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Original Research Article

Association between *Helicobacter pylori* infection and iron deficiency anemia among dyspeptic adult patients

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ABSTRACT

Background: *Helicobacter pylori* infection is a global public health problem that affects both developed and developing countries bearing a burden of one-third and half respectively. Previous studies on *H. pylori* infection and iron deficiency anemia were limited to children and pregnant women, indicating a paucity of evidence among dyspeptic adults. Hence, this study was aimed to assess the association of *H. pylori* infection and iron deficiency anemia among dyspeptic adult patients.
Methods: An institution based cross-sectional study was conducted from January to November 2023 among 328 dyspeptic adult patients aged 18 and above visiting Shashemene comprehensive specialized hospital. A structured questionnaire was used to collect data. RBC count, Hb and Hct were measured. Anemia was declared if Hb was <12 g/dl in females and <13 g/dl for men according to the WHO. The *H. pylori* infections status of the patients were detected using stool antigen test, and saline stool prepared was examined for intestinal parasites. Data were coded, entered and analyzed by SPSS version 25. Chi-square test and Logistic regression were used to assess association between variables, and a $p<0.05$ was considered statistically significant.
Results: Of 328 study participants, 38 (11.6%) were positive for *H. pylori*. The prevalence of anemia among HP infected was higher (50%) than uninfected (19.3%) patients ($\chi2=17.941$, $p=0.000$). *H. pylori* infection was significantly associated with Anemia ($p<0.001$).
Conclusions: There was association between *H. pylori* infection and iron deficiency anemia. Unhygienic water supply and poor sanitation are contributing factors.

Keywords: Helicobacter pylori, Iron deficiency anemia, Global public health

INTRODUCTION

Infection with *Helicobacter pylori* is a global public health problem that affects both developed and developing countries with a higher burden of more than half observed in developing countries compared to 34.7% in developed countries.[1-3] *H. pylori* is a gram-negative bacteria with a helix-shaped, curved rod. Gastritis, peptic ulcer disease, gastroduodenal ulcer, atrophic gastritis, gastric malignancies, and dyspeptic symptoms are all caused by it.[4,5] However, more than 80% of people who acquire *H. pylori* are usually asymptomatic. *H. pylori* is essential to the natural stomach ecology.[6]

Infection with *H. pylori* affects approximately 4.4 billion people globally.[1] Africa has the highest infection prevalence, at 70.1%, with prevalence ranging from 18.9% in Switzerland to 87.7% in Nigeria.[1] Pakistan and

India had the highest prevalence in Southern Asia, whereas Turkey had the highest prevalence in Western Asia, at 77.2%.[6] *H. pylori* was found in 74% of dyspeptic individuals in Uganda.[7] According to a meta-analysis conducted in Ethiopia, the prevalence of HPI varies from region to region, ranging from 7.7% to 91%.[8]

H. pylori Infection has been linked to hematological symptoms such as anemia and micronutrient deficiency (iron and vitamin B12).[9] It has also been associated with extra-gastric symptoms such as thrombocytopenic purpura, decreased growth velocity, iron shortage, and/or anemia.[10,11] Several studies have shown that eliminating *H. pylori* bacteria restores iron nutritional status without the need for iron supplementation.[12-15]

The mechanism or mechanisms by which *H. pylori* infection may cause iron deficiency and/or anemia are not fully understood, but likely mechanisms include an increase in intragastric pH; a decrease in ascorbic acid concentration in gastric juices, which disrupts iron absorption from the diet; chronic bleeding caused by an increase in micro-erosions in gastric mucous; neutrophil production of lactoferrins; and bacteria capture of iron.[16] Another possibility is an increase in hepcidin production, a key regulator of iron metabolism that slows iron absorption in the small intestine.[17]

Several studies on the association of *H. pylori* with iron deficiency anemia in Ethiopia focused on children and pregnant women. This revealed a paucity of evidence linking *H. pylori* infection to iron deficiency anemia in dyspeptic adults in Ethiopia, particularly in the Oromia region. This hinders HP infection prevention and control strategies in the study area. As a result, the aim of this study was to assess the association between HP infection and iron deficiency anemia among dyspeptic adult patients in the study area.

METHODS

Study design and period

Institution-based cross-sectional study was conducted from January 2023 to November 2023.

Study setting

The study was conducted at Shashemene Comprehensive Specialised Hospital, which is 250 kilometres from Addis Ababa along the Ethio-Kenya highway in the southern region of the country. It is one of the Comprehensive Specialised public hospitals, serving 2,731,154 estimated population, including 1,379,679 males and 1,381,475 females. Currently, the hospital offers curative and rehabilitative treatments with 232 beds and 383 employees. The hospital includes an accredited laboratory that can detect anaemia and *H. pylori* infection.

Population

All dyspeptic adult patients were considered as source population. Those dyspeptic patient from January 2023 to November 2023 were study population.

Inclusion criteria

All consecutively identified adult dyspeptic patients (age >18 years) who have dyspeptic complaints were included in the study until attaining sample size.

Exclusion criteria

Patients with chronic diseases, pregnant women and who had undergone gastrectomy. Patients who took treatment for *H. pylori* infection within last three month, donate blood within last three month and on treatment for anemia before data collection, and severally ill patients thus unable to respond to the questionnaire were excluded.

Sample size determination

The sample size was determined using single population proportion formula taking 30.9% prevalence of *H. pylori* infection from previous study with assumptions of confidence level at 95%, and margin of error (d) 5%.[18]

$$n=(Z\alpha/2)^2\times(p)\times(1-P)/d^2$$

Where;

n=sample size, $Z_{\alpha/2}$= critical value at 95% confidence level of certainty, p=proportion 30.9%, d=margin of error 5%.

When the non-response of 10% was added to the total sample size then the final sample size was 328.

Sampling technique and procedure

During the study period, a simple random sample procedure was used among dyspeptic adult patients who visited the hospital. The sampling frame for the current study was a list of dyspeptic adult patients obtained from the patient registration card. The individuals who matched the inclusion requirements were then given the chance to choose numbers from computer generated random numbers.

Data collection tools and procedures

Data were collected through face-to-face interview using structured questionnaires. Section one: Socio-demographic variables; age, sex, marital status, educational level, family size, income. Section two: environmental related variables; source of water used for drinking, habits of hand washing before meals and after

toilet use. Section three: behavioral related variables; habits of smoking, alcohol drinking, khat chewing, BMI. Section four: clinical related variables; like presence of *H. pylori* infection, presence of anemia, presence of intestinal parasite.

Study variables

Dependent variable

Dependent variable was presence of anemia.

Independent variable

Independent variables were-socio-demographic variables; age, sex, marital status, educational level, family size, income. Environmental related variables; source of water used for drinking, habits of hand washing before meals and after toilet use. Behavioral related variables; habits of smoking, alcohol drinking, khat chewing, BMI. Clinical related variables; like presence of *H. pylori* infection, presence of anemia, presence of intestinal parasite

Operational definition

Anemia

Hemoglobin level less than 13 mg/dl for male and less than 12 mg/dl for female considered as anemic according to WHO.

Data quality control

Standard operating procedures (SOP) were strictly followed and internal quality control materials were included from the test kits and performed based on manufacturer instructions. The questionnaire was checked by advisors and pretest was conducted at health center before the detail works were started. Proper training was given before starting data collection for data collectors and intensive supervision was done during data collection by the principal investigator

Data analysis and management

Data was entered and analyzed using SPSS version 25 and results were displayed using frequency and percentages. The Chi-square test ($\chi 2$) and logistic regression was performed. Figures and tables were used for data presentation. Continuous variables were reported using mean±SD. Anemia was defined according to the WHO definition as a hemoglobin concentration of <12 g/dl for adult women and <13 g/dl for adult men. For analysis purpose, 1. Anemic 0 non anemic categorized. Binary logistic regression were used to assess association between variables, and a $p<0.05$ was considered statistically significant.

RESULTS

Socio demographic characteristics

A total of 328 dyspeptic adult subjects were recruited for this study. Of these 208 (63.4%) were female and 120 (36.6%) were male with a median age of 32±11 (IQR) years and 34±13 (IQR) years female and male respectively. Majority of the participants were married 264 (80.5%), about one third of them were attended secondary school 112 (34.1%) and from rural area 199 (60.7%) (Table 1).

Behavioral characteristics

Among the study participants 55 (16.8%) were reported to have history of alcohol consumption while 67 (20.4%) were khat chewers. Frequent hand washing was reported among 267 (81.4%) participants. Pipe and well water was major source of drinking water among the study participants 221 (67.4%), 92 (28%) respectively (Table 2).

Prevalence of H. pylori infection and associated risk factors

Overall prevalence of *H. pylori* stool antigen was detected 38 (11.58% [(95% CI:8.53,15.55)]. The frequency of infection was higher in age groups 18-28, 20/38 (52.63%) and lower in age groups >49, 1/38 (2.63%), but the number of patients aged ≥49 years studied has been much smaller than those younger than 49 years. More infection was detected in those living in rural area than urban area (57.89% vs 42.1%). Among variables of study source of drinking water was statistically significant (AOR=5.136 95% CI (1.217, 21.685); p=0.026).

Sex (AOR=0.479 95% CI=0.217, 1.054; p=0.067), marital status (AOR=2.196 95% CI=0.96, 5.021; p=0.062) and habit of hand washing after toilet use (AOR=0.281 95% CI=0.077, 1.016; p=0.053) showed weak correlation with the infection.

However, age, smoking, presence of intestinal parasite, alcohol, income and other demographic characteristics are not significantly associated with *H. pylori* infection (Table 3).

Prevalence of anemia among dyspeptic patients and its association with H. pylori infection

Prevalence of anemia among dyspeptic patients was 22.9% (75/328). The mean hemoglobin was 13.45±1.54 g/dl and 14.12±1.92 g/dl for females and males respectively. The prevalence of anemia among HP infected was 50% (19/38) and 19.3% (56/290) in HP negative patients. The difference was statistically significant among infected individuals and uninfected one ($\chi 2=19.187$; p=0.000) (Table 5).

Table 1: Socio-demographic characteristics of dyspeptic adult patients 2023.

Variables	N	Percentage (%)
Sex		
Male	120	36.59
Female	208	63.41
Age (in years)		
18-28	141	42.99
29-38	104	31.71
39-48	56	17.07
>49	27	8.23
Marital status		
Single	64	19.51
Married	264	80.49
Educational level		
Illiterate	111	33.84
Primary school	77	23.48
Secondary school	112	34.15
College and above	28	8.54
Family size		
<5	209	63.72
>6	119	36.28
Residence		
Urban	129	39.33
Rural	199	60.67
Body mass index (kg/m^2)		
Underweight	42	12.80
Normal	269	82.01
Overweight	17	5.18

Table 2: Behavioral characteristics of dyspeptic adult patients

Variables	N	Percentage (%)
Alcohol consumption		
Yes	55	16.77
No	273	83.23
Cigarette smoking		
Yes	24	7.32
No	304	92.68
Khat chewing		
Yes	67	20.43
No	261	79.57
Hand washing		
Yes	267	81.40
No	61	18.60
Source of drinking water		
River water	15	4.57
Well water	92	28.05
Pipe water	221	67.38
Intestinal parasite		
Seen	28	8.5
Not seen	300	91.5
Anemic status		
Anemic	75	22.9
Non anemic	253	77.1

Table 3: Multivariable logistic regression analysis of factors associated with *H. pylori* infection.

Variables	Category	Positive, N (%)	Negative, N (%)	COR 95% CI	AOR 95% CI
Age (in years)	18-28	23 (16.31)	118 (83.69)	1	1
	29-38	11 (10.58)	93 (89.42)	0.61 (0.28, 1.30)	0.18 (0.06, 0.55)
	39 and above	4 (4.82)	79 (95.18)	0.26 (0.08, 0.78)	0.12 (0.04, 0.40)
Sex	Male	19 (15.83)	101 (84.17)	1	1
	Female	19 (9.13)	189 (90.87)	0.53 (0.27, 1.55)	1.27 (0.47, 3.46)
Alcohol consumption	Yes	12 (21.82)	43 (78.18)	2.65 (1.24, 5.65)	2.41 (0.86, 6.73)
	No	26 (9.52)	247 (90.48)	1	1
Smoking	Yes	10 (41.67)	14 (58.33)	7.04 (2.86, 17.31)	4.94 (1.34, 18.27)
	No	28 (9.21)	276 (90.79)	1	1
Khat chewing	Yes	13 (19.40)	54 (80.60)	2.27 (1.09, 4.73)	2.50 (0.80, 7.77)
	No	25 (9.58)	236 (90.42)	1	1
Source of drinking water	River	7 (46.67)	8 (53.33)	1	1
	Well	16 (17.39)	76 (82.61)	0.24 (0.08, 0.76)	0.23 (0.53, 0.97)
	Pipe	15 (6.79)	206 (93.21)	0.08 (0.03, 0.26)	0.06 (0.13, 0.25)

Table 4: Association between RBC indices and *H. pylori* infection.

Parameters	Mean (SD)		P value	95% CI
	+ve	-ve		
Hgb	12.95±1.48	13.8±1.73	0.005	0.26, 1.41
Hct	39.3±4.5	41.5±5.1	0.007	0.63, 3.8
MCV	90.3±9	90.8±9.5	0.742	2.65, 3.69
MCH	30.6±2.67	30.5±2.97	0.84	-1.03, 0.84
MCHC	33.19±1.5	33.24±2	0.877	-0.5, 0.58
RBC count	4.3±0.5	4.55±0.67	0.013	0.05, 0.434

*Hgb=hemoglobin; Hct=hematocrit; MCV=mean corpuscular volume; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; RBC=red blood cell.

Table 5: Association between *H. pylori* infection and anemia.

Anemic status	HP status		COR (95% CI)	AOR (95% CI)	P value
	Positive	Negative			
Anemic	19 (50%)	56 (19.3%)	4.747 (2.355-9.572)	5.521 (2.521-12.091)	0.001
Non anemic	19 (50%)	234 (80.7%)	1		

DISCUSSION

The overall prevalence of anemia in this study was found to be 22.9 % with [(95% CI=2.521-12.091)] dyspeptic adult patients, while *H. pylori* infection was present in 11.6% of dyspeptic adult patients with [(95% CI=8.3-14.9)]. Among those infected with *H. pylori*, anemia was significantly more ubiquitous (50%) compared to those non-infected individuals (19.3%).

The prevalence of *H. pylori* infection in this study was relatively low compared to those findings from other countries like, Vietnam 52.1%, Nigeria 81.7%, Cameroon 64.9% and various parts of Ethiopia such as Gondar 65.7%, Butajira 52.4% and Addis Ababa 29%.[18-23] However, it was slightly higher than results from studies conducted in Yirga Cheffe 7.7% and Batu 5.2%.[24,25] Differences in prevalence of infections are probably due to variations in sample size, population demographics, geographic location, and the diagnostic methods used.

Additionally, prior antibiotic use-common in areas where parasitic and respiratory infections are prevalent-might have contributed to reduced *H. pylori* detection.[26]

On the other hand the findings of present study is found in the national range of report by meta-analysis done in Ethiopia, reporting the prevalence of *H. pylori* infection ranging from 7.7% to 91%.[8,24]

Importantly, study found significant association between *H. pylori* infection and iron deficiency anemia, regardless of ulcer presence in dyspeptic patients. Infected individuals with *H. pylori* had chance of developing iron deficiency anemia 5.5 folds with (95% CI=2.521-12.091) than uninfected of patients from dyspeptic adults. Similar associations have been reported in research from China, where *H. pylori*-positive individuals had higher rates of developing iron deficiency anemia.[27]

A meta-analysis by Yuan et al also showed improved hemoglobin levels in those treated for *H. pylori* alongside

iron supplements, compared to those who received iron only.[14] Other studies from Alaska, Hudak et al meta-analysis done by Qu et al and Kibru et al support these findings, but study result from Haiti witnessed opposite link between iron deficiency anemia and *H. pylori*.[13,18,21,28,29]

Further analysis revealed significantly lower hemoglobin (12.95 g/dl vs. 13.8 g/dl) and hematocrit levels (39.3% vs. 41.5%) in *H. pylori*-positive patients, findings consistent with those of Kibru et al.[18]

No significant association found between *H. pylori* infection and alcohol consumption, aligning with findings from Southwest England and Butajira, which showed an inverse relationship.[18,30] Likewise, cigarette smoking showed no association with *H. pylori* infection, which is in line with results from China, Oilfield community, Hebei, Southwest England, Egypt Assosa general hospital.[30-32]

Although males had higher infection rate (57.89%) compared to females (42.1%), difference was not statistically significant. Difference was not significant (AOR=0.479 95% CI=0.217,1.054), p=0.067).This finding was similar with study conducted in Cameroon, Butajira, Jimma, which also reported slightly higher rates in males.[18,21,32] It was assumed that males are naturally more active and less hygienic than female, since prevalence of *H. pylori* infection and sanitation condition are inversely related.

Patients from rural areas had a higher prevalence (60.7%) of *H. pylori* infection than urban residents (39.3%), although this was not statistically significant. This trend, also observed in a study by Tadesse et al this may be due to lower sanitation standards and lack of clean water supply in rural part of the country.[33]

Lastly, the result of this study indicated that source of drinking water was significantly associated with *H. pylori* infection (p=0.034, river water and p=0.021 well water) which was in line with study done in Oilfield community in Hebei, China.[31] Study conducted in northwest Ethiopia revealed that seroprevalence of *H. pylori* infection was higher among individuals consuming unprotected surface water compared to those with access to piped tap water.[34]

Limitations

Adequate sample size was taken. Finding can be used as base line data for other researchers. Nature of study failed to establish cause and effect relationship between variables.

CONCLUSION

The present study found that the *H. pylori* infection was strongly associated with iron deficiency anemia. There is considerable reduced hemoglobin level, hematocrit level and red blood cell count among *H. pylori* positive patients than their counterparts. Prevalence of the infection was higher for those individuals' using unhygienic water supply, like river water and well water and poor sanitation. The findings of this study should be taken into account for developing intervention-based strategies on identified factors mainly on; source of drinking water and poor hygienic condition.

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