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Table of Contents: Volume 11 Number 1 January 2019

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Full Length Research Paper

Prevalence and associated factors of *Helicobacter pylori* Infection among HIV positive adults on Anti-retroviral Therapy

Addis G. Mariam[1*], Techalew Shimelis[2], Agete Tadewos[2], Fanuel Belayneh[3] and Demiss Niguse[2]

[1]Hawassa Comprehensive Specialized Hospital laboratory, Hawassa University, College of Medicine and Health Science.
[2]School of Medical Laboratory Sciences, Faculty of Medicine, Hawassa University, College of Medicine and Health Science.
[3]School of Public Health, Faculty of Health Science, Hawassa University, College of Medicine and Health Science.

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Human immunodeficiency virus (HIV) and *Helicobacter pylori* (*H. pylori*) infections are worldwide healthcare burdens. This study aimed to assess the prevalence and associated factors of *H. pylori* infection among HIV patients at Southern-Ethiopia. A Hospital based cross-sectional study was conducted at Hawassa University comprehensive specialized hospital on 390 HIV infected adults on antiretroviral therapy from September to November 2017. All vital data were collected by designed questionnaires and stool samples were collected using appropriate sample cap for *H. pylori* stool antigen diagnosis. The overall prevalence of *H. pylori* infection of HIV infected patients was 17.9%. About 42.6% of the participants had a history of dyspepsia and of them, 4.3% were positive for *H. pylori* infection. In addition, 48.9% of patients were using either aqua tablet (67 mg-Trocloresene sodium) or water filters for drinking water, of them 11.5% were positive for *H. pylori* infection. Having a history of dyspepsia: the adjusted odds ratio [AOR (95% CI): 4.8 (1.6–14.7)], and age ≤30 years [AOR (95% CI):3.7(1.6–8.8)] were associated factors of *H. pylori* infection. Moreover, the association of *H. pylori* infection ≤ 30 years old and history of dyspepsia indicates the need of further large-scale and cohort type studies to determine the other possible associated factors for the infection.

Key words: *Helicobacter Pylori*, HIV, stool antigen test, South-Ethiopia.

INTRODUCTION

Helicobacter pylori is a gram negative bacteria, spiral, flagellated bacillus that naturally colonizes humans' stomach. It lives extra-cellular spaces, mucous layer. Then this infection induces a host response that results in mucosal damage and a chronic active gastritis (Ostrow et al., 2010). *H. pylori* infection is associated with peptic

*Corresponding author. addisgebermariam@yahoo.com. Tel: +251-911-442884.

ulcer, gastric cancer, and lymphomas in human (Marshall et al., 2008). The infection has also been associated firmly with the development of gastric neoplasia, including gastric adenocarcinomas and gastric mucosa-associated lymphoid tissue lymphomas (Versalovic, 2003). In addition, the prevalence of *H. pylori* infection among People Living with Human immunodeficiency virus (HIV) varies from 10 to 76% depending on the period, geographical area and diverse in population (Nkuize et al., 2010; Fialho et al., 2011). Even if antiretroviral treatment (ART) had brought improvements including increased the life expectancy in HIV infected individuals, however, *H. pylori* infections are seen more frequent in ART patients compared to those did not receive ART (Palella et al., 1998). The gastro-intestinal tract (GIT) plays an important role in the patho-physiology of HIV/ Acquired Immuno-deficiency syndrome (AIDS) (Khamri et al., 2010). Further, *H. pylori* colonizes the gastric and duodenal mucosae and then it induces a specific local in addition with systemic immune response. The CD4+ T cells, dendritic cells, regulatory T cells and Th17cells components also play a role in HIV pathogenesis (Khamri et al., 2010; Mitchell et al., 2007). Few studies were done on the assessment of problem in Ethiopia and these studies were mainly based on serological tests and *that* has its own drawbacks difficulties in distinguishing between current and past infections, including with its low specificity.

Therefore, this study aimed to assess the prevalence and associated factors of *H. pylori* infection among HIV-infected adults in Hawassa University Compressive Specialized Hospital (HUCSH) by using stool antigen test.

MATERIALS AND METHODS

Study area and study population

This institution based cross sectional study was conducted at Hawassa University comprehensive specialized Hospital, Southern Nations Nationalities and Peoples Region (SNNPR) from September to November 2017. The Hospital was established in November 2005 and it provides teaching and health services. Nowadays, the hospital has over 400 beds and providing health services for patients including practical training for students. About 7125 HIV positive patients were attending the Hospital during the study period. All HIV-positive adults on ART age greater than or equal to 18 years old were eligible in the study. However, patients who were receiving anti-*H. Pylori* treatment within two weeks, and who were receiving anti-*H. Pylori* agents currently were excluded from the study.

Ethics clearance and consent to participate

The study was approved by the Institutional Review Board of Hawassa University, College of Medicine and Health Sciences. All the study participants were well versed about the protocol of the study, the involvement was voluntary and written informed consent was obtained from the study participant before data collection.

Sample size and technique

The sample size was calculated based on single population proportion formula and 64.2% prevalence of *H. Pylori* infection among peoples living with HIV in Addis Ababa, Ethiopia (Teka et al., 2015).

Based on the above-mentioned**,** formula, including with 10% non-response rate, the final sample size was calculated to be 390. To select participants from the study population, daily patients flow was assessed for a week in the ART clinic. Thus, the trend showed that the average weekly HIV patients flow was about 73. Lastly, every fifth HIV-infected patients were selected by systematic sampling method.

Data collection and assessment

Socio-demographic data and other relevant medical related information of the study subjects were collected by trained nurses using pre-tested and designed questionnaires. About two gram of stool sample was collected from each patients using sterile stool containers with a spatula in it. Instruction was given for each patient to avoid contamination of sample from the toilet, and covering immediately to avoid sample drying. Sample containers were properly labeled with unique number that was analogous with the patient's identity number found on the questionnaire. In addition, *H. pylori* stool antigen test was performed at Hawassa University Comprehensive Specialized Hospital Laboratory by *H. pylori* stool antigen test kit (CTK H.PYLORI, USA) according to the manufacturer instruction. Moreover, the test kit Sensitivity and specificity was 94.4 and 97.8%, respectively. Further, laboratory performance was strictly managed by following standard operating procedure from sample collection to result releasing.

Statistical analysis

All questionnaires were checked and entered into Epi Data version 3.1 and then exported to Statistical Package for Social Sciences (SPSS) version 20 for statistical analysis. Besides, categorical variables were summarized as frequencies and percentages, while mean values and standard deviations were tabulated for quantitative continuous variables. Chi-square was used for categorical variables. Bivariate analyses were conducted primarily to check the study groups differences in the distribution of categorical variables. Further, to control the possible effect of confounding variables, those variables having a P-value of less than 0.2 were entered in to multivariate logistic regression model. Finally, alpha level was set at 0.05 for statistical significance at 95% of confidence interval (CI).

RESULTS

Socio demographic characteristics of study participants

Among the 390 participants, 247 (63.3%) were females and the mean age of the study participant was 37 ± 9.7 with the range of 18 to 62 years old. About 19 (4.9%) of the respondents were aged below 24 years old, while 75 (19.2%) and 90 (23.1%) were aged in between 30-34 and 35-39 years, respectively. In addition, 368 (92.8%), 48(12.3%), 170 (43.6%) and 72 (44.1%) of the study subjects were urban inhabitants, had no formal education,

Table 1. Socio-demographic characteristics of HIV positive adults at Hawassa Comprehensive Specialized Hospital.

Variable	Frequency	%	Variable	Frequency	%
Sex			**Residence**		
Male	143	36.7	Urban	362	92.8
Female	247	63.3	Rural	28	7.2
Age group			**Education**		
18-24 years	19	4.9	Illiterate	48	12.3
25-29Years	57	14.6	Primary	170	43.6
30-34 years	75	19.2	Secondary	119	30.5
35-39 Years	90	23.1	Technical/Vocational	23	5.9
40-44 years	69	17.7	≥Universities	30	7.7
45-49 years	38	9.7	**Source of drinking water**		
50-54 years	30	7.7	Tap water	381	97.7
≥ 55 years	12	3.1	Well	4	1.0
Marital status			Spring	5	1.3
Single	35	9.0	**Household Waste disposal**		
Married	216	55.4	Open field	246	63.1
Divorced	59	15.1	Specified place	144	36.9
Separated	33	8.5			
Widowed	47	12.0			

primary level of education, and greater or equal to secondary education, respectively. About 35 (9.0%) were non-married and 216 (55.4%) were married, whereas 59 (15.1%) were divorced, 33 (8.5%) were separated and 47 (12.1%) were widowed (Table 1).

Behavioral characteristics of study participants

Participants who had a habit of continuously hand washing before meal, after defecation and before food preparation were 375 (96.2%), 363 (93.3%), and 368 (94.4%), respectively. About 35 (9.0%) and 9 (2.3%) of the study participant ever drank alcohol and ever smoked cigarette. Besides, 191 (48.9%) were using either aqua tablet (67 mg-Trocloresene sodium) or water filter to treat and purify water for drinking (Table 2).

Clinical characteristics and the prevalence of *H. pylori* infection

Patients on TDF/3TC/EFV of ART regimen were 192 (49.2%) followed by AZT/3TC/EFV: 75 (19.2%). The majority, 169 (43.3%) of the patients had been received ART for greater than or equal to five years. In addition, Participants with the previous history of opportunistic infection were 262 (67.2%) and about 43 (11%) of the participants had CD4+cells count less than or equal to 200 cells/µl. One hundred sixty six 166 (42.6%) of the participants had a history of dyspepsia. Moreover, the overall prevalence of *H. pylori* infection in the study participants was 70 (17.9%) and females had high prevalence rate 46 (11.8%) compared to males 24 (6.2%). The mean age of *H. pylori* infected participants was significantly higher (39.8±7.7 years) when compared to *H. pylori* negatives (36.4±8.8 years), p=0.003 and 31 (7.9%) *H. pylori* infection was observed in age group in between 31-40 years old. Among dyspeptic patients, 17 (4.3%) were positive for *H. pylori* infection. Furthermore, 191(48.9%) were using either aqua tablet (67 mg-Trocloresene sodium) treatment or water filters for drinking water and 45 (11.5%) of them were positive for *H. pylori* infection (Table 3).

Factors associated with *H. pylori* infection

In bivariate analysis: family size greater than or equal to six households had the crude odds ratio [COR (95% CI): 1.7 (1.0–2.9); p = 0.038] and age ≤30 years [COR (95% CI): 3.7(1.7-8.3); p = 0.001] were associated with *H. pylori* infection. In addition, having a history of dyspepsia [COR (95% CI): 2.7 (1.5-4.9); p = 0.001], being unmarried [COR (95% CI): 10.7(1.3–87); p = 0.03] and having a previous history of *H. pylori* infection [COR (95% CI):2.0(1.2-3.5); p = 0.012] were also associated with *H. pylori* infection (Table 4).

However, multivariate analysis was adjusted for possible confounding factors, only having a history of dyspepsia: the adjusted odds ratio [AOR (95% CI): 4.8 (1.6–14.7); p = 0.005], and age less than or equal to 300.005], and age less than or equal to 30 years [AOR (95% CI): 3.7(1.6–8.8); p = 0.003] were the associated

Table 2. Characteristics of HIV positive adults at Hawassa comprehensive specialized hospital.

Variable	Frequency	Percentage
Hand washing before eating		
Always	375	96.2
Sometimes	15	3.8
Hand washing after defecation		
Always	363	93.1
Sometimes	23	5.9
No	4	1.0
Hand washing before food preparation		
Always	368	94.4
Sometimes	22	5.6
Hand washing after cleaning		
Always	371	95.1
Sometimes	19	4.9
Alcohol Drinking		
Never drink	355	91.0
Tried once or twice	26	6.7
Time to time	9	2.3
Smoking cigarettes		
Never smoke	381	97.7
Tried once or twice	4	1.0
Time to time	3	0.8
Daily	2	0.5
Utilizing aqua tablet (water filter)		
No	199	51.1
Yes	191	48.9

factors of *H. pylori* infection (Table 4).

DISCUSSION

H. pylori infection has been known to be more associated with gastritis, duodenal ulcer, gastric cancer, and mucosa associated lymphoid tissue lymphoma (Lepper et al., 2004). The actual infection rates vary from nation to nation; and the developing countries have much higher infection rates (90%) due to different factors when compared to developed countries (1.2-12%) (Frenck et al., 2003).

The current study showed that the prevalence of *H. pylori* infection among HIV infected patients was 17.9%. The finding is lower than the studies reported from Iran (Kafil et al., 2011), India (Nkuize et al., 2010), Ghana (Sarfo et al., 2015), two studies of Nigeria (Anejo-Okopi et al., 2016; Ejilude et al., 2011) and other part of Ethiopia (Teka et al., 2015), which was 69.7, 33, 51.5, 46.8, 47.4 and 64.2%, respectively. Conversely, Perry et al. (2006) from Romania, reported low rate, which was 8.3%. The differences might be due to the socio-economic differences, environmental sanitation condition and the changes in health care practice across countries (Anejo-Okopi et al., 2016 and Mynepalli et al., 2014).

We found that the high prevalence of *H. pylori* infection in women (11.8%) when compared to males (6.2%). And similar findings were reported by Fialho et al. ((2011) from Brazil and Anejo-Okopi et al. (2016) from Nigeria.

We found that lower prevalence of *H. pylori* infection among patients with CD_4+ cells count below or equal to 200/mm^3 and the finding is in line with the studies conducted by Fialho et al. (2011) and Sarfo et al. (2015).

Table 3. Clinical characteristics and the prevalence of *H. pylori* infection among HIV positive adults at Hawassa comprehensive specialized hospital.

Variable	*H. pylori* stool antigen test 390 (%)		
	Positive(n=70)	Negative(n=320)	p-value
Gender			
Female	46(11.8)	201(51.5)	
Male	24(6.2)	119(30.5)	0.65
Age, year (mean ± SD)	39.8(7.7)	36.4(8.8)	0.003
≤30 years	9(2.3)	97(24.9)	
31-40 years	31(7.9)	136(34.8)	0.004
≥41years	30(7.7)	87(22.3)	
History dyspepsia			
Yes	17(4.3)	149(38.2)	0.001
No	53(13.6)	171(43.8)	
Residence			
Rural	68(17.4)	294(75.4)	
Urban	2(0.5)	26(6.7)	
Previous *H. pylori* infection			
No	47(12.1)	161(41.3)	0.01
Yes	23(5.9)	159(40.7)	
Current ART regimen			
TDF/3TC/EFV	29(7.4)	163(41.8)	
TDF/3TC/NVP	9(2.3)	27(6.9)	
AZT/3TC/EFV	17(4.3)	58(14.9)	
AZT/3TC/NVP	15(3.8)	63(16.2)	
Others	0(0.0)	6(1.5)	-
Utilizing aqua tablet (water filter)			
Yes	45(11.5)	146(37.4)	0.005
No	25(6.4)	174(44.6)	
Family size			
1-5 house holds	42(10.8)	148(37.9)	0.037
≥6 house holds	28(7.2)	172(44.1)	
History of opportunistic infection			
Yes	47(12)	215(55.1)	0.99
No	23(5.9)	105(26.9)	
CD_4^+ cells/µl, mean (±SD)	512.6(232)	497(246)	0.64
≤200 cells/µl	6(1.5)	37(9.5)	
201-400 cells/µl	22(5.6)	87(22.3)	0.32
>400 cells/µl	42(10.8)	196(50.2)	

AZT, zidovudine; TDF, Tenofovir; 3TC, lamvudine; EFV, efavreniz; NVP, neverapine.

In support, the low rate has been suggested that CD_4 cells play a role in inducing or perpetuating tissue and epithelial damage that may facilitate *H. pylori* colonization (Bontems et al., 2003). Further studies suggested that decreased gastric acid secretion might be predisposed to gastric colonization by other microorganisms that might compete with *H. pylori* bacteria and the use of either antibiotics or proton pump inhibitors in the low count of CD_4+ cells in HIV patients my decreases colonization of *H. pylori* (Panos et al., 2007; Nevin et al., 2014).

This study showed that 2.3% of participants with age ≤30 years were infected with *H. pylori*, and this was lower than study report from Nigeria with similar age group, (Anejo-Okopi et al., 2016).

Table 4. Factors associated with *H. pylori* infection among HIV positive adults at Hawassa comprehensive specialized hospital.

Parameter	At 95% confidence interval			
	Unadjusted odds ratio	p-value	Adjusted odds ratio	p-value
Family size	1.00		1.00	
1-5 households				
≥6 households	1.7(1.0-2.9)	0.038	0.95(0.34-2.6)	0.76
Age				
≤30 years	3.7(1.7-8.3)	0.001	3.7(1.6-8.8)	0.003
31-40 years	1.5(0.85-27)	0.15	1.4(0.77-2.7)	0.25
≥41years	1.00		1.00	
History dyspepsia				
Yes	2.7(1.5-4.9)	0.001	4.8(1.6-14.7)	0.005
No	1.00		1.00	
Educational				
≤ Primary level	0.7 (0.41-1.2)	0.18	0.7(0.39-1.2)	0.23
≥Secondary level	1.00		1.00	
Residence				
Urban	0.33(0.08-1.4)	0.14	0.7(0.07-1.4)	0.13
Rural	1.00		1.00	
Marital status				
Single	10.7(1.3-87)	0.03	4.8(0.56-42.6)	0.15
Married	1.3(0.63-29)	0.43	0.92(0.4-2.1)	0.85
Divorced	1.2(0.49-3.1)	0.66	0.85(0.31-2.3)	0.76
Separated	1.7(0.55-5.7)	0.34	1.6(0.45-5.6)	0.47
Widow	1.00		1.00	
Previous *H. pylori* infection				
No	1.00		1.00	
Yes	2(1.2-3.5)	0.01	0.45(0.15-1.3)	0.14
Drink house treated water				
Yes	1.00		1.00	
No	2.1(1.2-3.7)	0.005	2.2(0.76-6.2)	0.15
CD_4^+, cells/µl				
≤200	2.1(1.2-3.7)	0.18	2.2(0.66-7.2)	0.20
201-400	0.89(0.5-1.6)	0.68	1.0(0.52-1.89)	0.97
>400	1.00		1.00	
Hemoglobin level				
<12 g/dl	0.6(0.28-1.2)	0.13	0.51(0.22-1.1)	0.10
≥12 g/dl	1.00		1.00	

In addition, the current study indicated that the presence of dyspepsia was found to have a significant association with *H. pylori* infection. It in line with the study reported by Anejo-Okopi et al. (2016) that indicated that the association of dyspepsia with *H. pylori* infection. Furthermore, the association of *H. pylori* with dyspepsia condition has triggered a major paradigm change in patients' management (Jemilohun et al., 2011).

The present study revealed that no association in between hemoglobin level and *H. pylori* infection. This in line with the study conducted by Fraser et al., 2010 and Kermati et al., 2007. However, one study from Turkish teenager reported that association between *H. pylori* infection and anemia (Süoglu et al., 2007). This might be attributed to favors of poor hygienic status for parasitic infestation and sharing of a similar transmission route with *H. pylori* infection and the condition of co-morbidity might increase risks of anemia.

We found that no association of *H. pylori* infection with CD_4+ cells. In support, different studies depicted that CD4+ cells has been shown to be raised in *H. pylori* gastritis, but gastric inflammation has been correlated with lower *H. pylori* bacteria load, and pro-inflammatory genetic profiles are associated to lower *H. pylori* sero-prevalence. Besides, *H. pylori* infection requires an intact mucosal cellular immunity, and that the loss of the CD4+ cell population in the gastric mucosa may prevent *H. pylori* persistence (Sarfo et al., 2015; Aebischer et al., 2010).

The present study indicated that the association of *H. pylori* infection with age less than or equal to 30 years of participants and this in line with the report of other studies (Anejo-Okopi et al., 2016; Abebaw et al., 2014; Chen et al., 2013). Moreover, current study showed that no significant association of *H. pylori* infection with family size, educational status, marital status, alcohol consumption, residence and occupation. Furthermore, 48.9% were using either aqua tablet treatment or filters for drinking water and 11.5% of them were positive for H. pylori infection. This might indicate the utilization of poor proportions of aqua tablet and water or inappropriate water filtration.

Limitations of the study

This study was conducted on HIV patients who had many underline disease conditions as a confounding factor that was not completely controlled, so as to have impact on the outcome of the statistical associations between *H. pylori* infection and different variables of interest. The other limitations were Immuno-chromatographic stool antigen test characteristics, (non-ELISA method), lack of HIV negative controls and cross sectional nature of the study that did not show cause and effect relationship between the variables.

Conclusion

The overall prevalence of *H. pylori* infection in the study participants was 17.9%. About 42.6% of the participants had a history of dyspepsia and of them, 4.3% were positive for *H. pylori* infection. In addition, having a history of dyspepsia and age ≤30 years were associated factors of *H. pylori* infection. HIV-positive subjects receiving ART co-infected with *H. pylori* tend to have higher levels of CD4+ T-lymphocytes (>200 cells/µl) when compared to patients withCD4+ T-lymphocytes <200 cells/µl and patients with low immune status, reflected by CD4+ T-lymphocyte levels below 200 cells/µl, are less probable to be infected with *H. pylori*. Moreover, dyspepsia in HIV-positive patients suggests the need to investigate alternative etiologies, besides *H. pylori* infection. In addition, this study indicated the need for further large-scale study in HIV patients to determine the possible factors for infection. Furthermore, cohort type studies are recommended to formulate a cause and effect relationship between associated factors and *H. pylori* infection among HIV infected patients.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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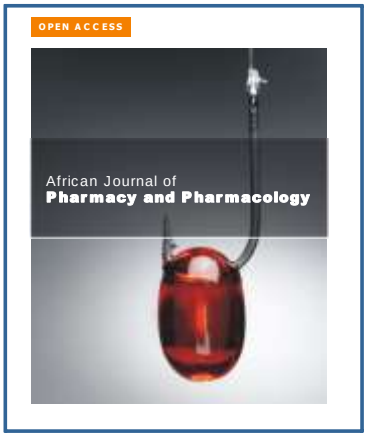

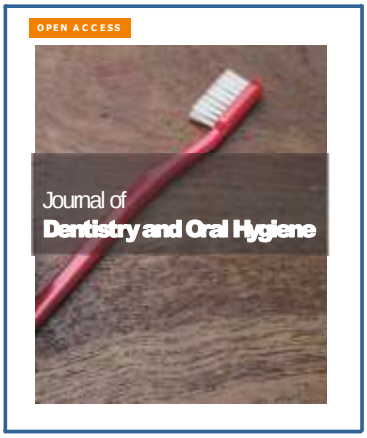

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