



Prevalence of helicobacter pylori infection and clinical characteristics in immune thrombocytopenia patient at St. Paul's Hospital Millennium Medical College Addis Ababa from September 2016 to June 2019

This paper is submitted to the Department of Internal Medicine for the partial fulfillment of the Requirements for certificate in Internal Medicine Specialty.

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LIST OF ACRONYMS AND ABBREVIATION

APS = antiphospholipid antibody syndrome

H.pylori = helicobacter pylori

ITP = immune thrombocytopenia

SLE =systemic lupus erythematosus

SPHMMC = Saint Paul hospital millianume medical collage

HIV = human immunodeficiency virus

ICH= Intra-cranial hemorrhage

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Abstract

Background

H.Pylori infection is highly prevalent in ITP patient and its eradication has been shown to induce response.

Helicobacter pylori has also been postulated to play a role in the pathogenesis of idiopathic thrombocytopenic purpura (ITP)

H.Pylori is highly prevalent in Ethiopia with adult prevalence of 52.2%. There is no study done assessing the prevalence of H.Pylori ITP patient in Ethiopia and comparing the clinical characteristic between H.Pylori infected and non-infected groups in ITP patient in Ethiopia.

METHOD

A retrospective study of adult patients seen at St Paul hospital millennium medical college Department of Internal Medicine study in hematology unit from September 2016 to June 2019. A total of 43 patient were included in assessing prevalence of H.Pylori infection.

RESULT

From the 43 immune thrombocytopenia patient identified H.Pylori infection was found in 9/43(20.9%) by H.Pylori stool Ag , Mean age at diagnosis was 33.63 ± 4.975 age ranges (16- 75) and mean age in H.Pylori negative and positive patient is [34.91 vs 28.78]. The ratio male to female is 1:3.3 the mean platelet count of 18,000 with 67.4% have a count $< 30,000$. Majority of patient (79.1%) presented with symptomatic thrombocytopenia. Mucocutaneous bleeding occur in 62.8%. complete and partial response was seen in 83.7% .There is no significant difference in platelet count , bleeding type and Gender predominance in H.Pylori infected and none infected group .

CONCLUSION

ITP is majorly a disease of young females in Ethiopia. And the prevalence of H.Pylori infection is in ITP patient a lower than the general prevalence .most of patient presented with low platelet count with bleeding .There no major difference in clinical characteristics between H.Pylori infected and non-infected group . Most patient have response to treatment

Chapter one

1. Introduction

1.1. Background

Helicobacter pylori is a Gram-negative bacterium that is considered as a causative agent of peptic ulcer disease, gastric lymphoma, and gastric carcinoma. *Helicobacter pylori* trigger an intense leucocyte infiltration of the gastric sub mucosa, an action that is mediated by pro-inflammatory cytokines. This pathogenic mechanism is common to many other diseases (1)

Helicobacter pylori (*H. pylori*) is found in half the population of the world. Its prevalence is highly variable in relation to geography, ethnicity, age, and socioeconomic factors – higher in developing countries and lower in the developed world.(2)

In Meta-analysis done from January 1, 1970 through January 1, 2016. Including 184 studies were included in the final analysis, comprising data from 62 countries. Africa had the highest pooled prevalence of *H. pylori* infection (70.1%; 95% CI, 62.6-77.7), whereas Oceania had the lowest prevalence (24.4%; 95% CI, 18.5-30.4). Among individual countries, the prevalence of *H. pylori* infection varied from as low as 18.9% in Switzerland (95% CI, 13.1- 24.7) to 87.7% in Nigeria (95% CI, 83.1-92.2). Based on regional prevalence estimates, there were approximately 4.4 billion individuals with *H. pylori* infection worldwide in 2015.(3)

Immune thrombocytopenia(ITP) is a heterogeneous disease characterized by increased platelet destruction and thrombocytopenia. A number of features suggest this destruction is immune-mediated and that it may involve not only the destruction of the platelet, but also inhibition of platelet release by the megakaryocyte .(4)

A platelet count less than $100 \times 10^9/L$ was established as the threshold for diagnosis.(5)

ITP is classified to different group based of the causes. Primary ITP is an autoimmune disorder characterized by isolated thrombocytopenia peripheral blood platelet count $<100 \times 10^9/L$) in the absence of other causes or disorders that may be associated with thrombocytopenia. The diagnosis of primary ITP remains one of exclusion.(6)

Secondary ITP All forms of immune-mediated thrombocytopenia except primary. This can be secondary to medications or to a concurrent disease, such as an autoimmune condition (eg, [SLE], [APS], immune thyroid disease, or Evans syndrome), a lymphoproliferative disease (eg, chronic lymphocytic leukemia or large granular T-lymphocyte lymphocytic leukemia), or chronic infection, eg, with *Helicobacter pylori*, human immunodeficiency virus (HIV), or hepatitis C virus (HCV). (7)

Different studies has shown there is a higher prevalence of *H.pylori* in ITP patients, a causative role of *H.pylori* for ITP and response for ITP with treatment of *H.Pylori* infection

1.2 Statement of the problem

H. pylori which is a common infection around the world with global prevalence of is >50%.[2]

Africa had the highest pooled prevalence of H pylori infection (70.1%; 95% CI, 62.6-77.7), It's also highly prevalent in Ethiopia When we see the prevalence in Ethiopia classified according to age group age 2-4 is 48%, age 6 is 80% and adults >90%.(2)

H.pylori infection is highly prevalent in ITP patient and H .pylori is considered as one of the cause of secondary ITP and its eradication has been shown to induce response in ITP patient (6)

Studies has also shown the prevalence of H.pylori infection in ITP mirrors the .prevalence of H pylori infection in the general population (6)

Ethiopia is one of the highly prevalent country for H.pylori infection and according to the studies the prevalence among ITP patient is going to parallel the general prevalence which is going to be high. But there is no study done in Africa including Ethiopia assessing H.pylori prevalence among H.pylori infection

1.3 Significance of the study

Despite H.pylori being a common infection in Africa especially in Ethiopia with adult prevalence of > 95 % there is no study done in assessing H.pylori prevalence in ITP among adult patient Africa or Ethiopia [2]

Since studies has shown the prevalence of H.pylori infection in ITP mirrors the .prevalence of H pylori infection in the general population [7]

This study will evaluate the prevalence of H.Pylori infection in ITP patient. Evaluate the clinical characteristics and response to ITP treatment and compare the finding among H.Pylori infected patient and not infected patient and those who are infect with H.Pylori treated and those who are not.

It will help in understanding the prevalence of H.Pylori infection in ITP patient and the clinical characteristic of this patient in SPHMMC. It helps in how sensitive physician in our set up should be reading H.Pylori testing and treating according to response and according to prevalence. Whether there is a difference in clinical characteristics and treatment response among those who are infected with H.Pylori and those who are not infected

Chapter Two

2. Literature review

2.1 prevalence of H.Pylori

The global prevalence of *H. pylori* infection is >50%. The prevalence may vary significantly within and between countries.(2)

In meta-analysis from 62 countries. Africa had the highest pooled prevalence of *H. pylori* infection (70.1%; 95% CI, 62.6-77.7), whereas Oceania had the lowest prevalence (24.4%; 95% CI, 18.5-30.4). Among individual countries, the prevalence of *H. pylori* infection varied from as low as 18.9% in Switzerland (95% CI, 13.1- 24.7) to 87.7% in Nigeria (95% CI, 83.1-92.2). Based on regional prevalence estimates, there were approximately 4.4 billion individuals with *H. pylori* infection worldwide in 2015.(3)

It's also highly prevalent in Ethiopia When we see the prevalence in Ethiopia classified according to age group age 2-4 is 48%, age 6 is 80% and adults >90%.(2)

In the study done in Ethiopia and published in 2019 The trend of *H. pylori* infection showed a decreasing pattern in the last three decades from 1990 to 2017;64.4% in the first decade (1990–2000), 62.2% in the second decade (2001–2011) and 42.9% in the third decade (2012–2017). in the subgroup analysis showed a lower prevalence of 39.9% in Oromia. General prevalence of 52.2%(8)

2.2 prevalence of ITP

Published data on the epidemiology of ITP among adults are currently sparse. ITP is generally considered to be a relatively rare disease with both acute and chronic forms; as such, the true disease burden in the population is difficult to estimate. (9)

Before 1995, there were no population-based estimates of ITP disease burden in the literature. (10)

A nationwide population-based study in France done from 2009-2011 . Incidence was 2.9/100 000 person-years, with peaks among children and in those >60 years of age. ITP was more frequent among males in these subgroups. The incidence was lower in overseas Caribbean French departments, suggesting a lower incidence among Afro-American people. (11)

In another article that assesses the prevalence among black patients which reviewed 6 articles, the proportion of blacks among patients with ITP was lower than the proportion of blacks in the population. In 5 of the published studies, the 95% confidence interval (CI) for the observed percent of blacks among the ITP patients did not overlap with the percentage of blacks in the population ,One of these articles commented on their observation that only 4 (6%) of 67 patients with ITP were black, compared with 25% of their hospital patients. (12)

A study from Nigeria shows a rarity of ITP in indigenous black people Hospital incidence of the disease was computed from all hospital admissions in 11 year. There were eleven cases (7 females, 4 males), aged 10 to 55 (median, 21) years. (13)

Another study done in Ethiopia Between January 1982 and December 1989, thirty-four cases of chronic idiopathic thrombocytopenic purpura (ITP) were seen in adult Ethiopians in the Department of Internal Medicine in-patient and hematology referral clinic, of Tikur Anbessa teaching hospital. (14)

2.3 The prevalence of H.Pylori infection and its effect of eradication in ITP patient

Since its discovery, *H. pylori* have been associated with other disorders outside of the gastrointestinal (GI) tract including diseases in hematologic, cardiopulmonary, metabolic, neurologic, and dermatologic systems(1)

The first study that show the association of ITP and *H.Pylori* infection was done in Italy in 1998 showing Regression of autoimmune thrombocytopenia after eradication of *Helicobacter pylori* 18 patients (13 female; mean age 45 [SD 14] years) with AT were evaluated. *H pylori* infection was found in 11 patients. There was no difference in sex between infected and uninfected patients; mean age, however was lower in infected patients (43 [14] vs 49 [12] years, $p>0.05$). Platelet count was similar in infected and uninfected patients (95 [39] vs 103 [24] 103/L, $p>0.05$). Eight of the 11 *H pylori*-positive patients had the bacterium eradicated after treatment. Patients in whom *H pylori* was eradicated had a significant increase in platelet count after 2 and 4 months , six out of these eight patients had disappearance of auto antibodies against platelets ($p<0.003$). Antibodies against platelets and platelet count did not change during follow-up either in *H pylori* negative patients or among those treated but in whom *H pylori* was not eradicated(15)

The data so far reported indicate that the prevalence of *H.pylori* infection in ITP mirrors the prevalence of *H pylori* infection in the general population(16)

Another Study that was done in Italy in 2000 a prospective open study to verify the prevalence of *H.pylori* infection and the effects of its eradication in a larger proportion of patients with chronic ITP .*H pylori* infection has been documented in 13 patients (43.33%) by C urea breath test and confirmed by histological examination. Bacterium eradication with antibiotics, obtained in 12 of 13 infected patients (92.3%), led to a complete response in 4 (33.33%) and to a partial response (platelets $90 \times 10^9/L$ - $120 \times 10^9/L$) in 2 (16.66%). The response was maintained for a median of 8.33 months, but 1 patient relapsed 7 months after eradication. Search for *H pylori* infection seems appropriate in ITP patients at diagnosis. Bacterium eradication provides a new good option for a none immunosuppressive treatment in some ITP patients(17)

A study was done in Japan to examined the effect of *H. pylori* eradication on secondary ITP The prevalence of *H. pylori* infection and the effect of its eradication on platelet count in 48 Japanese patients with autoimmune thrombocytopenic purpura (AITP), including 40 chronic ITP and eight secondary AITP, were investigated. *H. pylori* infection was found in 25 ITP patients (62.5%) and in 2 secondary AITP (25%).

H. pylori eradication was obtained in 19 of 19 infected ITP patients(100%), who were not in remission (platelets $< 100 \times 10^9/l$) at the time of infection assessment. During follow-up (median 14.8 months), 12 of 19 *H. pylori*-eradicated patients (63.2%) showed a significant increase in platelet count accompanied by a significant decrease of platelet associated immunoglobulin G (IgG). This response was maintained in all responding patients throughout the follow-up period. However, two infected patients with secondary

AITP did not show platelet increase after eradication. The assessment of *H. pylori* infection and its eradication should be attempted in ITP, as this approach could be an effective strategy, at least for some of these patients. (18)

Another study in Japan investigated the prevalence of *H. pylori* infection and the effects of its eradication in 61 patients with ITP. *H. pylori* infection was found in 50 patients (83%), an incidence significantly high not only healthy volunteers in Japan (60%) but also subjects in other reported ITP series (approximately 43%-71%)., the mean age of *H. pylori*-positive ITP patients (58.0 years) was significantly higher than that of *H. pylori*-negative ITP patients (40.5 years). Bacterium eradication efforts were performed in 29 infected ITP patients and succeeded in 27 patients (93%). The 29 patients with eradicated *H. pylori* infections showed significant increases in platelet counts compared with patients with uneradicated infections or who were *H. pylori*-negative. During the follow-up period (median, 11.0 months), 16 (55%) of 29 patients achieved a major or a minor response. The assessment of *H. pylori* infection and its eradication should be attempted in cases of ITP, because this approach may be a good new strategy for treating some ITP patients, especially elderly Japanese patients(19)

A retrospective study was performed to determine the prevalence of *Helicobacter pylori* (*H. pylori*) infection, the effect of *H. pylori* eradication on platelet counts, and the characteristic clinical features of chronic immune or idiopathic thrombocytopenic purpura (ITP) with *H. pylori* infection. *H. pylori* infection was found in 300 patients, a group that was significantly older ($P < .005$) and had more cases of hyperplastic megakaryocyte in the bone marrow ($P = .01$) than patients without *H. pylori* infection. *H. pylori* eradication therapy was performed in 207 *H. pylori*-positive ITP cases, and the platelet count response was observed in 63% of the successful eradication group and in 33% of the unsuccessful eradication group ($P < .005$). In the successful group, the complete remission and partial remission rates were 23% and 42%, respectively, 12 months after eradication. In the majority of responders, the platelet count response occurred 1 month after eradication therapy, and the increased platelet count continued without ITP treatment for more than 12 months. *H. pylori* eradication therapy was effective even in refractory cases, which were unresponsive to splenectomy. In conclusion, *H. pylori* infection was involved in most ITP patients older than 40 years in Japan, and eradication therapy should be the first line of treatment in *H. pylori*-positive ITP patients. (20)

Another systematic review of the literature published in English, selecting articles reporting 15 or more total patients .they identified 25 studies including 1555 patients, of whom 696 were evaluable for the effects of *H. pylori* eradication on platelet count. The weighted mean complete response (platelet count $> 100 \times 10^9/L$) and overall response (platelet count $> 30 \times 10^9/L$ and at least doubling of the basal count) were 42.7% (95% confidence interval [CI],31.8%-53.9%) and 50.3% (95% CI, 41.6%- 59.0%), respectively. In 222 patients with a baseline platelet count less than $30 \times 10^9/L$, the complete response rate was 20.1% (95% CI, 13.5%-26.7%) and the overall response rate was 35.2% (95% CI,28.0%-42.4%). The response rate tended to be higher in countries with a high background prevalence of *H. pylori* infection and in patients with milder degrees of thrombocytopenia. These findings suggest that the detection and eradication of *H. pylori* infection should be considered in the work-up of patients with seemingly typical ITP. (21)

Another study done in Malaysia shows 50 ITP adult patients from haematology clinics were recruited. A 13C urea breath test for *H. pylori* infection was performed in all patients. Those with *H. pylori* infection were treated with standard eradication regimen. Platelet counts were monitored regularly after eradication

therapy to assess response. The median age of patients recruited was 50 years.

The majority of patients were female (76%). Chinese was the largest ethnic groups (56%) followed by Malays (28%) and Indians (16%). 11 of the 50 patients (22%) were found to have *H. pylori* infection and all but one had eradication therapy.

Overall, some response was observed in 3 patients (30%) with a CR seen in 2 patients and PR in one patient. However, all these patients had a drop in their platelet counts at 6th month follow up. The prevalence of *H. pylori* infection is

relatively low in our adult ITP patients (22%) and eradicating the infection did not have any sustained effect in the platelet recovery(18)(22)

Another study done in Spain analyzed the response to eradication of *H. pylori* in a series of 56 adult patients with chronic ITP. Forty patients had *H. pylori* infection (71%) that was eradicated in 23 of 32 evaluable patients (72%). Platelet counts did not significantly vary according to *H. pylori* treatment outcome. Three of 56 patients (5%) achieved a partial response attributable to *H. pylori* eradication.(23)

CHAPTER 3

3 .OBJECTIVE OF THE RESEARCH

3.1 General objective

To determine the prevalence of H.Pylori infections and clinical characteristics among immune thrombocytopenia in adult patient who had or having follow up at SPHMMC from September 2016 to June 2019

3.2 Specific objective

- To determine the prevalence of H.Pylori infection in ITP patient
- To determine clinical characteristics of ITP patients
- To compare clinical characteristics between H.Pylori negative and positive groups

Chapter 4

4 Materials and method

4.1 study Area

This study is conducted in St paul's Millennium Medical College is one of the teaching hospitals in Addis Ababa, capital city of Ethiopia. The late Emperor Haile Selassie established it in 1968. It was re-established in 2010 through a decree of the council of Ministers. The college has more than 2800 clinical, academic , administrative and support staffs that provide medical specialty services to patients who are referred from all over the country. The college sees an average of 1200 emergency and outpatient clients daily. [22]

One of the departments is internal medicine, which has many subunits including Hematology Unit. The hematology unit provides numerous services to the public including since July 2016 follow up a hematology clinic twice a weekly at which about a total of 80-90 patient are seen per weekly. It also provides chemotherapy at outpatient and inpatient unit around 30 patient are currently enrolled. The unit also consists of inpatient ward admission unit.

4.2 Study period

The study was conducted from November 2018 to August 2019.

4.3 Study design

The study design is retrospective study.

4.4 Source population and study population

4.4.1 Source population

The source population are all patients having or had follow-up at SPHMMC haematology Clinic from September 2016 to June 2019

4.4.2 Study population

The study population are those patients who are or were diagnosed with ITP at SPHMMC haematology clinic during the study period.

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion Criteria

Patient age > 15 and was diagnosed with ITP

4.5.2 Exclusion Criteria

Those patients who had not been tested and couldn't be tested for H.pylori during the study, because either they are not willing or not available during the study period

4.6 Sampling

The sources population for the study is 48 since this is a few number the plan is to include all the patient

4.7 Data collection method and tools

4.7.1 Data collection Methods

Data for the research was collected through chart review all patient charts with the diagnosis of ITP at Haematology clinic was collected by using data from HMIS registration book and will be reviewed

4.7.2 Data collection tool and personnel

The socio-demographic data pregnancy status at diagnosis, any medication use was collected using self-prepared questionnaire from the chart and telephoning the patient. The questionnaire have three parts. The first part was assess socio-demographic status like age, sex, marital status, occupation, educational status, and address. Second part was assess H.Pylori infection and associated confounding infection and the third part asses the platelet count and the treatment responses to H.Pylori eradication

Trained data collector and principal instigator collected data from the questionnaire and is analysed by the principal investigator

4.8 Study Variables

4.8.1 Independent Variables

Age

Sex

Educational status

Marital status

Occupation

Area of residency

HIV

Hep b infection

Hep c infection

Pregnancy

Drug intake

H.Pylori infection

4.8.2 DEPENDENT VARIABLE

ITP

4.9 Operational definition

H.pylori infection Patient are considered as having H.Pylori infection if they have H.Pylori stool Antigen , H.Pylori serum antibody positive or urease breath test positive

H.Pylori eradication therapy include 2 standard antibiotics and PPI triple therapy for 2 weeks

H.Pylori treatment response

Is assessed after four weeks of 2 standard antibiotics completion and after PPI is discontinued after 2 weeks with H.Pylori stool Ag

Adult age > 15

4.10 Data Analysis

Data was collected with chart review and first checked manually for completeness and analysed using SPSS version 25. During the analyses P-value < 0.05 with 95% confidence interval (CI) for OR (odds ratio) was used in judging the significance of the associations. Descriptive statistical analysis (mean, median) was utilized for demographic statistics and the degree of spread using standard deviations or range for continuous variables. Frequency distribution tables were employed for categorical data as well as pie and bar charts. Mean and Univariate and Bivariate analyses between dependent and independent variables will be performed using chi square (χ^2) and binary logistic regression.

4.11 Data quality control

Data quality was controlled by rechecking the questioner to avoid duplications, incomplete information and invalid information before analysis. Regular checkup for completeness and consistency of the collected data was done using checklist by the data collector.

4.12 Ethical considerations

Ethical clearance was obtained from SPHMMC and department of internal medicine; Letter for cooperation from each level was obtained. Names and other identification that will reveal patients identity was kept strictly hidden. Data was abstracted from patient's chart to data collection form by investigator who is already involved with care of the study population. All abstracted data didn't contain patient identification.

4.13 Dissemination of results.

The findings of the study will be submitted to the department of internal medicine, public health department and all efforts will be made to publish the results to the local and international journals and to present it in national scientific conferences.

CHAPTER 5; RESULT

5.1 Sociodemographic data

A total of 48 patient identified from September 2016 to June 2019. However, five patient chart cannot be traced so they were not included in the study. Patients that were assessed in the study are 43 this include 33 (76.7%) female and 10(23.3%) male patient with a median age is 27 years. The majority of the patient age range 20-29, which accounts for 37.2%. Employed group account for 55.9%. Marital status 27.9% are single, 69.8% are married and 2.3% are divorced.

Educational status 9.3 % can't read and write 11.6% can read and write, 16.3 % received primer education 34.9 % secondary education 27.9 %have attended collage/ university

TABLE 1 1 **Socio demographic data**

Age group		
		Number (Percent)
	15-19	7 (16.3%)
	20-29	16 (37.2%)
	30-39	7 (16.3%)
	40-49	3 (7%)
	50-59	6 (14%)
	60-69	3 (7%)
	>69	1 (2.3%)
Gender		
	MALE	10 (23.3%)
	FEMALE	33 (76.7%)
Marital status		
	Single	12 (27.9%)
	married	30 (69.8%)
	divorced	1 (2.3%)
Occupation		
	farmer	2 (4.7%)
	private employed	7(16.3%)
	government worker	9(20.9%)
	student	8 (18.6%)
	unemployed	11 (25.6%)
	self employed	6 (14 %)
Residency		
	Urban	23 (53.5%)
	semi- urban	13 (30.2%)
	Rural	7 (16.3%)
Educational status		
	uneducated	4 (9.3%)
	read and write	5 (11.6 %)
	primer education	7 (16.3%)

	secondery education	15 (34.9%)
	collage/ universty	12 (27.9%)

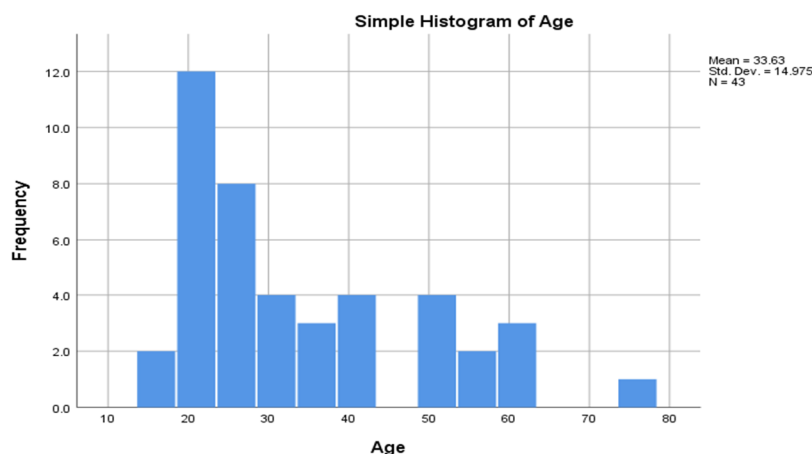


FIGURE 1 1 AGE DISTRIBUTION HISTOGRAM

5.2 Cofounding factor

From the 33 female 14(42.4%) was pregnant and 19 (57.6 %) was not pregnant at the time of diagnosis. HIV status 3 patient were HIV positive (7%) (2 male and 1 female) and 1(2.3%) patient was positive for hepatitis B and 1(2.3%) patient was positive for hepatitis C. Patient who were taking medication at the time of diagnosis was 8(18.6%) patient and only 2 patient were taking medication has been associated with ITP. One of the patient 32-year-old female who was taking penicillin g benzathine the other one is 19-year-old female patient who was taking ibuprofen.

TABEL 2 COFOUNDING FACTOR

pregnancy status		Number (percent)
	not pregnant	19 (57.6%)
	pregnant	14 (42.4%)
HIV test		
	negative	40 (93%)
	positive	3 (7%)
Hepatitis B Surface antigen		
	negative	42(97.7%)
	positive	1(2.3%)

Hepatitis C Ab		
	negative	42(97.7%)
	Positive	1(2.3%)

5.3 CLINICAL CHARACTERISTICS

H.Pylori infection was detected in the 9(20.9%) out of 43 patient which were positive for H.Pylori test investigated with H.Pylori stool Ag (40 patients) or H.Pylori anti body test (3 patients) from the blood and all the positive result was from the stool ag. Treatment for H.Pylori was given for seven out of the 9 H.Pylori infected patient. The mean platelet count at presentation is 18,000. Majority 79.1% of patient presented with bleeding. Transfusion was required for 14(32.6%).Treatment for ITP was given for 38(88.3%) patient 37(86%) of them with prednisone; one(2.3%) patient with po dexamethasone and 5 (11.6%)patient didn't require treatment.

H.Pylori test		Number (percent)
	Negative	34 (79.1%)
	Positive	9 (20.9%)
Platelet count		
	<10,000	14 (32.6%)
	10,000 - 30,000	16 (37.2%)
	31,000 - 60,000	9 (20.9%)
	>60,000	4 (9.3%)
Transfusion required		
	Yes	29 (67.4%)
	No	14 (32.6%)
Treatment given for H.Pylori		
	Given	7 (16.3%)
	not given	2 (4.7%)
	not needed	34 (79.1%)
Treatment given for ITP		
	Predensinol	37 (86%)
	Dexamethasone	1 (2.3%)
	Not needed	5 (11.6%)

Bleeding at diagnosis		
	Yes	34 (79.1%)
	No	9 (20.9%)
Response to treatment		
	partial response	17 (39.5%)
	complete response	19 (44.2%)
	no response	2 (4.7%)
	steroid dependent	5 (11.6%)
Bleeding type		
	petechia	2 (4.7%)
	purpura	1 (2.3%)
	gum bleeding	2 (4.7%)
	epistaxis	13 (30.2%)
	menorrhagia	4 (9.3%)
	intracranial bleeding	1 (2.3%)
	no bleeding	9 (20.9%)
	petichea+ gum bleeding+ epistaxis	9 (20.9%)
	menorrhagia+ epistaxis	2 (4.7%)

TABEL 1 4 COMPARISON CLINICAL CHARACTERISTICS BETWEEN H.PYLORI INFECTED AND NOT INFECTED PATIENT

H.Pylori		Negative	Positive
Number of patient		34	9
	Mean age	34.91±14.975	28.78±13.98
	Median	28.00	26.00
	Age Range	19-75	16-60
Gender			
	MALE	7(20.6%)	3(33.3%)
	FEMALE	27(79.4%)	6(66.7%)
Platelet count			
	<10,000	9(26.5%)	5(55.6%)
	10,000 - 30,000	14(41.2%)	2(22.2%)
	31,000 - 60,000	8(23.5%)	1(11.1%)
	>60,000	3(8.8%)	1(11.1%)
Bleeding			
	Yes	25(73.5%)	9(100%)

	No	9(26.5%)	0
Transfusion required			
	Yes	25(73.5%)	4(44.4%)
	No	9(26.5%)	5(55.6%)
HIV			
	Positive	31(91.2%)	0
	Negative	3(8.8%)	9(100%)
Hepatitis B s Ag			
	Positive	1(2.9%)	0
	Negative	33(97.1%)	9(100%)
Hepatitis c Ab			
	Positive	0	1(11.1%)
	Negative	34(100%)	8(88.9%)
Pregnancy			
	Pregnant	12(44.4%)	4(66.7%)
	Not pregnant	15(55.4%)	2(33.3%)

Clustered Bar Percent of Age (Binned) by h.pylori test

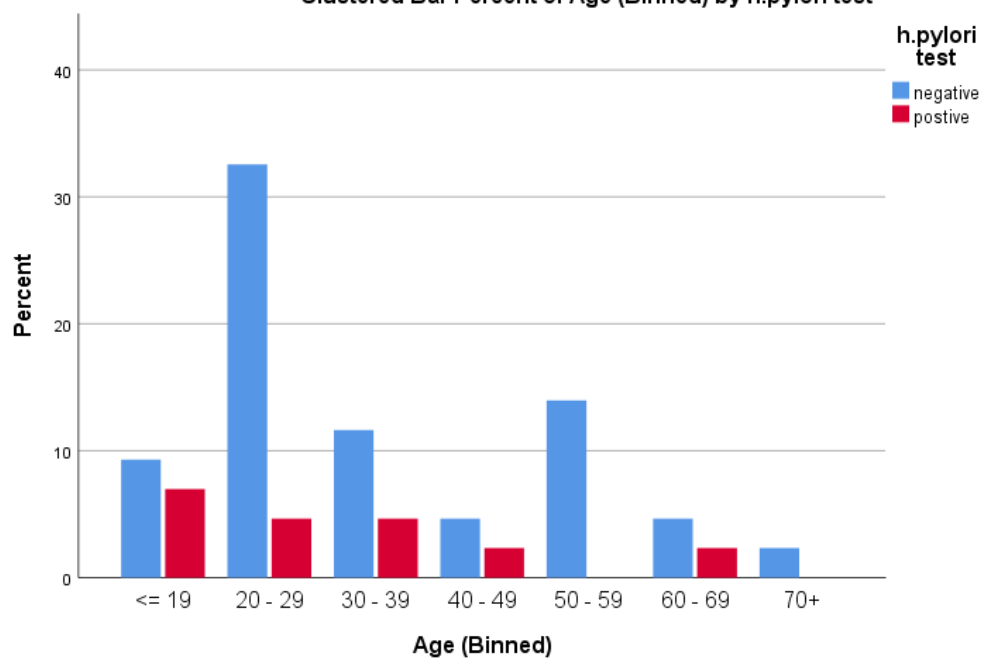
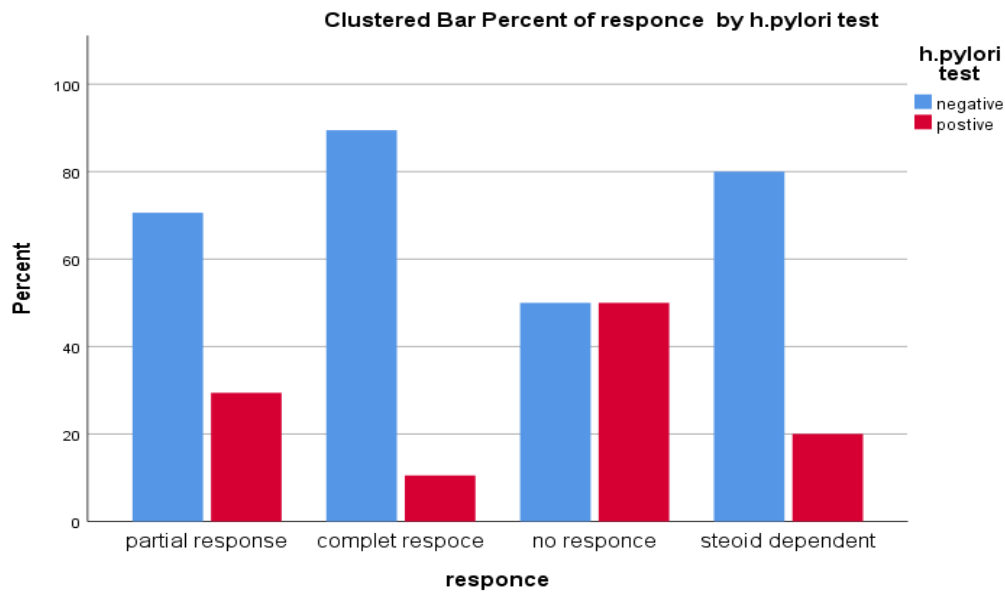


FIGURE 2 AGE DISTRIBUTION BETWEEN H.PYLORI POSITIVE AND NEGATIVE PATIENTS



There was no association found between age, sex, platelet count, H. Pylori positivity and response to treatment based on Pearson's correlation coefficient, chi square test taking $p < 0.05$ as a statistically significant test.

CHAPTER SIX DISCUSSION and CONCLUSION

There were 43 patient identified which was comparable to other studies which asses the associate of ITP and H.Pylori association one study from the one that is done in Ethiopia previously with 34 patient (14) ITALY included 30 patient (17) And in 2 reports from japan one included 48 patient the other included 61 (18)(19)patients

Epidemiology and clinical characteristics

The median age of ITP diagnosis is 27 ± 14.975 age range (16- 75) with the predominate age group of < 40 with Peak age of 20- 29. which is comparable to study done in south Africa which has a mean age of 32 ± 14 years and a bit higher than the previous study done in Ethiopia mean of 24.9 years age range of (13-57) (14). But when compared to other studies done in England shows the mean age is 57 ranges (18-99) with increase prevalence in age group >60(9) and a nationwide study in comparing different ethnic group France has showed a pick incidence in adult 60 years of age (11). These differences in age between our study and the Western world could be attributed to a number of factors, including 1) younger age structure of our population 2) presence of co infection 3) association of pregnancy and ITP since around 42.4% were pregnant at diagnosis

This study shows The ratio of male to female 1:3.3 showing female predominance, previous study in Ethiopia shows that female to male ratio of 2.1:1 not exaggerate as this study (14)in South Africa female to male ratio is 4.2:1, which more exaggerated female predominance this study is in between the two (24) ITP usually affect young females.

The mean platelet count at diagnosis is in this study is 18,000. The majority of patient (67.4%) have a platelet count $\leq 30,000$. Around 20.9% of the patient presented with no bleeding and a majority of patient presented with bleeding 79.1 majorly muco cutaneous bleeding 62.8% from this epistaxis account for 30.2%. Major bleeding, menorrhagia occurred 14%, around 2.3% presented with CNS bleeding and no patient presented with GI bleeding. The platelet count is comparable to study done in Ethiopia previously (14)and a bit higher than the south African study (24) but lower platelet count than other studies in most countries like Japan ,Italy and UK with comparable prevalence in intracranial bleeding (21) . Bleeding at presentation is consistent South African study (24)

These differences could be attributed to factors such as poor health seeking behavior in our population; the probability of making diagnosing ITP is poor in the health center and peripheries unless they are symptomatic. Late presentations to hospital as well as severe thrombocytopenia at initial presentation. The lower incidence of intracranial bleeding can be explained by lower risk of major bleeding like ICH in ITP patient despite low platelet count

H.Pylori infection was found in 9/43 (20.9%) patient by H.Pylori stool Ag which is lower than Italy 13/30(43.3%) (17)and the Japanese study 27/48 (56.5 %)which is relatively lower compared to the

general prevalence in our county which is about >90%. This could be due to increase sensitivity of health care worker to over treat H.Pylori infection every now and then in our set up right and left use of antibiotics and omeprazole. The test that is used to diagnosed H.Pylori which is either H.Pylori stool ag or H.Pylori Ab has a sensitivity of (90-92%) and (87-92%) respectively (25,26) and specificity of 90% (25). Comparing this with other studies done in Japan and Italy they make the diagnosis of H.Pylori infection depending on 2 positive results from 2 different tests histologic test with 13C urea breath test or rapid urease test which in combination have a better diagnostic sensitivity (17)(18). The presence of other overwarming causes for ITP may contributed to it. Health education primarily to improve knowledge and awareness on the transmission dynamics of the bacteria, behavioral changes, adequate sanitation.

Mean age in H.Pylori infected and not infected group, the H. pylori infected group are younger with mean age of 28.78 ± 13.98 than those who are not infected with H.Pylori, which is 34.91. compared to systemic review of 22 article (1998-2007) comparing finding from different countries(ITALY ,JAPAN , UK) showed also there is a difference from study to study the majority shows those patient who are infected with H.Pylori have a higher mean age who are not. it also included studies showing lower mean age than those who are not (21)

As with other studies the ratio of male to female is comparable between H.Pylori infected and not infected patient this result is comparable to those that is done in ITALY There was no difference in sex ratio between infected and uninfected patient(15) and the one that is done in England (18)

There is no difference in the mean platelet count mean in H.Pylori negative(19,000)and H.Pylori positive 17,000 , bleeding presentation between H.Pylori infected and not infected group of patient and around 77.8% have a platelet count < 30,000 which is comparable to other studies (21)

The mainstay treatment of ITP is oral corticosteroids, particularly prednisone. This was the drug of choice in most of our patient who required treatment 97.7% and oral dexamethasone was given in 2.3%(1 patient) from the total patient 11.6 % didn't require treatment .

Response to treatment 44.2 % have a complete response, 39.5 achieve a partial response, 11.6% become steroid dependent and 4.2 % have no response. Commenting on the response is difficult because the duration of follow up is 2months –4years and most patient have a follow up duration around 6 months , in the patient who have a longer duration of follow up some off the patient tends to be on off treatment. There is no major in response in those who are H.Pylori infected and not infected

Strength

Since it's the first study done in Ethiopia and Africa assessing the prevalence of H.Pylori in ITP it serve as a starting point for the studies yet to come.

Limitation

Because of the retrospective nature of the study, relying on aggregated data documented in patient's records. In some circumstances, these records were not adequately completed and certain information was lacking Duration of follow up is from 2month - 4yr. and assessing and following maintenance of

response to treatment is difficult. The test that was used to diagnose H.Pylori (H.Pylori stool Ag, H.Pylori ab has only (87-92%) sensitivity and histological study of H.Pylori was not done which is more sensitive for the diagnosis of H.Pylori

Conclusion

ITP is predominately- young predominantly female disease with higher prevalence in younger age < 40. Prevalence of H.Pylori infection is 20.9% of the patient, which is low. There is no difference in age group, gender predominance, clinical presentation, initial platelet count between H.Pylori infected and non-infected group. Majority of patient have complete or partial response with no difference with or without H.Pylori infection. Whether eradication of H.Pylori have effect in ITP treatment response requires further study with longer duration of follow up

Recommendation

Prevalence of H.Pylori infection prevalence is relatively low in our study group when compared to the general population. Because of limitations we have in diagnosing, investigating all ITP patients for H.Pylori still merits the patients until further studies shows lower prevalence.

Making the diagnosis of H.Pylori should be done using at list 2 positive result from two different diagnostic technique and one being histologic test

Further prospective studies with large population size, gold standard diagnostic technique (histologic diagnostic test for H.Pylori) and longer duration of follow up are required to assess the causal association of H.Pylori and ITP

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Annex I

Consent

The confidentiality of patients who are subject of this study will be kept. Names and other identification that will reveal patients identity will be kept strictly hidden and will not be revealed in the checklist.

Section I: Socio-demographic characteristic

S.R	Question	Response category
1	Age(in years)	
2	Sex	1. Male 2. female
3	Residence	1. urban 2. semi-urban 3. rural
4	Occupation	1. Daily labor 2. Farming 3. Private work 4. Governmental Employee 5. Other (specify
5.	Marital status	1. Single 2. married 3. Divorced
6	Educational Level	1. Uneducated 2. Can read/write 3. Primary education 4. Secondary education 5. Higher level education (College/University)

II Assessing h.pylori infection and Cofounding factor

1)HIV test

Positive ☐ Negative ☐

2)test for hepatitis B

Positive ☐ Negative ☐

3)Test for hepatitis C

Positive ☐ Negative ☐

4) h.pylori test

Positive ☐ Negative ☐

5)If the answer to question number four is positive how was it assessed

h.pylori anti body ☐ h.pylori stool Antigen ☐ urase breath test ☐

6)was the patient pregnant at the time of diagnosis

yes ☐ no ☐

7)was the patient taking any medication at the time of diagnosis

yes ☐ no ☐

8)if the answer to question no 8 is yes specify the drug

Assessing H.pylori and ITP association

1)What was the platelet count at diagnosis?

<10,000 ☐ 10000-30,000 ☐ 31,000-60,000 ☐ >60,000 ☐

2)was there any bleeding at the diagnosis or during follow up?

Yes ☐ No ☐

3) if the answer is yes to the above question what kind of bleeding does the patient had ?

Petechiae ☐ purpura ☐ Epitasis ☐ GI bleeding ☐ intracranial bleeding ☐

4) What was given for the patient having platelet count < 10,000 or having GI or intracranial bleeding?

IVIG ☐ prednisone ☐

5) did the patient requires platelet transfusion at diagnosis ?

Yes ☐ No ☐

6) What was give to the patient for ITP management ?

Predensonol ☐ IVIG ☐ Retiximab ☐ splenctomy ☐

Dexametason po ☐ Dexametason IV ☐

7) If patient who are positive to h.pylori test is positive were they treated with triple therapy

Yes ☐ NO ☐

8) was it possible to archive h.pylori eradication after triple therapy?

Yes ☐ NO ☐

8) Was the patient off PPI for at list 2 weeks when eradication of h.pylori was assessed?

YES ☐ NO ☐

9) did the ITP respond to H.pylori eradication alone?

YES ☐ NO ☐

10) if the patient was a persistent (>3months) or chronic ITP patient (>12 months) or post splenectomy and H.Pylori infection was it possible to achieve response by H.pylori eradication?

Yes ☐ NO ☐

11) IF the answer is yes for the above question what was the response that was achieve

Partial ☐ complete ☐ no responses ☐ steroid dependent ☐