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Effect of H. Pylori on Fibrinogen Level among Sudanese Patients at Khsartoum State

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: *Helicobacter pylori* (*H. pylori*) is a gram-negative, spiral shaped pathogenic bacterium that specifically colonizes the gastric epithelium causing chronic gastritis, peptic ulcer disease, and/or gastric malignancy.
Aim: To assess the effect of *H. pylori* on fibrinogen level of Sudanese patients with diabetes millets (D.M) living in Khartoum state.
Subjects and Methods: This was case control study conducted among Sudanese diabetic patients during the period from May 2018 to July 2021. A total of 181 diabetics patients are involved in this study. Citrated blood and stool samples were collected from each participant. All stool samples were tested for the presence of *H. pylori* antigen by using commercially available *H. pylo*ri antigen detection card. Based on the result examination for *H. pylori* the study population are sub grouped in two groups one group 124 of cases with Positive *H. pylori* antigen and another group 57 of controls with negative *H. pylori* infection. Both groups were assessed for the fibrinogen level. Data was gathered and analyzed by using SPSS version 20.
Results: Our results revealed that cases have slightly higher values of fibrinogen levels 326.29± 89.99 mg/dl compared to 309.47± 90.82 mg/dl for control group. However, the statistical analysis indicate that the difference was remain insignificant with P-value of 0.246. Among cases group gender concerned the fibrinogen concentration mean in the plasma of male 336.2±98.5 mg/dl was higher than female 311.1±73.4 mg/dl.

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Conclusion: they were insignificant association between fibrinogen level and presence of *H. pylori* infection among Sudanese diabetic patients. gender concerned the fibrinogen concentration in the plasma in *H. pylori* among males showed higher levels than females.

Keywords: Diabetes millets; H. pylori infection; fibrinogen level; citrated plasma; hyperfibrinogenemia; H. pylori antigen.

1. INTRODUCTION

"Helicobacter pylori is a gram-negative bacterium that colonizes the stomach and causes persistent infection. The infection is typically acquired in the first few years of life" [1,2]. "The associated risk factors of *H. pylori* infection include living in crowded households, low socioeconomic conditions and infected family members" [3,4]. "The infection is common worldwide with highest prevalence rates reaching 80–90% in developing countries and underprivileged communities, while a much lower prevalence of 20–50% is recorded in developed countries" [5,6,7].

"Associations of *H. pylori* infection with DM incidence have been reported. Recent meta-analyses showed a significant 1.7 to 2-fold higher prevalence of *H. pylori* infection in persons with T2DM vs. non-diabetic individuals" [8]. "In some of the studies that reported a positive association between *H. pylori* infection and DM" [9], "the association became on-statistically significant after adjustment for potential confounders such as age and socioeconomic status. Other studies reported no significant association between *H. pylori* and DM", [10] or "a significant association only in persons with BMI>25". [(11)] "Several studies did not control adequately for socioeconomic status and for traditional risk factors of DM, such as obesity and physical inactivity" [12].

"Furthermore, most of the evidence is based on small-scale hospital-based case–control studies, in which the source population, selection of control population and representativeness of the sample were not fully described" [13]. "For these reasons, inference and generalizability of findings from such studies should be done with caution. On the other hand, recent well-designed studies show convincing evidence of the potential involvement of *H. pylori* infection in the occurrence of DM, and possibly in IGT" [14].

"Diabetic patients have higher cardiovascular morbidity than non-diabetic subjects. Several studies have shown that homeostatic factor especially hyperfibrinogenemia is implicated as a source of atherosclerosis and its complications . Studies have reported that fibrinogen levels were higher in diabetics than in controls. Very few studies have been done regarding the association of *H. pylori* with fibrinogen in type 2 diabetes mellitus" [15].

"In a review aimed to evaluate the possible relationship between *H. pylori* and T2DM according to epidemiological surveys of 70 studies retrieved from databases, including Scopus, PubMed, and Google Scholar about the relationship between *H. pylori* and T2DM, and discuss the reported background mechanisms of this correlation. According to the results of their study, the different studies have shown that *H. pylori* is more prevalent in Type 2 diabetic patients than healthy individuals or nondiabetic patients. The reason is development of *H. pylori* infection-induced inflammation and production of inflammatory cytokines as well as different hormonal imbalance by this bacterium, which are associated with diabetes mellitus. On the other hand, by tracing *anti-H. pylori* antibodies in patients with diabetes mellitus and occurrence of symptoms such as digestive problems in >75% of these patients, it can be concluded that there is a relationship between this bacterium and T2DM. Considering the evidence, it is crucially important that the probability of infection with *H. pylori* is evaluated in patients with T2DM so that medical process of the patient is followed with higher cautious" [16].

H. pylori infection has been associated with an increased risk of developing ischemic heart disease (IHD). It has been suggested that a persisting low-grade acute phase response results from the chronic inflammation caused by *H. pylori* infection, which may give rise to increased circulating levels of certain coagulation factors and fibrinogen level [15]. Increase fibrinogen and coagulation factors activity among diabetes patients may put them in high risk of developing ischemic heart disease and subsequently IHD.

2. MATERIALS AND METHODS

2.1 Study Setting and Population

This was case control study conducted among Sudanese diabetic patients during the period from May 2018 to July 2021. A total of 181 diabetics patients are involved in this study. Citrated blood, stool samples were collected from each participant. All stool samples were tested for the presence of *H. pylori* antigen by using commercially available *H. pylori* antigen detection card. Based on the result examination for *H. pylori* the study population are sub grouped in two groups one group 124 of cases with Positive *H. pylori* antigen and another group 57 of controls with negative *H. pylori* infection. Both groups were assessed for the fibrinogen level.

2.2 Inclusion and Exclusion Criteria

Confirmed Sudanese diabetic patients living in Khartoum state of various ages and genders were included in this study. Any patient with disease other than diabetes mellites or have any fibrinogen disorder, were excluded from this study.

2.3 Detection of *H. pylori* Antigen in Stool Sample

The stool samples were evaluated by the card test according to the manufacturer's protocol. A single red band appearing across the central window in the site marked with the control line was considered negative. A red band appearing in the site marked with the result line and in the site marked with the control line was considered positive. A total absence of the control band, regardless of the appearance of the result site was considered invalid.

2.4 Estimation of Fibrinogen Level

Several steps have been followed according to manufacture protocol to assess the fibrinogen level in the blood samples of cases and controls. The citrated platelet poor plasma (PPP) of control pool plasma was used and the following dilutions in buffer were made: Dilution: 1:5 1:10. Then in plastic plane tube 90ul of buffer + 10ul of control plasma was added to obtain a 1:5 dilution. Then each of a second and a third plastic plain tubes 50 ul of buffer was added. In the second tube 50 ul from the first tube was added to 50 ul buffer to obtain a dilution of 1:10. Alternatively, a calibration curve which was provided with each kit. The same calibration curve could be used when using the same lot of reagents and performing a daily quality control. The PPP samples were diluted 1:10 with Imidazol buffer solution. Then the diluted samples were assayed for fibrinogen assay using the automated coagulometer and the clotting time of each sample was blotted 29 on the log-log paper and the corresponding concentration was gotten from the curve. Reference values: 200 - 400 mg/dl.

2.5 Quality Control

Pathological and normal control plasma were used to assure the accuracy of the result.

2.6 Data Collection and Analysis

The cases and controls demographic data as well as laboratory test data were obtained and recorded. Data was analyzed by using computer software package for social science (SPSS). Independent T test was used to compare between cases and controls in the level of plasma fibrinogen. The probability value <0.05 was considered to indicate a statistically significant value

3. RESULTS

This study was involved a total of 181 participants, about one third of them 58 (32.0%) are aged 53 – 63 years, while only 6 (3.3%) of them are aged less than 20 years old (Table 1). More than half 103 (56.9%) of the study participants are males while he rests 78 (43.1%) are females (Table 2). Our results revealed that cases have slightly higher values of fibrinogen levels 326.29± 89.99 mg/dl compared to 309.47± 90.82 mg/dl for control group. However, the statistical analysis indicate that the difference was remain with P-value of 0.246 (Table 3). Our study results showed that among cases group the mean of male's fibrinogen level 336.2±98.5 mg/dl was lower than females' level 311.1±73.4. While among control group the mean of male's fibrinogen level 306.2±76.1 mg/dl was lower than females' level 312.6 ±104.3mg/dl (Table 4). The current study results showed that there were insignificant association between cases and controls age groups and the level of fibrinogen (Tables 5,6).

Table 1. Distributions of age group among study of case populations

Age group	Frequency	Percent
less than 20 years	6	3.3
20-30	10	5.5
31-41	22	12.2
42-52	47	26.0
53-63	58	32.0
64-74	31	17.1
75-85	7	3.9
Total	181	100.0

Table 2. Distributions of gender among study of case populations

Gender	Frequency	Percent
Female	78	43.1
Male	103	56.9
Total	181	100.0

Table 3. The mean and Std of Glucose and fibrinogen among study of case and control populations

Parameter	*Case (N=124) (mean ±Std)*	*Control (N=57) (mean ±Std)*	*P. value*
Fibrinogen	326.29± 89.99	309.47± 90.82	0.246

The table shows the mean ± SD (mini - max) and probability (P). Independent T-test was used for comparison. P value ≤ 0.05 was considered significant

Table 4. Cases and controls fibrinogen level according to their gender

Participants	Gender	Fibrinogen level mg/dl
Case	Female	311.1±73.4
	Male	336.2±98.5
Control	Female	312.6 ±104.3
	Male	306.2±76.1

Table 5. Association between age group and fibrinogen level among H. pylori positive result

Age group	Fibrinogen
less than 20 years	390.0±36.3
20-30	375.4± 88.9
31-41	329.8±119.5
42-52	332.9±76.9
53-63	321.6±87.5
64-74	293.9± 96.1
75-85	326.2±89.9

Table 6. Association between age group and, fibrinogen level among H. pylori negative result

Age group	Fibrinogen
less than 20 years	231.0±21.0
20-30	356.0±80.2
31-41	354.8±109.1
42-52	280.1±101.0
53-63	327.8±80.6
64-74	298.4±100.4
75-85	241.0±72.3

4. DISCUSSION

"In the present study they were insignificant different in fibrinogen level among case and control which found fibrinogen level was 326.2 and 309.4 mg/dl in control group which agreement with" Yusuf et al.,[17] "which found the median serum fibrinogen level was 434 mg/dl *in H. pylori* positive patients and 486 mg/dl in *H. pylori* negative patients, with no significant difference between the two groups, p = 0.78. In the study conducted by" Longo et al.,[18] which found Fibrinogen level was 471.5 ± 23.6 in case and 297.2 ± 14.7 in control and the P.value was (0.0001).

"H. pylori infection could be linked to the early stages of coronary atherosclerosis rather than advanced coronary atherosclerosis" [19]. "Stroke is commoner than coronary heart disease in Africans with severe and uncontrolled hypertension. Progression of carotid lesions already associated with *H. pylori* infection may explain the onset of carotid plaques and stroke" [(20)] "in this screening population. However, carotid atherosclerosis is not related to *H. pylori* infection in the United Kingdom",[21] "whereas *H. pylori* seropositivity is associated with carotid plaques and cerebrovascular and cardiovascular events in Italy" [21]. "Our data clearly demonstrate that severity of *H. pylori* infection was significantly associated with the most important traditional risk factors for CVD, such as diabetes mellitus, arterial hypertension, high levels of serum fibrinogen and total cholesterol, and low HDL-cholesterol. In these *H. pylori* seropositive, male sex was the only independent predictor of both cerebrovascular and coronary heart diseases. *H. pylori* infection showed an extremely broad spectrum of disease outcomes. These findings lend support to the notion that chronic *H. pylori* infection with exacerbation of inflammation (elevated fibrinogen), male sex (smoking) and dyslipidemia may contribute to early onset of atherosclerosis" [22,23] "in those Africans facing demographic transition. Severity of Seropositivity in this infected group may reflect virulent strains bearing the cytotoxin-associated protein (CagA), with changes in inflammatory markers and higher risk of myocardial infarction" [24,25].

"As in previous studies, we did not observe any influence of *H. pylori* status on the white blood cell or platelet counts", [26,27] "but the mean plasma fibrinogen level was reduced by approximately 5% after *H. pylori* eradication therapy. By multivariate analysis, eradication treatment, regardless of its effect on *H. pylori* infection, was the only independent predictor of a reduction in the fibrinogen level. Conceivably, this is due to the effect of antibiotic treatment on the total pathogen burden or to the intrinsic anti-inflammatory properties of macrolide antibiotics" [28]. "Previous studies in patients with ischemic heart disease have shown similar decreases in plasma fibrinogen after treatment of *H. pylori* infection" [29] "although there is also evidence against any effect of *H. pylori* eradication treatment on fibrinogen" [27].

5. CONCLUSION

From our findings we conclude that, there was insignificant association between fibrinogen level and *H. pylori* infection among Sudanese diabetic patients. Also, there was insignificant association between fibrinogen level and gender among cases group. Further studies on the existing modalities which lower fibrinogen and finding newer treatment measures that can lower the fibrinogen levels without adverse effects, should be done.

All individuals signed informed consent prior to their enrolment in the study. Also, the study was planned according to the ethical guidelines following the Declaration of Ethics Committee of Karary University of Medical Sciences approved it.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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