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ORIGINAL ARTICLE

PREVALENCE AND RISK FACTORS OF *HELICOBACTER PYLORI* INFECTION AMONG PREGNANT WOMEN IN NORTHWEST ETHIOPIA

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ABSTRACT

Background: *Helicobacter pylori is a gram-negative bacterium that causes chronic gastrointestinal disease and other related disorders in pregnancy. Globally, the disease is prevalent and the burden of infection is paramount in people living with poor socioeconomic conditions. Hence, the present study sought to determine the prevalence and risk factors of H. pylori infection among pregnant women in Northwest Ethiopia.*

Method: *A facility-based cross-sectional study was conducted from January to March 2020 at the University of Gondar antenatal care clinic. A total of 325 study participants were enrolled using simple random sampling technique. A pre-tested structured questionnaire was employed to collect socio-demographic characteristics, clinical parameters and predisposing risk factors. Five grams of stool specimen were collected from each participant and stored at -20^{o}C until laboratory tests could be carried out. The test used the SD BIOLINE H. pylori Ag Rapid test kit. The data analysis was done via SPSS version 20. Chi-square testing was used to observe the association between variables and logistic regression analysis was also performed to identify potential risk factors. P-value less than 0.05 was taken as statistical significance.*

Result: *The prevalence of H. pylori was found to be 40.3% (131/325). Helicobacter pylori antigen detection was significantly associated with family size (four and above) (AOR= 11.89; 95% CI = 1.18 to 119.46, P = 0.036), educational status (AOR= 7.48, 95% CI = 2.63 – 21.25, P ≤ 0.001), and gastrointestinal illness (AOR= 4.32; 95% CI = 2.28 to 8.18, P ≤ 0.001).*

Conclusion: *The present study revealed that the magnitude of H. pylori infection is high among pregnant women. Empowering women with education and improving socioeconomic status is the step ahead for prevention and control of H. pylori infection in the study area.*

Keywords*: Helicobacter pylori, Pregnant Women, Prevalence, Ethiopia.*

BACKGROUND

Helicobacter pylori is a gram-negative bacterium known to colonized the stomach and plays a role in causing multiple gastrointestinal disorders, such as peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue lymphoma (1, 2). The bacteria evades the bactericidal activity of the gastric luminal contents and enters the mucous layer. Urease production and motility are essential for this first step of infection. Urease hydrolyzes urea into carbon dioxide and ammonia, thereby permitting *H. pylori* to survive in an acidic milieu (3). The enzyme activity is regulated by a unique pH-gated urea channel, UreI, that is open at low pH and shuts down the influx of urea under neutral conditions (4). Motility is essential for colonization and *H. pylori fl*agella have adapted to the gastric niche (5).

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The prevalence of *H. pylori* varies greatly among countries and population groups within the same country since the infection is mainly correlated with socioeconomic conditions (6, 7). Globally, one half of the worlds' population is infected by *H. pylori* (8). In Ethiopia, a pooled prevalence of 52.2% (9) was reported even though reports of prevalence of *H. pylori* at country-level ranges between 7.7% (10) and 91% (11). Moreover, based on a systematic review and meta-analysis study, almost half of the pregnant women globally were infected with *H. pylori* including very high prevalence in Africa and South America compared with other continents (12).

Since humans are the only natural reservoir, person-to-person transmission is most likely with the main route of transmission being through oral-oral, fecal-oral, or gastric-oral (13, 14) contact. Living in rural areas, poor sanitation, overcrowding, lower educational levels, and low socioeconomic status were the most frequent independent risk factors for *H. pylori* infection (15).

During pregnancy, bacterium infection seems to be associated with hyperemesis gravidarum, a severe form of nausea and vomiting. Its presence is mainly related with pregnancy related disorders such as iron deficiency anemia, thrombocytopenia, fetal malformations, miscarriage, pre-eclampsia and fetal growth restriction (16). A few studies have explored possible associations between these symptoms and the presence of chronic gastrointestinal infections (17, 18).

Pregnancy is characterized by a decreased cell-mediated cytotoxic immune response with preservation of humoral and innate immunity (19) and by itself may increase the susceptibility to *H. pylori* infection (20). This is probably due to the fact that there are immunologic adaptations in pregnancy to ensure maternal tolerance towards the semi-allogeneic fetus (19).

Pathogenicity caused by the bacillus relies on several strain-specific factors. Some strains express specific genes conferring pro-inflammatory, cytotoxic and vacuolating properties which could enhance the in vivo pathogenicity (21). Urease and flagella are the virulence factors in all strains and they are vital for pathogenesis and colonization (22).

Serological and stool antigen tests are the first choice for *H. pylori* infection diagnosis in pregnancy, since they are easy to perform and low-cost. The serological test isn't able to differentiate current and past *H. pylori* infection due to late disappearance of anti-IgG *H. pylori* antibodies. This limits the ability to assess the actual incidence and association of *H. pylori* infection with potential risk factors. In the present study the stool antigen test was used to measure the current infection status of pregnant women.

In Ethiopia, despite various studies conducted on the burden of *H. pylori* infection and its associated risk factors on different study groups, little information is available on the prevalence of *H. pylori* infection among pregnant women, including in the present study area. Therefore, this study was designed to determine the prevalence of *H. pylori* and to point out the possible risk factors among pregnant women attending the antenatal care clinic at University of Gondar Comprehensive Specialized Hospital.

METHOD

Study design, period and area: A facility-based cross-sectional study was conducted from January to March 2020 to determine the prevalence and risk factors of *Helicobacter pylori* infection among pregnant women attending the antenatal care clinic at University of Gondar Comprehensive Specialized Referral Hospital, Gondar, Northwest Ethiopia. It is one of the largest public hospitals in Amhara regional state, which services over 5 million people. The hos-

pital is in Gondar town, the historic former capital city of Ethiopia hundreds of years ago.

Data collection and processing:

Questionnaire survey: Socio-demographic, clinical, behavioral and environmental data were collected using a pre-tested structured questionnaire, after informed consent was obtained from pregnant women. The data was collected by trained data collectors through face-to-face interview with each study participant. A pre-test was conducted among five percent of the total sample size selected randomly from study participants. The data was collected using the local "Amharic" language version of the questionnaire which was translated from "English" version. Some of the collected information included: the women's age, parity, trimester, educational level, occupational status, types of toilet, and source of drinking water.

Stool sample collection and processing: Using clean and labelled containers, approximately 5 grams of stool specimens were collected from pregnant women who volunteered to participate in the study. Then, using ice coolers, the stool samples were transported to the Immunology and Molecular biology Laboratory at the University of Gondar and stored at -20^{o}C until laboratory tests could be carried out. Each stool specimen was processed and examined for *H. pylori* using an antigen test.

***H. pylori* testing:** The SD BIOLINE *H. pylori* Ag Rapid test kit was used to diagnose *H. pylori*, after considering previous study recommendations on the specificity and sensitivity of *H. pylori* diagnosis methods in the study area (23). All test activities were done according to manufacturer's instructions (STANDARD DIAGNOSTIC, INC. Korea). The presence of only one band ("C" band) within the result window indicates a negative result while the presence of two colour bands ("T" band and "C" band) within the result window indicates a positive result. In cases where the purple colour band was not visible within the result window (of the "C" window) after performing the test, the result was considered invalid and the specimen were re-tested using a new test kit. Test results were interpreted within 10–15 minutes.

Study population and sampling technique: Study participants were pregnant women who had antenatal care follow-up during the study period at the University of Gondar Comprehensive Specialized Hospital. The sample size was determined using the single population proportion formula based on a 29% prevalence of *H. pylori* among pregnant women from a previous study (24) with 5% marginal error (d=0.05) and 95% confidence interval (Z=1.96)). Accordingly, the total sample size was determined to be 332 with 5% non-response rate.

Inclusion and Exclusion Criteria: Study participants who had no history of having been treated with antibiotics, colloidal bismuth compounds, proton pump inhibitors (PPI) or H2 blockers in the last four weeks prior to screening were included in this study and those who had been previously treated were excluded from the study.

Data management and analysis: After the data was entered, the data were cleaned and checked for completeness and analyzed using Statistical Package for Social Sciences (SPSS) version 20 software. The frequency, mean and proportion were used to describe study participants' characteristics. A chi-square test was used to observe the association between dependent and independent variables. Binary logistic regression and multivariate regression analysis were performed to identify potential risk factors of *H. pylori* infection. *P*-value less than 0.05 was considered as statistically significant.

RESULT

Socio-demographic characteristics of the study participants: Among the 332 pregnant women who gave consent, seven stool samples were discarded due to poor quality and inadequacy. Thus, 325 pregnant women participated in the study. The mean age of participants was 26.8 ± 4.9 (age range 17- 42 years). More than one-third of the study participants, 123 (37.8%), were between 22 – 26 years. Around 77% of participants were urban residents. Three hundred nineteen (98.2%) of study participants were married. Regarding their occupational status, (36.3%) of them were housewives (Table 1).

Table 1: Socio-demographic Characteristics of Study Participants attending Antenatal Care Clinic at University of Gondar Comprehensive Specialized Hospital

Variable		Frequency	Percentage (%)
Age (Years)	17 - 21	43	13.2
	22 - 26	123	37.9
	27 - 31	109	33.5
	32 - 36	39	12.0
	37 - 42	11	3.4
Ethnic group	Amhara	324	99.7
	Tigray	1	0.3
Religion	Orthodox	312	96
	Muslim	12	3.7
	Others	1	0.3
Residence	Rural	75	23.1
	Urban	250	76.9
Educational level	Illiterate	82	25.2
	Primary school	59	18.2
	Secondary school	142	43.7
	Degree and above	42	12.9
Marital status	Single	3	0.9
	Married	319	98.2
	Divorced	2	0.6
	Widowed	1	0.3
Occupational status	Governmental employee	77	23.6
	Private work	27	8.3
	Daily laborer	7	2.2
	House wives	118	36.3
	House worker	55	16.9
	Merchant	21	6.5
	Student	8	2.5
	Other	12	3.7
Household family size	One	5	1.5
	Two	117	36.0
	Three	73	22.5
	Four and above	130	40.0

Prevalence of *H. pylori* in relation with Socio-Demographic Characteristics of Study participants: The overall prevalence of *H. pylori* infection among pregnant women was found to be 40.3% (131/325) (95% CI = 34.9 – 45.9). The highest prevalence of *H. pylori* was observed in the age group of 27 – 31 (38.2%), though the difference was statistically insignificant among age groups (P>0.05). In univariate logistic regression analysis, the odds of being infected by *H. pylori* was around six times higher among illiterate study participants than those who had a degree and above educational level (crude odds ratio (COR) = 5.74; 95% CI = 2.51 - 13.14). In addition, a significant difference was observed among household family size across *H. pylori* positivity (p<0.05) (Table 4). A significantly higher number of positivity was found among urban residents 103 (78.6%), but the difference was not significant (P = 0.55) (Table 2).

Table 2: *Helicobacter pylori* infection status in relation with Socio-demographic Characteristics of Pregnant Women attending Antenatal Care Clinic at the University of Gondar Comprehensive Specialized Hospital

Variable	Total tested No (%)	Stool antigen test		P-value
		Positive No (%)	Negative No (%)	
Age category				
17 - 21	43 (13.2)	18 (13.7)	25 (12.9)	
22 - 26	123 (37.8)	43 (32.8)	80 (41.2)	
27 - 31	109 (33.5)	50 (38.2)	59 (30.4)	0.56
32 - 36	39 (12.0)	16 (12.2)	23 (11.9)	
37 - 42	11 (3.4)	4 (3.1)	7 (3.6)	
Religion				
Orthodox	312 (96.0)	126 (96.2)	186 (95.9)	
Muslim	12 (3.7)	5 (3.8)	7 (3.6)	0.71
Others	1 (0.3)	0 (0)	1 (0.5)	
Residence				
Rural	75 (23.1)	28 (21.4)	47 (24.2)	
Urban	250 (76.9)	103 (78.6)	147 (75.8)	0.55
Marital Status				
Single	3 (0.9)	0	3 (1.5)	
Married	319 (98.2)	128 (97.7)	191 (98.5)	0.09
Divorced	2 (0.6)	2 (1.5)	0	
Widowed	1 (0.3)	1 (0.8)	0	
Monthly income				
Less than 1000	123 (37.8)	51 (38.9)	72 (37.1)	
1000 - 2000	78 (24.0)	30 (22.9)	48 (24.7)	0.91
Above 2000	124 (38.2)	50 (38.2)	74 (38.1)	

Pearson's chi-square test showed that none of the life style and possible environmental risk factor variables were significantly associated *with H. pylori* infection (Table 3).

Table 3: Prevalence of *H. pylori* infection among pregnant women with respect to life style, and environmental possible risk factors at University of Gondar Comprehensive Specialized Hospital Antenatal Care Clinic

Variable	Total tested	No. HpSA +	X^2	P-value
Khat chewing				
Yes	1	0	0.68	0.41
No	324	131		
Alcohol consumption				
Yes	63	23	0.47	0.49
No	262	108		
Tea and coffee consumption				
Yes	250	97	1.02	0.31
No	75	34		
Frequency of tea and coffee consumption/Day				
One	55	139		
Two	12	34		
Three	17	47	0.61	0.89
Four and above	13	30		
History of IP during pregnancy				
Yes	141	48	4.06	0.04
No	184	83		
Eating unwashed vegetables and fruits				
Yes	38	12	1.36	0.24
No	287	119		
Hand washing before meal				
Yes	324	130	1.48	0.22
No	1	1		
Hand washing with soap after toilet				
Yes	312	126	0.02	0.89
No	13	5		
Source of drinking water				
Tap water	290	115		
River, Lake or Stream	10	6		
Well	9	2	6.23	0.18
Pipe	11	7		
Packed	5	1		
Toilet use				
Yes	283	112	0.49	0.49
No	42	19		

X^2 – Chi-square

Prevalence of *H. pylori* infection among pregnant women with respect to clinical parameters at the University of Gondar Hospital antenatal care clinic: The majority of pregnant women, 202 (62.1%) were multigravida. One hundred thirty (40.0%) women were in their second trimester followed by those in their first 107 (32.9%) and in their third trimesters 88 (27.1), though no significant difference was observed between trimesters (P > 0.05). More than half of study participants had history of hyperemesis gravidarum and gastrointestinal illness (57.2%) and (59.7%), respectively.

On univariate logistic regression analysis, the odds of having *H. pylori* infections were significantly higher in those who had history of hyperemesis gravidarum (COR = 1.61; 95% CI = 1.02 to 2.54). In line with this, a majority of the participants who had a clinical sign of hyperemesis gravidarum were in the first trimester (P < 0.05). Pregnant women who had history of gastrointestinal illness were approximately four times more prone to *H. pylori* infection (COR= 3.9; 95% CI = 2.37 to 6.43) than those who didn't have previous history. Moreover, 67.5% of pregnant women who had a history of intestinal parasitic illness had hyperemesis gravidarum during pregnancy (Table 4).

Table 4: Univariate analysis showing association of *H. pylori* infection among pregnant women with respect to some Socio-demographic and clinical parameters at the University of Gondar Comprehensive Specialized Hospital Antenatal Care Clinic

Variable	Total	No. HpSA +	COR (95% CI)	*P-value*
Educational status				
Illiterate	82	55	5.74 (2.51 – 13.14)	≤ 0.001
Primary School	59	12	0.72 (0.28 – 1.83)	0.49
Secondary School	142	53	1.68 (0.78 – 3.61)	0.19
Degree and above	42	11	1	
Household family Size				
One	5	1	1	
Two	120	25	1.05 (0.11 – 9.84)	0.96
Three	74	13	0.85 (0.09 – 8.26)	0.89
Four and above	126	92	10.82 (1.17 – 100.29)	0.03
Gravidity				
First	123	43	0.67 (0.39 – 1.11)	0.12
Second	79	33	0.89 (0.50 – 1.57)	0.68
Three and above	123	55	1	
Trimester				
First	107	40	0.75 (0.42 – 1.33)	0.33
Second	130	52	0.84 (0.48 – 1.45)	0.53
Third	88	39	1	
History of hyperemesis gravidarum				
Yes	186	84	1.61 (1.02 – 2.54)	0.04
No	139	47	1	
History of gastrointestinal illness				
Yes	194	102	3.90 (2.37 – 6.43)	≤ 0.001
NO	131	29	1	

DISCUSSION

Helicobacter pylori plays a pivotal role in abdominal symptoms and gastroduodenal diseases, including peptic ulcer and gastric malignancies (25). The infection is mainly acquired during childhood and causes asymptomatic chronic infection (8). It is widely believed that an activation of latent *H. pylori* occurs during pregnancy due to hormonal and immunological changes having an impact not only on maternal health, but also on the fetus and sometime consequences can be observed later in life (16).

In the present study, the overall stool antigen detection rate of *H. pylori* infection among pregnant women was 40.3%. The current study finding was lower compared with studies conducted in Kulito Health Center, South Ethiopia (54.7%) (26) and other countries report like; Uganda (45.2%) (27), Mexico (52.2%) (28), Belgium (52.4%) (20) and Chile (68.6%) (29). However, we found higher prevalence of *H. pylori* infection compared with studies done in Addis Ababa (21.9%) (30), 29% from Nigeria (31) and other studies in Zanzibar and France with a prevalence of 17.5% and 21.5%, respectively (32, 33). The variation in detection rate of *H. pylori* infection might be due to difference in study area, study design, laboratory methods used, study population, socio-economic status, and personal life style. However, there was no statistically significant association between *H. pylori* infection and sociodemographic characteristics like; age group, marital status, occupational status (table 2), and some expected behavioral and environmental risk factors like habits of drinking alcohol, cigarette smoking, Khat chewing, drinking tea and coffee, water source for drinking purpose (table 3). Besides, clinical parameters like: gestational period (week), gravidity (number of pregnancy), parity (number of children) (table 4 and 6).

The present study showed that *H. pylori* infection was significantly higher in the pregnant women with hyperemesis gravidarum ($P<0.05$): 64.1% of the study participants with history of hyperemesis gravidarum were positive to *H. pylori* infection. This also supported by studies conducted on the prevalence of *H. pylori* infection among pregnant women with hyperemesis gravidarum in Turkey and Nigeria which were (80%) (34) and (72.4%) (24), respectively. Moreover, comparably lower prevalence were found among pregnant women with hyperemesis gravidarum in Saudi Arabia (35) and Turkey (36). Possible reasons may be the accumulation of fluid and displacement of intracellular and extracellular fluid that may occur as a result of the increased level of steroid hormones and HCG during pregnancy, which leads to changes in pH and motility of gastrointestinal tract, and this changes in turn the activities of *H. pylori* infection(37). However, insignificant differences were observed between pregnant women with and without hyperemesis gravidarum in relation to *H. pylori* infection (38, 39) and other studies (40-42).

In this study, gastrointestinal illness was found to be a risk factor for *H. pylori* infection (AOR= 4.32; 95% CI = 2.28 to 8.18, $P \leq 0.001$) (Table 5), the result revealed that 52.6% of pregnant women with a history of gastrointestinal illness were positive to *H. pylori* infection. But this finding was higher compared with a comparative study conducted among pregnant and non pregnant women in Addis Ababa, Ethiopia (34.7%) (30). Besides, this study finding was relatively lower in comparison with a study done in Chile (72.5%) (43). The coincidence of gastrointestinal illness with *H. pylori* infection might be due to the role of the bacteria in controlling the secretion of stomach acid. Since the bacteria infect the stomach wall, it controls the secretion of stomach acid, causing low stomach acid. This results in difficulty in assimilating nutrients from animal protein and once stomach acid has decreased, it will lead to gastritis or stomach inflammation which always accompanies infection in the gastrointestine (44).

Regarding educational status, illiteracy was positively associated with *H. pylori* infection (AOR= 7.48, CI = 2.63 – 21.25, $P \leq 0.001$). This study finding agreed

with other studies (45-47). In addition, this result was also pronounced in a study conducted among children that pointed out the impact of educational status of the family in *H. pylori* infection (48). The observed association may show the role of education by influencing personal and household hygiene practices.

Pregnant women who had four and above family members were found almost twelve times more prone to *H. pylori* infection than those who had one family member (AOR= 11.89; 95% CI = 1.18 to 119.46, P = 0.036). The possible reason might be that an increase in family size could lead to poor socioeconomic conditions, over-crowdedness and poor hygienic conditions which are all predisposing factors to *H. pylori* infection (49).

Table 5: Prevalence of *H. pylori* across risk factors among pregnant women attending Antenatal Care Clinic at University of Gondar Comprehensive Specialized Hospital

Variable	Frequency	HpSA + No./%	COR	*P-value*	AOR	*P*-value
Family size						
One	5	1 (0.8)	1			
Two	120	25 (19.1)	1.05	0.964	1.23	0.86
Three	74	13 (9.9)	0.89	0.890	0.61	0.68
Four and above	126	92 (70.2)	10.82	0.036	11.89	0.03
Educational level						
Illiterate	82	55 (67.1)	5.74	≤ 0.001	7.48	≤ 0.001
Primary school	59	12 (20.3)	0.72	0.490	1.41	0.55
Secondary school	142	53 (37.3)	1.68	0.186	2.08	0.13
Degree and above	42	11 (26.2)	1			
History hyperemesis gravidarum						
Yes	186	84 (64.1)	1.61	0.040	1.16	0.64
No	139	47 (35.9)	1			
History gastrointestinal illness						
Yes	194	102 (52.6)	3.90	≤ 0.001	4.32	≤ 0.001
No	131	29 (22.1)	1			

HpSA +, *Positive for H. pylori stool antigen;* ***COR****, Crude odds ratio;* ***AOR****, Adjusted odds ratio*

Table 6: Univariate analysis showing association of *H. pylori* infection with clinical parameters of pregnant women attending Antenatal Care Clinic at University of Gondar Comprehensive Specialized Hospital

Variable	Total tested	No. HpSA +	X^2	P-value
Gastric cramping				
Yes	156	54	4.04	0.04
No	169	77		
Abdominal discomfort				
Yes	182	64	4.55	0.03
No	143	67		
Dyspepsia				
Yes	131	47	0.18	0.11
No	194	84		
Heart burn				
Yes	156	63	0.001	0.98
No	169	68		
Vomiting				
Yes	98	40	0.01	0.90
No	227	91		
Nausea				
Yes	166	61	1.79	0.18
No	159	70		

CONCLUSION

The present study revealed that the magnitude of *H. pylori* infection is high among pregnant women. Feco-prevalence was significantly associated with educational status, family size and gastrointestinal illness. Empowering women with education and improving socioeconomic status are likely next steps for prevention and control of *H. pylori* infection in the study area.

Declarations

Ethics approval and consent to participate: The study was approved by the Research and Ethical Review Committee of the School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. Permission was also sought from University of Gondar Hospital after submitting the ethical approval. Informed consent was obtained from all study participants before commencing the study. A code number was given to each study subject. The diagnosis results remained confidential and necessary treatments were given by physicians for those found to have infection.

Consent for publication: Not applicable in this section

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

***Competing interests*:** The authors declare that they have no competing interests.

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Authors' contributions: AD and AK conceived the study. AD, AK, AA, YT and GB involved in data collection and analysis. AD prepared the first draft of the manuscript. All the authors were involved in critical review and approving the final version of the manuscript.

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List of Abbreviations: HCG- human chorionic gonadotropin, **HPSA**: *Helicobacter pylori* stool antigen test

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