pre-pregnancy weight. After admission, these women have stayed for 4.7 days on average with standard deviation of 2.09. Sixteen of these cases were readmission cases (Table 2).

Characteristics	Category	Frequency(No.)	Percentage (%)	
		N = 102	100%	
Gravidity	I	48	47.1	
	II - IV	45	44.1	
	> IV	9	8.8	
Prior abortion	No	55	53.9	
	Yes	47	46.1	
Pregnancy condition	Planned	86	84.3	
	Unplanned	16	15.7	
Number of embryo/fetus	Single	97	95.1	
	Twin	5	4.9	
Gestational age in weeks	Mean ± SD	9.62	± 1.98	
	First trimester (≤ 12 weeks)	83	81.4	
	Second trimester (> 12 weeks)	19	18.6	
Weight loss	< 5%	29	28.4	
	> 5%	27	26.5	
	Unknown	46	45.1	
BMI	< 18.5	22	21.6	
	18.5 - 24.5	80	78.4	
Previous admission with HEG	Yes	16	15.7%	
Duration of Hospitalization	1 - 4 days	73	71.6	
	5 - 9 days	29	28.4	
	(Mean ± SD)	4.7 ± 2.09		

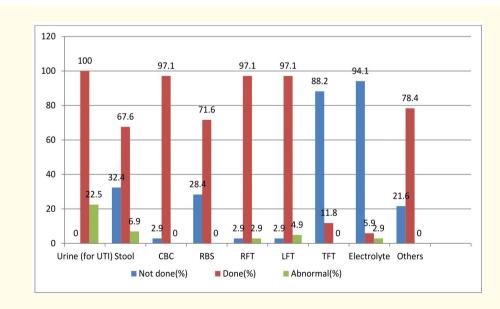
Table 2: Obstetric and clinical characteristics of women with HEG, 2015, JUMC.

All 102 of the patients had at least one condition mentioned as risk factors. Twenty (19.6%) have more than one factors identified. Gastrointestinal diseases in 27.5% and UTI in 17.6% are the most frequent conditions identified in association with HEG (Figure 1).



**Figure 1:** Associated conditions and/or co-morbidities identified in women with HEG, JUMC, 2015.

Urine analysis is performed in all of the patients and 22.5% had abnormalities other than ketonuria. The degree of ketonuria identified was severe (+3/+4) in 90 (88.2%) of them. CBC, RFT, LFT were done in 97.1% of the patients each. Whereas no abnormality was found in CBC of all patients, 3 (2.9%) patients had abnormal RFT, and 5 (4.9%) had abnormality in LFT. Serum electrolytes were determined for 6 (5.9%) cases and half of these (3 / 2.9%) had abnormal reports. There was no case with hypoglycemia or hyperthyroidism (Figures 2 and 3).



**Figure 2:** Laboratory examinations performed and abnormalities identified in women with HEG, JUMC, 2015.

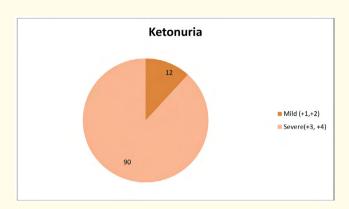


Figure 3: Degree of ketonuria on urine dipstick of women with HEG, JUMC, 2015.

Management of HEG cases included intravenous fluids hydration, vitamin supplementation, antiemetic, and dietary modification. Antiemetic therapy included promethazine (73.5%), metoclopramide (41.2%), prochlorperazine (23.5%), and more than one antiemetic drugs were used in 39 (38.2%) of cases. In addition, antacids were added in the management for 92.2% and steroid treatment for 10.8%. With regards to response to therapy, 61.8% responded to monotherapy, while 27.5% responded to combination therapy (Table 3).

Management protocol	Categories	Frequency (No.)	Percentage (%)
Anti-emetic therapy	Promethazine	75	73.5
	Metoclopramide	42	41.2
	Chlorpromazine	24	23.5
	>1 antiemetic drugs	39	38.2
	Antacids	94	92.2
	Steroid treatment	11	10.8
Fluid & electrolyte replacement		102	100.0
Vitamin supplementation		102	100.0
Dietary modification & advice		102	100.0
Other medications		22	21.6
Response to therapy			
Single antiemetic agent		63	61.8
Multiple antiemetic agents		28	27.5
Antiemetic agents+ Steroids		11	10.8
Total		102	100.0

Table 3: Management protocol and response to therapy of women with HEG, JUMC, 2015.

Only maternal religion showed significant association among socio-demographic factors. Gestational age at admission (9-12 Weeks), twin gestation in current pregnancy, history of previous admission, presence of UTI and abnormal OFT/electrolytes on admission showed significant association (p < 0.05) with prolonged hospitalization. In addition, women who require treatment with antacid, steroids, and multiple anti-emetic drugs are also associated with prolonged hospitalization (Table 4).

Factors	Prolonged Hospital stay		P-value
	No	Yes	
Age of patient (mean +SD)*	25 + 3.8	25 + 4.5	0.813
Religion of patient(Muslim)	45 (64.3)	25 (35.7)	0.018
Gravidity of patient	36 (75)	12 (25)	0.294
GA at admission (9 - 12 Weeks)*	38 (64.7)	18 (35.3)	0.002
Degree of weight loss	17 (63)	10 (37)	0.085
Twin pregnancy	2 (40)	3 (60)	0.033
History of previous admission	7 (43.8)	9 (56.2)	0.008
Degree of ketonuria	62 (68.9)	28 (31.1)	0.090
Abnormal U/A other than ketone	12 (52.2)	11 (47.8)	0.021
Abnormal OFT/ electrolytes	1 (20)	4 (80)	0.02
Requirement of antacid	58 (78.4)	16 (21.6)	0.005
First line used antiemetic drug (metoclopramide)	14 (70)	6 (30)	< 0.0001
Requirement of multiple anti emetic drugs	20 (51.3)	19 (48.7)	< 0.0001
Requirement of steroids	2 (18.2)	9 (81.8)	< 0.0001

**Table 4:** The relationship between maternal socio-demographic and clinical factors with prolonged hospital stay in women with HEG, JUMC, 2015.

\*P-value calculated by independent sample t-test, in all others chi-square test is used

# **Discussion**

The prevalence of HEG in JUMC is 4.8% of all pregnant women presenting to the hospital in the first half of pregnancy, up to 20 weeks of gestation. This finding is similar to previous studies from other similar institutions in Ethiopia and abroad. A study from Addis Ababa in three teaching hospitals showed prevalence of HEG to be 4.4% [32] and in tertiary institutions in Egypt is 4.5% [20]. This study is inconsistent with other studies that showed the prevalence of HEG to be 0.5% [32]. Estimates of HEG vary greatly and range from 0.3% in a Swedish registry to as high as 10.8% in a Chinese registry of pregnant women [19].

From previous international studies about HEG, the present study demonstrates high prevalence of HEG among pregnant women at JUMC. This difference in the prevalence of HEG is apparent because of the difference in methodology and definition of HEG used, in our study, HEG was defined as severe vomiting, ketonuria, pre-pregnancy weight loss > 5% occurring in pregnancy starting before the  $20^{th}$  week of gestation and without coincidental medical conditions while in other studies vomiting occurring in pregnancy starting before the  $20^{th}$  week of gestation, and of such severity to require the patient's hospital admission, without coincidental medical conditions.

This study showed that majority of women (91.2%) were in the age group 20-35 years old which is in agreement with other studies mentioned that majority of women (86.4%) were in the same age group [27].

This study revealed that about 47.1% of women were primigravida which is consistent with other studies and about 36.2% of those diagnosed with HEG were primigravida [20,31]. Primigravidity was found to be significantly associated with HEG. This may be due to stress and exposure to high levels of HCG for the first time.

It was noticed that the majority of women were admitted at the first trimester which is consistent with other studies who reported the same results [3]. The mean of gestational weeks at this study is  $9.62 \pm 1.98$  weeks which is consistent ( $9.8 \pm 0.47$  weeks,  $9.53 \pm 2.26$ 

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weeks) with other studies respectively [14,27]. The risk factors revealed at the present study as the highest percentages were gastrointestinal diseases, more than one risk factor and urinary tract infection in 27.5%, 19.6%, and 17.6%, respectively. These findings are consistent with others studies 26.6%, 19%, and 16% respectively [14]. But inconsistent with others studies who mentioned that hyperthyroid diseases, psychiatric illness, preexisting diabetes mellitus were all statistically significant risk factors for HEG [3].

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Concerning the duration of hospital stay, this study indicated that more than two thirds of women had from 1-4 days hospital stay which is consistent with others studies [16,20]. In this study, it was noticed that an average hospital stay of  $4.7 \pm 2.09$  days per patient which is consistent with other studies (4 days) who reported the similar results [16,33].

About 15.7% of cases were re-admissions to hospital due to recurrence of HEG after treatment. These findings are consistent with other studies. But inconsistent with some other studies, about 25% of patients required re-admission to hospital due to recurrence of symptoms [16].

The routine initial investigations done for women with HEG at the present study were urine analysis, complete blood count, renal function test, liver function test, pelvic ultrasound, random blood sugar and stool examination which is consistent with others studies [20,33].

Conventional therapies instituted were bed rest, fluid and electrolyte replacement, antiemetic therapy, vitamin supplementation and dietary modification which is inconsistent with others studies [22,28].

Among frequently used antiemetic drugs promethazine, metoclopramide and combination therapy were used in 73.5%, 41.2%, and 38.2% respectively. The response to therapy is consistent with others studies [28]. The usage of steroid treatment in this study was 10.8% which is in agreement with others studies [22,23].

### Conclusion

The overall hospital rate of HEG at JUMC was 4.8% which was considered to be high as compared to the universal prevalence. The most common risk factors of HEG were gastrointestinal diseases and urinary tract infection. The management protocol for HEG included hospitalization, fluid and electrolyte replacement, antiemetic therapy, vitamin supplementation and dietary modification and advice.

# Recommendations

A larger study is needed to establish the difference in prevalence, risk factors and management protocol of HEG among different maternity health care settings. In addition, the findings of high readmission rate and prolonged hospitalization require further exploration as to their relation with patient related or medical personnel problems. Exploration of this high prevalence of HEG leads to the recommendation that physicians and nurses should pay more attention to these women who were diagnosed with the problem.

### Limitation of the study

Lack of adequate literatures, recall bias and temporal bias were the major limitations.

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