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Original Research

Prevalence and Possible Predictors of Helicobacter Pylori Infection Among Adult Patients with Sickle Cell Disease in Ahmadu Bello University Teaching Hospital North-West, Nigeria

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Abstract

Background: Helicobacter Pylori *(H. pylori)* infection occurs worldwide. Patients with Sickle Cell Disease (SCD) may present with abdominal symptoms due to different pathophysiological mechanisms. SCD patients are predisposed to infections due to immune deficiency, abdominal symptoms like dyspepsia and recurrent abdominal pain have been associated with *H. pylori* infection. This study determined H. *pylori* prevalence in adult SCA patients and its relationship with socio-demographic, clinical, and laboratory parameters.

Methodology: Adult patients with SCA in Steady State were enrolled after informed consent. Sociodemographic, clinical, and laboratory parameters were documented using a structured questionnaire. *H. pylori* IgG antibody was detected using lateral flow Rapid Diagnostic Test (FaStep USA). Data were analyzed using EpiInfo 7.2.

Results: The median age of participants was 23(20, 26) years. Most of the participants (56.8%) were from lower socioeconomic classes. Sickle cell painful vaso-occlusive crises and blood transfusion in the previous 12 months were 2(1, 4) and 0(0, 1) respectively. Ninety (53.3%) of the participants had abdominal symptoms. Non-specific abdominal pain was the most common. The median frequency of abdominal pains was 1(0, 2). *H pylori* infection was found in 23.1%. The Odds for *H. Pylori* infection was high in participants with abdominal symptoms, antacid use, and multiple abdominal symptoms {OR=1.552, 1.306, and 2.584 respectively) though not statistically significant. At the same time those with recurrent abdominal pain and male sex had lower Odds (OR=0.875 and 0.831respectively), though not statistically significant.

Conclusion: H. pylori infection is not uncommon among SCA patients. Physicians should be vigilant in SCD patients with multiple abdominal symptoms by screening early and instituting management.

Keywords: Abdominal Pain, *H. Pylori*, Predictors, Sickle Cell Disease, Nigeria

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Quick Response Code:

Introduction

Helicobacter pylori(H. pylori) is a fastidious gram-negative micro-aerophilic bacillus that colonizes the luminal surface of human gastric epithelium.(1,2) *H. pylori* is transmitted through fecal-oral or oral-oral route(3) and prevalence rates differ significantly between geographic regions with estimated infection rates of 20-50% among the general population in Western developed countries.(4) However, a higher prevalence of up to 80% has been reported among the general population in less developed countries.(5) In a previous study in Zaria, Nigeria, Ajiboye *et al* (6) reported a prevalence of 73.6% among persons with non-ulcer dyspepsia while Jemikalajah & Okogun (7) reported a prevalence of 12.7% in South-South Nigeria.

Persons with Sickle Cell Disease (SCD) are predisposed to different infections due to defective splenic function, impaired complement activation, deficiencies of micro-nutrients such as Zinc as well as some phenotypic variations among the different haplotypes of SCD.(8) Thus, persons with SCD may be more prone to infection by *H. pylori* and may be afflicted with more acute and chronic complications of SCD if they have been infected with *H. pylori*.

Patients with Sickle Cell Anaemia (SCA) suffer from recurrent exacerbations of signs and symptoms referred to as Sickle cell crisis. These crises include the most common painful Vaso-occlusive/bone pain crisis, sequestration crises, hyper-haemolytic crises, or hypo-plastic crises. Similarly, abdominal pain frequently occurs in patients with SCA. This abdominal pain may arise from hepatic, biliary, intestinal, or other intra-abdominal pathologies or may be secondary to the ill-defined abdominal pain crisis. The abdominal pain crisis presents as mild, transient, or severe abdominal pain not related to any specific abdominal pathology.(9),(10)

Helicobacter pylori (*H. pylori*) infection has been implicated in the pathogenesis of gastric cancer, dyspepsia, and peptic ulcer especially in persons taking non-steroidal anti-inflammatory drugs (NSAIDs).(11) Due to the frequent painful Vaso-occlusive crises, patients with SCA will often ingest NSAIDs and may likely be more predisposed to peptic ulcer and other related diseases as reported by Woods *et a*l.(11)

Abdominal symptoms in patients with SCA include epigastric pain, vomiting, diarrhea, and recurrent abdominal pain. However, these symptoms occur in other illnesses such as peptic ulcer, malaria, and other infectious disease conditions. *H. pylori* infection which is common worldwide may also present with epigastric pain and dyspepsia.(12) Particularly in Sickle Cell Patients.(4)

H. pylori has been linked to growth retardation, development of Iron deficiency anaemia, gastritis, peptic ulcer, chronic idiopathic thrombocytopenic purpura, and recurrent abdominal pain especially in children with a paradoxical reduction in the incidence of asthma.(13,14) Hence, *H. pylori* infection may have the potential to instigate or worsen the precarious health status of patients with SCA and thus may adversely affect their activities of daily living. This study determined the sero-prevalence of *H. pylori* among adult (age ≥18 years) patients with SCA and assessed the relationship between *H. pylori* status and some socio-demographic, clinical, and laboratory parameters among participants in Zaria, North-West, Nigeria with a view to identifying predictors (clinical or laboratory) that can be used as indicators for screening of SCA patients.

Materials and Methods

Study area: This study was conducted at the Ahmadu Bello University Teaching Hospital (ABUTH) a federal government-owned Tertiary Hospital in North-West Nigeria. The Hospital has a 500-bed capacity and runs a specialist Haematology clinic weekly where there are over 600 registered Sickle Cell Disease (SCD) patients. Zaria is a town that occupies the high plains of Northern Nigeria, 652 meters above sea level and 950 kilometers from the Atlantic coast at $11^0$31'N and $7^0$42'E.(15)

Sample size calculation

The sample size was determined using the formulae from OpenEpi version 3

$$N = [DEFF*Np(1-p)]/[d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$$(16)

Where: Population size (for finite population correction factor or FPC)(*N*): 600 SCD patients on ABUTH Database

Hypothesized % frequency of outcome factor in the population (*p*): 31%+/-10

Confidence limits as % of 100(absolute +/- %) (*d*):10%

Design effect (for cluster surveys-*DEFF*): 2 (due to consecutive enrolment).

The minimum sample size (n) calculated = 145

However, an attrition rate of 20% was assumed and therefore, 145 x 20/100 = 29 was added (145 + 29 = 174). Thus, a total of 174 participants were enrolled in the study.

Study design: This was a hospital-based cross-sectional study spanning over 3 months (1st September to 30th November 2019) conducted among 174 eligible consenting SCD patients aged ≥ 18 years who were consecutively enrolled into the study after signing an informed consent form.

Ethical Consideration: Ethical approval for the study was obtained from the hospital's Health Research Ethics Committee prior to commencement of the study (ABUTHZ/HREC/H45/2019).

Study procedure: Three milliliters (3ml) of blood were drawn from a suitable vein in the cubital fossa after a standard aseptic procedure and dispensed into plain sample bottles. These were left to stand for 30 minutes and thereafter centrifuged at 3000rpm for 5 minutes. The sera were dispensed into plain containers and frozen at -20^0C for a maximum of seven days before analysis.

H. pylori IgG detection technique: This was carried out using a lateral flow Rapid Diagnostic Test (RDT) Cassette by *FaStep* China.(17) Two drops of serum were added to the designated test device and the results read visually at 10 minutes. The test device has an inbuilt control line that must appear to indicate the test is correctly done. These were initially validated by known positive and negative sera. A positive result was recorded when 2 lines appeared whereas the result was reported negative if only the control line appeared. The absence of the control line invalidates the test.

Steady State Haematological Values: These were retrieved from the patients' case notes; the HCT, WBC, and Platelets values for 3 previous steady state visits were extracted and the mean value for each patient was determined as the steady-state values.

Definition of Terms:

Steady State: This refers to a point in time where the patient is not experiencing an acute painful crisis or any change due to therapy.(18)

Recurrent Abdominal Pain (RAP): This was defined as three or more episodes of upper abdominal pain severe enough to require medical attention during the past three months preceding the study. (19) Patients who have received proton pump inhibitors, amoxicillin, metronidazole, or clarithromycin within two weeks prior to the study were excluded.

Multiple Abdominal Symptoms: This refers to the occurrence of more than one abdominal symptom (e.g. Dyspepsia and Epigastric pain) at the same time.
Dyspepsia: This was defined as a predominant epigastric pain lasting at least one month that can be associated with other gastrointestinal symptoms such as epigastric fullness, nausea, vomiting, and or heartburn.(20)
Socio-Economic Status: The Socio-Economic status of participants was defined based on the standard occupational classification designed by the Office of Population Census and Surveys (OPCS) and modified by Esan *et al*.(21)Where:

Class 1: skilled workers e.g. professional & managerial officers & retirees of this cadre.
Class 2: unskilled workers e.g. artisans and traders
Class 3: dependents e.g. retirees of class 2, those not on pension, housewives of class 2, and students whose parents are unskilled.

Data Analysis
Data obtained were checked for completeness and analyzed using EpiInfo 7.2. Qualitative variables were summarized as frequencies, percentages, and charts. Continuous variables were assessed for normality using skewness and kurtosis following which non-normality distributed variables were summarized as medians {interquartile ranges – (25^{th} percentile, 75^{th} percentile)}. The socio-economic class was re-classified as upper (Class 1 and 2) and lower (class 3).
Risks were estimated using odds ratio (OR) and 95% Confidence Intervals (CIs). Distributions of non-normally distributed continuous variables between bivariate qualitative variables were assessed using Mann Whitney U (MWU) tests. The level of statistical significance was set at $p \leq 0.05$.

Results

There were 174 participants with SCA enrolled, out of which 169 participants with complete data were analyzed. The median age of participants was 23(IQR 20,26) years. Females constituted 121 (71.6%). Most of the participants 96 (56.8%) were from the lower (Class 3) socioeconomic class while the remaining 73(43.2%) were from the upper socioeconomic class. The median number of Sickle cell painful vaso-occlusive crises and blood transfusions in the previous 12 months were 2(1, 4) and 0(0, 1) respectively.

Over half of the participants, 90/169(53.3%) had abdominal symptoms with non-specific abdominal pain occurring in 45/90(50%) and dyspepsia in 8/90(8.9%) while 12/90(13.3%) had multiple abdominal symptoms (Figure 1). The median frequency of abdominal pains was 1(0, 2) with only 33(19.5%) of participants having recurrent abdominal pain. None of the participants reported a history of smoking cigarettes. There was a history of intake of antacid in 49 (29.0%) of participants. The median HCT, WBC, and platelets are summarized in Table 1.

The relationship between *H. pylori* infection and Clinical/Haematological Variables is shown in table 2. The prevalence of *H pylori* infection was 39/169(23.1%). Participants with abdominal symptoms had increased odds of having *H pylori* {OR=1.552(95% CI 0.747, 3.223), p=0.237}. Males were less likely to have *H. pylori* infection with an OR of 0.831(95% CI 0.371, 1.881, p=0.663). Participants from lower socioeconomic status had a lower risk of having *H. pylori* infection OR=0.748(95% CI 0.365, 1.534, p=0.4270)}. Participants with *H. pylori* infection were older than those without (24(10.0) years vs 22(6.3) years, MWU=1999.5000, p=0.045). There was a slightly increased odds that participants with a history of antacid intake had *H. pylori* infection OR=1.306{(95% CI 0.605, 2.816), p=0.496)}. Participants with multiple abdominal symptoms had markedly increased odds of having *H pylori* infection OR=2.584{(95% CI 0.771, 8.655), p=0.150)}. While those with recurrent abdominal pain had OR=0.875{(95%CI 0.347,2.204), p=0.823)}.

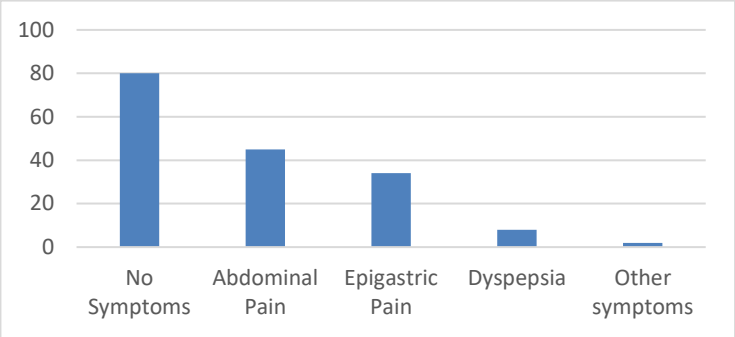

Figure 1: Frequency of abdominal symptoms in study participants (n=169)

Table 1: Summary of Haematological Parameters of participants (n=169)

	HCT (%)	WBC (x 10^9/L)	PLT WBC (x 10^9/L)
25th Percentile	19.7	8.7	306.5
Median	22.2	11.1	394.0
75th Percentile	25.2	13.4	497.0

*Haematocrit (HCT), White Blood Cell Count (WBC), Platelet Count (PLT)

Table 2: Relationship between H. pylori infection and Clinical/Haematological Variables

H. pylori		Mean Rank	MWU	p value
Crises (in last 12 months)	Positive	90.65	2314.500	0.405
	Negative	83.30		
Transfusion (in last 12 months)	Positive	94.79	2153.000	0.108
	Negative	82.06		
Abdominal Pain Frequency	Positive	86.87	2462.000	0.774
	Negative	84.44		
HCT (%)	Positive	89.88	2344.500	0.479
	Negative	83.53		
WBC (x 10^9/L)	Positive	77.77	2253.000	0.294
	Negative	87.17		
PLT (x 10^9/L)	Positive	81.73	2407.500	0.636
	Negative	85.98		

*Haematocrit (HCT), White Blood Cell Count (WBC), Platelet Count (PLT)

Discussion

This prevalence of *H. pylori* (23.1%) among persons with SCD found in this study is not remarkably different from the 28% sero-prevalence report by Enitan *et al* from North-Central Nigeria(22) and 29.7% among internally displaced persons in South-South by Owowo *et al* (23). Ayodele *et al* and Kooffreh-Ada *et al* found a higher prevalence of 39.8% among suspected peptic ulcer disease and 42.6% among patients with dyspepsia respectively in South-South Nigeria (24,25). Omosor *et al* who reported a higher prevalence of 52% also from South-South Nigeria(26). Our finding is remarkably lower than the 87.7% sero-prevalence in Northern Nigeria reported by Smith et al(23=27), and Umar *et al* who reported 69% prevalence in Kano, North-West Nigeria.(28) Even though these studies were carried out on apparently healthy participants, they reflect the general geographical differences in the prevalence of *H. pylori* infection across the world.(29,30)

Our findings suggest that SCA patients with more than two abdominal symptoms (multiple abdominal symptoms) are more likely to have *H. pylori* infection, this concurs with the report of Woods *et al* that showed an increased risk of *H, pylori*-induced PUD among SCA patients.(11) Similarly, the absence of a relationship between recurrent abdominal pain and *H. pylori* infection in this study may be related to the fact that abdominal pain in SCA is caused by different pathophysiological mechanisms e.g. hepatic, biliary, mesenteric, splenic, and other pathologies.(9)

Even though previous studies in adults with dyspepsia have indicated a high prevalence of *H. pylori*,(24,25,31-33) this study, in contrast, noted that most participants had abdominal symptoms, but non-specific abdominal pain was the commonest symptoms and dyspepsia occurred less frequently. This difference may be explained by the method of participant selection in the other studies where only participants with dyspepsia were enrolled. Out of the thirty-nine patients with *H. pylori*, the majority had abdominal symptoms, while the remaining had no abdominal symptoms. There was no statistically significant difference in frequency, presence, or absence of abdominal symptoms among *H. pylori* positive. This may be a pointer that no abdominal symptom is specific to *H pylori* infection(1,34).

The finding of reduced risk of *H. pylori* infection among participants from low socioeconomic class is in contrast with other studies within and outside Nigeria, which noted that the majority of *H. pylori* infection occurred among persons from the lower socioeconomic class(33,35-37), which were attributed to poor hygiene because of irregular/insufficient potable water to persons in the lower socioeconomic class. However, the lower prevalence of *H. pylori* in our study may be explained by Zaria being an urban and cosmopolitan city with different ethnic groups.(38,39) Even though some previous studies on patients with *H. pylori* by Rahman *et al*(40) and Guclu *et al*(41) reported high white cell and platelet counts respectively compared to *H. pylori* negative patients. Our finding of comparable steady-state haematological parameters (Table 1) between participants with and without *H. pylori* infection is not unexpected. This is because *H. pylori* do not affect haemopoietic cells and thus may not cause significant haemopoietic changes except if H. pylori infection sequel leads to significant gastrointestinal bleeding that may result in anaemia and reactive thrombocytosis.

Limitations: The IgG antibody detection test used for this study tends to overestimate the prevalence of H. *pylori* and the reliance on participant self-reporting of symptoms of abdominal pain may be affected by recall bias.

Conclusion:

The prevalence of *H. pylori* infection in patients with Sickle Cell Disease in ABUTH Zaria is similar to the prevalence in the general population. However, patients with SCD presenting with multiple abdominal symptoms have a higher risk of *H. pylori* infection compared to those with only one or no abdominal symptoms.

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