

## ORIGINAL ARTICLE

# NAUSEA AND VOMITING IN FIRST-TRIMESTER PREGNANCY: IS HELICOBACTER PYLORUS A RISK FACTOR?

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## ABSTRACT

**Background:** Nausea and vomiting in pregnancy could lead to adverse fetal and maternal outcomes. The aim of this study was to investigate the association between Helicobacter pylori infection and both the frequency and severity of nausea and vomiting in pregnant women before 20 weeks of gestation.

**Materials & Methods:** This descriptive cross-sectional study was conducted on all one hundred pregnant women with nausea and vomiting during the study period, from May 1, 2022, to April 30, 2023, in the Obstetrics and Gynecology Department of the Maternity Teaching Hospital in Dohuk, Kurdistan Region of Iraq. The H.pylori infection was assessed through IgG testing by ELISA.

**Results:** The H. Pylori test was positive in 56% of pregnant women with Nausea and Vomiting (N&V). There was a highly significant association between cesarean section and pregnant women with preterm birth. There was a significant association between increased age and gestational age of pregnant women with N&V and positive H. Pylori test ( $p < 0.05$ ). There was a highly significant association between normal General Urine Examination (GUE) of pregnant women with N&V and positive H. Pylori test ( $p < 0.001$ ).

**Conclusions:** The prevalence of H. pylori infection among pregnant women with nausea and vomiting is high.

**KEY WORDS:** Nausea; Vomiting; Pregnancy; H. pylori; Infection.

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## INTRODUCTION

The nausea and vomiting in pregnant women or 'morning sickness', is reported for about 50–80% of pregnant women in the first trimester.<sup>1</sup> Nausea and vomiting are commonly shown between the 4<sup>th</sup> to 8<sup>th</sup> weeks of pregnancy and might continue to the 20<sup>th</sup> or 22<sup>nd</sup> weeks.<sup>2</sup> Generally, it is a mild and self-limited condition. However, it could deteriorate more severe symptoms which is called hyperemesis

gravidarum (HG).<sup>1</sup> The HG is defined as persistent nausea and vomiting in pregnancy associated with ketosis and weight loss. The HG, especially in severe cases may lead to dehydration, electrolyte imbalance, acid-base disturbance, deficient nutrition, and mortality in severe cases. Hospitalization for HG severe cases is reported in about 0.3-2% of pregnant women.<sup>3</sup> The prevalence of HG is ranged between 0.3 to 1.5% of all pregnancies.<sup>4</sup>

The exact pathogenesis of nausea and vomiting in pregnancy is not fully understood till now. However, the etiology is likely multi-factorial including different factors such as hormonal disturbances, psychological factors, gastrointestinal disturbances, infection, immune responses, metabolism abnormalities, and anatomic changes.<sup>5</sup> At first and second trimesters of pregnancy, the HG is the main cause of hospitalization and the HG is the second cause after preterm labor for pregnancy hospitalization in general. Hyperemesis gravidarum

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could be related to severe maternal co-morbidities like encephalopathy and fetal co-morbidities like intrauterine growth retardation and fetal mortality.<sup>4</sup> Helicobacter pylori (H. pylori) or Campylobacter pyloridis are gram-negative bacteria regarded as the main cause of gastritis and the commonest risk factor of peptic ulcers. Additionally, H. pylori plays a major role in the etiology of stomach lymphoma and carcinoma.<sup>6</sup> The prevalence of these bacteria in poor countries reached 70 to 90% of the population, while in rich countries the H. pylori prevalence reached about 25 to 50% of the population.<sup>4</sup> Diagnosis of H. pylori included different non-invasive tests like blood antibody test, stool antigen test, and carbon urea breath test. An invasive diagnostic method for H. pylori is by endoscopic biopsy, histology inspection, and culturing.<sup>7</sup> However, serology testing is highly sensitive, simplest, and less expensive than biopsy.<sup>8</sup> H. pylori infection among pregnant women that is acquired before pregnancy is activated with immunological and hormonal changes during pregnancy. The H. pylori infection had many adverse effects on fetal and maternal health status.<sup>9</sup> The association between H. pylori infection and vomiting and nausea at earlier weeks of gestation might be attributed to fluid replacement caused by elevated steroid hormones that also stimulate PH alteration like acidity variances that may induce H. pylori infection activation. Another explanation for this association is the reduced defensive mechanism against H. pylori infection and low gastrointestinal motility during gestation.<sup>10</sup> The aim of this study was to investigate the association between Helicobacter pylori infection and both the frequency and severity of nausea and vomiting in pregnant women before 20 weeks of gestation.

## MATERIAL & METHODS

A Descriptive cross-sectional study was carried out in the Obstetric department of Maternity Teaching Hospital in Duhok city-Kurdistan region/Iraq through the interval from 1<sup>st</sup> of May, 2022 till 30<sup>th</sup> of April, 2023. The studied population was all pregnant women who presented or were admitted to the Obstetric department of the hospital with nausea and vomiting during the study duration. A sample of 100 pregnant women with nausea and vomiting (N&V) were selected by convenience sampling after meeting inclusion and exclusion criteria. Inclusion criteria were pregnant women aged 18-42 years old, gestational age of fewer than 20 weeks confirmed by ultrasound, excessive pregnancy-related nausea and/or vomiting that prevents adequate intake of food and fluids, measuring weight loss (>5% of pre-pregnancy

weight), signs of dehydration, ketonuria (+1 or more) and hemoconcentration (normal female hematocrit value 36.1-44.3%). Exclusion criteria were hydatidiform molar pregnancy, thyroid dysfunction, gastroenteritis, cholecystitis, pyelonephritis, and liver dysfunction. The research protocol was approved by the Ethics Committee of the Kurdistan Higher Council of Medical Specialists, approval from hospital authorities, and oral informed consent of women.

The data of women was filled in a prepared questionnaire designed by the researchers after direct interviews with selected women. The questionnaire contained general characteristics of pregnant women with N&V (age, residence, gravidity history, parity history, miscarriage history, gestational age, and previous mode of delivery) and Investigation findings of pregnant women with N&V (N&V severity, complete blood count, H.pylori infection and general urine examination finding). All cases were subjected to the following: full history taking, clinical examination, transabdominal or transvaginal pelvic sonogram, laboratory investigations including complete blood count, serum electrolytes, liver and kidney function tests, urine analysis, thyroid functions, and H.pylori IgG testing by ELISA.

The collected data were entered and interpreted statistically by SPSS program 26. Suitable statistical tests (Chi-square and Fisher's exact tests) were used for categorical variables. The p-value of  $\leq 0.05$  was regarded as significant.

## RESULTS

This study included one hundred pregnant women with Nausea & Vomiting (N&V) presented with a mean age of  $28.6 \pm 5.5$  years; 53 (53%) of them were in the age group 20-29 years. Most of the pregnant 89 (89%) women with N&V were living in the urban areas. More than half 55 (55%) of pregnant women had a gravidity history of 2-4, while 62 (62%) of them had a parity history of 1-4 and 23 (23%) of them had positive miscarriage history. The mean gestational age of pregnant women with N&V was  $8.6 \pm 2.7$  weeks; 62 (62%) of them had gestational age of less than 10 weeks. The cesarean section history was the previous mode of delivery for 7 (10%) of pregnant women with N&V. (**Table 1**)

The severity of N&V was distributed as follows; grade 0 21 (21%), grade I 55 (55%), grade II 18 (18%), and grade III 6 (6%). The CBC was normal in all studied pregnant women with N&V. The H. Pylori test was positive in 56 (56%) of pregnant women with N&V. The general urine examination was abnormal in 30 (30%) of pregnant women with N&V. (**Table 2**)

**Table 1: General characteristics of pregnant women with N&V.**

Variable	No.	%age
<b>Age (years)</b>	28.6±5.5*	
<20 years	4	4.0
20-29 years	53	53.0
30-39 years	41	41.0
≥40 years	2	2.0
<b>Residence</b>		
Urban	89	89.0
Rural	11	11.0
<b>Gravidity history</b>		
Primi-gravida	28	28.0
Gravida 2-4	55	55.0
Gravida ≥5	17	17.0
<b>Parity history</b>		
Nulliparous	30	30.0
Para1-4	62	62.0
Para≥5	8	8.0
<b>Miscarriage history</b>		
Yes	23	23.0
No	77	77.0
<b>Gestational age (weeks) weeks*</b>	8.6±2.7*	
<10 weeks	62	62.0
≥10 weeks	38	38.0
<b>Previous mode of delivery</b>		
Vaginal delivery	63	90.0
Cesarean section	7	10.0
<b>Total</b>	100	100.0

\*mean ±SD

**Table 2: Investigations findings of pregnant women with N&V.**

Variable	No.	%age
<b>Severity of nausea and vomiting</b>		
Grade 0	21	21.0
Grade I	55	55.0
Grade II	18	18.0
Grade III	6	6.0
<b>Complete blood count</b>		
Normal	100	100.0
Abnormal	0	-
<b>H. Pylori test</b>		
Positive	56	56.0
Negative	44	44.0
<b>General urine examination</b>		
Normal	70	70.0
Abnormal	30	30.0
<b>Total</b>	100	100.0

There was a significant association between the increased age of pregnant women with N&V and positive H. Pylori test ( $p=0.05$ ). Among the 56 women who tested positive for H. Pylori, 28 (50%) were in the 20-29 age group, 26 (46.4%) were in the 30-39 age group, and 2 (3.6%) were in the ≥40 age group, while among 44 women who tested negative, 4 (9.1%) were in the <20 age group, 25 (56.8%) were in the 20-29 age group, and 15 (34.1%) were in the 30-39 age group. No significant differences were observed between pregnant women with positive H. Pylori test and pregnant women with negative H. Pylori test regarding residence ( $p=0.06$ ), gravidity ( $p=0.18$ ), parity ( $p=0.19$ ), miscarriage ( $p=0.9$ ), and previous mode of delivery ( $p=0.28$ ). A significant association was observed between increased gestational age of pregnant women with N&V and positive H. Pylori test ( $p=0.01$ ). Among women with positive tests, 29 (51.8%) women had a gestational age of <10 weeks, and 27 (48.2%) women had a gestational age of ≥10 weeks, while among women with negative tests, 33 (75%) women had a gestational age of <10 weeks and 11 (25%) women had a gestational age of ≥10 weeks. (Table 3)

**Table 3: Distribution of women's general characteristics according to H. Pylori test.**

Variable	H. Pylori test				P-value
	Positive (n=56)		Negative (n=44)		
	No.	%	No.	%	
<b>Age</b>					
<20 years	0	-	4	9.1	0.05 <sup>S</sup>
20-29 years	28	50.0	25	56.8	
30-39 years	26	46.4	15	34.1	
≥40 years	2	3.6	0	-	
<b>Residence</b>					
Urban	47	83.9	42	95.5	0.06 <sup>NS</sup>
Rural	9	16.1	2	4.5	
<b>Gravidity history</b>					
Primi-gravida	12	21.4	16	36.4	0.18 <sup>NS</sup>
Gravida 2-4	35	62.5	20	45.5	
Gravida ≥5	9	16.1	8	18.2	
<b>Parity history</b>					
Nulliparous	13	23.2	17	38.6	0.19 <sup>NS</sup>
Para1-4	39	69.6	23	52.3	
Para≥5	4	7.1	4	9.1	
<b>Miscarriage history</b>					
Yes	13	23.2	10	22.7	0.9 <sup>NS</sup>
No	43	76.8	34	77.3	
<b>Gestational age</b>					
<10 weeks	29	51.8	33	75.0	0.01 <sup>S</sup>
≥10 weeks	27	48.2	11	25.0	
<b>Previous mode of delivery</b>					
Vaginal delivery	40	93.0	23	85.2	0.28 <sup>NS</sup>
Cesarean section	3	7.0	4	14.8	

\*P-value Chi-square and Fisher's exact tests, S=Significant, NS=Not significant.

There was a highly significant association between normal General Urine Examination (GUE) of pregnant women with N&V and positive H. Pylori test ( $p < 0.001$ ). Among women with positive tests, 54 (96.4%) women had a normal GUE and 2 (3.6%) women had an abnormal GUE, in women with negative tests, 16 (36.4%) women had a normal GUE and 28 (63.6%) women had an abnormal GUE. While a significant association was found between H. pylori infection and the presence of nausea and vomiting among pregnant women, no significant correlation was observed between H. pylori infection and the severity of nausea and vomiting ( $p = 0.3$ ). This suggests that although H. pylori may contribute to the occurrence of nausea and vomiting, it does not appear to influence their severity. (**Table 4**)

**Table 4: Distribution of investigation findings according to H. Pylori test.**

Variable	H. Pylori test				P-value
	Positive (n=56)		Negative (n=44)		
	No.	%	No.	%	
<b>Severity of nausea and vomiting</b>					
Grade 0	9	16.1	12	27.3	0.3 <sup>NS</sup>
Grade I	31	55.4	24	54.5	
Grade II	13	23.2	5	11.4	
Grade III	3	5.4	3	6.8	
<b>General urine examination</b>					
Normal	54	96.4	16	36.4	<0.001 <sup>S</sup>
Abnormal	2	3.6	28	63.6	

\*P-value Chi square test, S=Significant, NS=Not significant.

## DISCUSSION

The complications of nausea and vomiting, if left untreated, can be serious maternal and fetal ones. Identification of risk factors is an important concern in management planning to improve the quality of life.<sup>3</sup>

The mean age in the current study reported the age of pregnant women with N&V as 28.6 years and 53% were within the age group 20-29 years. This finding is close to the results of Shahab and Hamadamin's study<sup>11</sup>, which reported that 60% of pregnant women with N&V were in the 20-29 age group. The maximum risk of nausea and vomiting in pregnancy, according to a recent Indonesian study, occurs at the age of 20-35 years, while the lower risk was at younger or older maternal ages.<sup>12</sup>

Our study found that 89% of pregnant women with N&V were urban residents. A study conducted by Fejzo and Trovik reported that nausea and vomiting in pregnancy are more common in urban areas.<sup>13</sup>

In our study, over half of the pregnant women had a history of gravidity of 2-4. On the other hand, 62% of them had a parity history of 1-4, while 23% had a positive miscarriage history. These results are in line with the outcome of various studies that have found the impact of gravidity, parity, and pregnancy loss on the incidence of nausea and vomiting in pregnancy.<sup>14,15</sup>

Our study found that 62% of pregnant women with N&V had a gestational age of less than 10 weeks. The finding coincides with the results of Zhu's study.<sup>16</sup> The history of cesarean section in the current study showed that 10% of pregnant women with N&V had a previous C-section. Similarly, research conducted<sup>17</sup> recorded that the occurrence of nausea and vomiting in pregnancy increased after a cesarean section delivery.

The severity of N&V in the current study was as follows: grade 0 comprised 21%, grade I 55%, grade II 18%, and grade III 6%. This is in closeness with findings from Jin et al. in their meta-analysis, where the N&V severity among pregnant women was specified as grade 0 (40%), grade I (46%), grade II (10%), and grade III (4%).<sup>18</sup>

The interesting finding in the present study was that, out of pregnant women with N&V, 56% tested positive for *H. pylori*. As a matter of fact, this coincides with various literature showing the significant role of *H. pylori* in the development of nausea and vomiting in pregnancy.<sup>19,20</sup>

Our study demonstrated that general urine examination was abnormal in 30% of pregnant women with N&V. Adane showed that the incidence of urinary tract infection contributed to N&V among pregnant women.<sup>21</sup>

In the current study, advanced maternal age significantly influenced having a positive *H. pylori* test with  $p=0.05$ .<sup>22</sup> Our study also showed a significant association between increased gestational age in pregnant women with N&V and a positive *H. pylori* test ( $p=0.01$ ).<sup>23</sup> Massadah reported that *H. pylori* infection in pregnant women with N&V was more evident with increased gestational age. Furthermore, our study found a highly significant association between normal GUE and a positive *H. pylori* test ( $p<0.001$ ).<sup>24</sup> Although the results of this study showed a strong correlation between the presence of *H. pylori* infection and symptoms of nausea and vomiting in the first months of pregnancy, the inverse association of infection with symptom severity should be revisited. The reasons for this difference included individual differences in immune response or pregnancy's hormonal milieu. Heightened steroid hormones cause high gastric pH, where *H. pylori* can wreak havoc and lead to nausea and vomiting among pregnant women. However, the degree of symptoms may be determined by other attributes in addition to those, such as a genetic risk factor, nutritional health or underlying medical conditions. This study also is limited

in that the diagnostic modality used (ELISA-based IgG testing) cannot accurately identify active *H. pylori* infections and cannot differentiate between chronic (smoldering) and active infections. Further studies using more sensitive and specific diagnostic methods for *H. pylori*; such as urea breath test or stool antigen tests, are required to accurately elucidate the role of *H. pylori* in NVP.

## CONCLUSION

In conclusion, the prevalence of *H. pylori* infection among pregnant women with nausea and vomiting is high. Risk factors for *H. Pylori* infection in pregnant women with nausea and vomiting are increased age and increased gestational age of pregnant women. This study recommended physicians search for *H. Pylori* infection among pregnant women with nausea and vomiting.

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**CONFLICT OF INTEREST**  
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#### AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	NSQ, MY
Acquisition, Analysis or Interpretation of Data:	NSQ, MY, AYM
Manuscript Writing & Approval:	NSQ, MY, AYM

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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