Asian Journal of Medicine and Health
2(4): 1-7, 2017; Article no.AJMAH.31952

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No Association between *Helicobacter Pylori* Infection and Type 2 Diabetes Mellitus; A Case-control Study in the North-Western Part of Ghana

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Authors' contributions

This work was carried out in collaboration between all authors. Authors PA and RKDE designed the study, performed the statistical analysis and wrote the protocol. Author KOD wrote the first draft of the manuscript. Authors ID, PK and BT undertook all the experimental procedures. Authors PA and KOD managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2017/31952
Editor(s):
(1) Nicolas Padilla-Raygoza, Department of Nursing and Obstetrics, Division of Health Sciences and Engineering, Campus Celaya Salvatierra, Mexico.
(2) Maria Manuel Azevedo, Department of Microbiology, Faculty of Medicine, University of Porto, Porto, Portugal.
Reviewers:
(1) Nagahito Saito, Fujioka Hospital, Saga, Japan.
(2) Alba E. Vega, Universidad Nacional de San Luis, Argentina.
Complete Peer review History: http://www.sciencedomain.org/review-history/18028

Original Research Article

Received 31st January 2017
Accepted 27th February 2017
Published 3rd March 2017

ABSTRACT

Background: Patients with diabetes mellitus are prone to infections as a result of impaired immune status as a consequence of hyperglycemia. Previous studies addressing the relationship between *Helicobacter pylori (H. pylori)* infection and diabetes mellitus have yielded conflicting results.
Objective: This study aimed to determine the prevalence and the determinants of *H. pylori* infection among type 2 diabetes patients (T2DM) and its associated predisposing factors.
Methods: This case-control study enrolled 112 T2DM patients and 83 healthy adults (controls) who attended the Wa Regional Hospital. Sociodemographic characteristics were collected using questionnaire and anthropometrics were measured according to standard procedure. Stool samples were analysed for *H. pylori* infection using the *Onsite H. pylori* stool antigen rapid test cassettes while fasting blood glucose (FBG) was also estimated by using the glucometer.

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Results: There was no significant difference in the prevalence of *H. pylori* infection between the two groups [46% (cases) vs 39% (controls); p= 0.3073]. The mean ages of *H. pylori* positive T2DM patients and *H. pylori* negative T2DM patients were 56.83±10.50 and 52.81±11.65 years respectively. The mean FBG increased as BMI increased in diabetes and non-diabetes, with obese diabetic patients showing abnormal mean FBG level (7.76±1.44 mmol/l). Diabetes patients showed a higher mean FBG (6.526±0.1683) than the non-diabetes (4.272±0.1099) as body mass index (BMI) increased and the difference was statistically significant (p<0.0001).
Conclusion: *H. pylori* infection was not significantly associated with T2DM. Hyperglycemia, BMI and gender were not *H. pylori*-related predisposing factors in type 2 diabetic patients.

Keywords: H. pylori; fasting blood glucose; body mass index; type 2 diabetes mellitus.

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a global metabolic disorder, causing 3.8 million adult deaths annually [1]. The pathogenesis of T2DM is multifactorial, with risk factors such as diet, obesity, lack of physical exercise, genetic predisposition, and socioeconomic factors [1]. Insulin resistance, chronic inflammation, insulin secretion deficiency as a result of defect in pancreatic β-cells are the possible mechanisms in the pathogenesis of T2DM [1]. There are multiple evidence supporting the increased susceptibility of diabetes patients to chronic infections [2]. Diabetes mellitus has been shown to induce impairment of cellular and humoral immunity thereby enhancing a person's susceptibility to *Helicobacter pylori (H. pylori)* infection [1,3,4]. Also, diabetes mellitus decreases gastrointestinal motility and acid secretion thereby promoting the colonization and subsequently increases infection of the gut by pathogens [1]. It has been proposed that sialic acid circulating in the blood of diabetes mellitus patients act as specific antigen receptor for *H. pylori* on cells surfaces [5].

H. pylori is a chronic bacterial infection that affects approximately 50% of the global population particularly in developing countries [2,6-8]. However, there has been conflicting data on the association between diabetes mellitus and *H. pylori.* Whereas some researchers found significant association between *H. pylori* infection and diabetes [9-11], others found no such association [12,13]. Additionally, it has been suggested that *H. pylori* infection is common in diabetes patients with poor glycemic control as a consequence of impaired function of their immune system [4]. However, it is still difficult to make causal inferences from T2DM and *H. pylori* infection in Ghana. We therefore determined the prevalence and the determinants of *H. pylori* infection among T2DM patients in Wa in the North-western part of Ghana.

2. METHODS

2.1 Study Design/Area

This case-control study was conducted from January, 2016 to May, 2016 at the Wa Regional Hospital (WRH) in the Upper West Region of Ghana.

2.2 Participants/ Inclusion/ Exclusion Criteria

The study recruited a total of 195 participants; 112 T2DM, and 83 healthy adult non-diabetes mellitus individuals (controls). Non-diabetics with random plasma glucose >11.1 mmol/l were excluded. Again, any participant on any of the following medications: antibiotics, antacids, bismuth, and peptic ulcer medicines such as proton pump inhibitors (PPIs) and H2 blockers were excluded as these drugs may interfere with *H. pylori* stool antigen testing.

2.3 Ethical Considerations

The participation of the respondents who are all indigenes of Ghanaians was voluntary and written informed consent was obtained from each of them. The study was approved by the University of Cape Coast Institutional Review Board (UCCIRB). Approval was also sought from the Department of Medical Laboratory Technology and the WRH authorities. All procedures were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments.

2.4 Data Collection

An open-ended questionnaire and case notes were used to capture the socio-demographic and the clinical information of the participants.

2.5 Anthropometric Measurement

Height (to the nearest meter) and weight (to the nearest 0.1 kg) in light clothing were measured using a wall-mounted graduated ruler and weighing balance respectively. The body mass index (BMI) was then calculated as the ratio of the weight (kg) to the square of the height (m^2). BMI of <18.5, 18.5 – 24.9, 25.0 – 29.9, ≥30.0 underweight, normal, overweight, and obese respectively [14].

2.6 Sample Collection and Biochemical Analysis

Participants were given clean containers and instructed on how to properly collect stool samples. Samples were then screened for active *H. pylori* infection using *Onsite H. pylori* stool antigen rapid test cassettes (Biotech Simplifying Diagnostics, USA). Additionally, Fasting blood glucose (FBG) was estimated in accordance with manufacturer's instructions (ONETOUCH SELECT, India) after proper patient preparation.

2.7 Statistical Analysis

Data was analysed with SPSS version 21 (IBM Corp., USA). Exploratory analysis was done to obtain descriptive statistics such as mean ± SD, frequency, and percentages. T-test was used to compare means of cases and non-cases. Multivariate logistic regression analysis was used to evaluate BMI, FBG, and gender as risk factors for *H. pylori* infection. Chi-square analysis was used to determine the relationship between BMI and FBG level among cases and $P < 0.05$ was interpreted as statistically significant.

3. RESULTS

Most of the patients were within the age group of 40-50 years; 42 (37.5%) and 35 (42.2%) for cases and controls respectively with approximately equal age-wise distribution for both groups. The ages of the cases and controls were similar (p=0.362). Additionally, there was no significant difference between the prevalence of *H. pylori* infection between cases and controls [46% (cases) vs 39% (controls); p=0.3908], (Table 1).

Table 2 shows the socio-demographic and clinical characteristics of T2DM patients in relation to *H. pylori* status. Cases within the age group of 40-50 years had the highest infection rate of 18 (44.6%) with those within the age bracket of 81-90 recording the lowest infection rate of 1 (1.9%), however the infection rate

Table 1. Socio-demographic and clinical characteristics of study participants

Variables	Cases (N=112)	Controls (N=83)	P-value
Age (years)	55.6±9.9	54.3±10.5	0.362
Age group (years)			0.887
40-50	42 (37.5)	35 (42.2)	
51-60	36 (32.1)	25 (30.1)	
61-70	27 (24.1)	16 (19.3)	
71-80	5 (4.5)	5 (6.0)	
81-90	2 (1.8)	2 (2.4)	
Sex			**0.006**
Male	29 (25.9)	37 (44.6)	
Female	83 (74.1)	46 (55.4)	
FBG (mmol/l)	6.53±1.78	4.27±1.00	**0.000**
Weight (Kg)	69.63±11.02	65.47±6.81	**0.001**
BMI (Kg/m^2)	26.15±4.54	24.38±2.62	**0.001**
BMI group			**0.001**
Underweight	3 (2.7)	0 (0.0)	
Normal	43 (38.4)	48 (57.8)	
Overweight	45 (40.2)	33 (39.8)	
Obese	21 (18.8)	2 (2.4)	
***H. pylori* status**			0.3908
Positive	52 (46)	32 (39)	
Negative	60 (54)	51 (61)	

among the various age groups did not differ significantly (p=0.914). In addition, *H. pylori* infection rate was predominant among the female diabetes patients 38 (73.1%) compared to their male counterparts 14 (26.9%), however the difference was not statistically significant (p=0.817).

Also multinomial logistic regression analysis of gender, BMI, glycemic status, and age as risk factors of *H. pylori* infection among patients with diabetes were shown not to have any significant association (p>0.05) [Table 3].

Table 2. Socio-demographic and clinical characteristics of cases stratified by *H. pylori* status

Variables	Total	*H. pylori* status		P-value
		Positive	Negative	
	(N=112)	(N=52)	(N=60)	
Age (years)	55.6±9.9	55.4±10.3	54.9±9.5	0.432
Age group (years)				0.914
40-50	42 (37.5)	18 (34.6)	24 (40.0)	
51-60	36 (321)	16 (30.8)	20 (33.3)	
61-70	27 (24.1)	14 (26.9)	13 (21.7)	
71-80	5 (4.5)	3 (5.8)	2 (3.3)	
81-90	2 (1.8)	1 (1.9)	1 (1.7)	
Sex				0.817
Male	29 (25.9)	14 (48.0)	15 (52.0)	
Female	83 (74.1)	38 (46.0)	45 (54.0)	
FBG (mmol/l)	6.53±1.78	6.64±1.72	6.43±1.84	0.527
FBG group				
Normal	71 (63.4)	31 (59.6)	40 (66.7)	0.440
High	41 (36.6)	21 (40.4)	20 (33.3)	
Weight (Kg)	69.63±11.01	68.19±11.02	70.87±10.95	0.202
BMI (Kg/m^2)	26.15±4.54	25.88±4.86	26.38±4.28	0.567
BMI group				0.902
Underweight	3 (2.7)	2 (3.8)	1 (1.7)	
Normal	43 (38.4)	20 (38.5)	23 (38.3)	
Overweight	45 (40.2)	20 (38.5)	25 (41.7)	
Obese	21 (18.8)	10 (19.2)	11 (18.3)	

Table 3. Multinomial logistic regression of factors associated with *H. pylori* infection among persons with type 2 diabetes

	OR (95% CI)	P-value
Age group (years)		
40-50	0.750 (0.044-12.816)	0.843
51-60	0.800 (0.046-13.812)	0.878
61-70	1.077 (0.061-19.046)	0.960
71-80	1.500 (0.055-40.633)	0.810
81-90	Reference	-
Sex		
Male	Reference	-
Female	0.905 (0.388-2.110)	0.817
BMI group		
Underweight	Reference	-
Normal	0.435 (0.037-5.161)	0.509
Overweight	0.400 (0.034-4.736)	0.467
Obese	0.455 (0.036-5.813)	0.544
Glycaemic status		
Normal	Reference	-
High	1.355 (0.626-2.930)	0.440

4. DISCUSSION

This case-control study determined the prevalence of *H. pylori* infection in T2DM in the Upper West region, Ghana. The prevalence of *H. pylori* infection in T2DM and non-diabetics were 46% and 39% respectively. This non-significant difference in prevalence among T2DM and non-diabetic population recorded in the present study agrees with similar studies conducted in Hong Kong (42.9% vs. 56.3%, p>0.05) and in Greece (37.3% vs. 35.2%) [12,13]. However, a similar case-control study in Abakaliki, South-Eastern Nigeria recorded lower prevalence (18% vs. 13%, p= 0.52) [15]. Considering that the study design and *H. pylori* testing methods were similar, the variance in the prevalence recorded in this study compared to the Oluyemi et al. [15] study could be due to the differences in population demographics and probably the immune status of the participants.

In another study in rural Rajasthan, India, a higher prevalence was recorded among T2DM patients and non-diabetic controls (88% vs. 67% respectively; p<0.05) [5]. That study recruited a relatively smaller number of participants (33 T2DM and 39 controls) and also employed serological means to detect anti-*H. pylori* – IgG. Although differences in geographical distribution of *H. pylori* infection could be a factor in explaining this discrepancy, the obvious limitations associated with serological approaches for detecting *H. pylori* infection is well documented in literature [16-18].

Our findings are however at variance with other previous studies. In a similar case-control study in India, Devrajani et al. [11] demonstrated that T2DM patients had higher risk of developing *H. pylori* infection [11]. Other studies conducted in Turkey and India also found significant associations between *H. pylori* infection and T2DM [19-21]. There may be some underlying molecular, genetic, demographic and/or socio-economic factors underpinning these diverse findings in different geographic areas. Future studies that employ animal models as well as genomic assays in human subjects may be fundamental in explaining the molecular basis of these apparent discrepant findings concerning any plausible association between T2DM and *H. pylori* infection.

Obesity is a known risk factor for T2DM [22]. Not surprisingly, a significantly higher proportion of the cases in this study were obese. On average, the BMI of cases belonged to the pre-obese category (25.0 – 29.9) compared to controls (26.15 vs 24.38; p=0.001). This findings agrees with previously published data [9,22,23]. However, among the T2DM patients, there was no significant difference in the BMIs of T2DM patients who were positive for *H. pylori* and those who were negative for *H. pylori* infection. As T2DM is mostly acquired through lifestyle choices as one ages, the lack of association between BMI and *H. pylori* infection may not be surprising considering that *H. pylori* is known to be mostly acquired in childhood through fecal-oral or oral-oral route [24]. Moreover, a multivariate logistic regression analysis that interrogated the association of *H. pylori* infection with factors such as age, gender, BMI, and glycemic status in T2DM patients found none of these as significant risk factors.

The association between *H. pylori* infection and gender is debated in the literature. Some previous studies have suggested that gender is a predisposing factor to acquiring *H. pylori* infection, with males being more susceptible than females [25,26]. Additionally, meta-analyses reported a male predominance in adults but not in children [26-28]. On the other hand some studies rather suggest female preponderance [29]. In contrast to these two schools of thought, our study demonstrates comparable proportions of males and females are affected by *H. pylori* infection (48% males vs 46% males; p=0.817). This finding agrees with others who found no association between gender and *H. pylori* infection [30,31]. Clearly, the relationship between gender and *H. pylori* infection is not a simple linear one and must be approached taking into consideration the environmental and/or genetic basis of the population under study.

Although our study employed the *H. pylori* stool antigen detection system which is non-invasive and allows for large numbers of samples to be screened, its sensitivity is less than the accepted gold standard which is histology [32,33]. Thus, it is possible that some participants who tested negative might as well have been positive. Additionally, our study did not interrogate the virulence factors associated with the *H. pylori* strains detected in this study. This could have enriched the epidemiological impact of this study as these virulence factors have been linked to the incidence of gastric cancer [34].

5. CONCLUSION

The prevalence rate of *H. pylori* infection in type 2 diabetes mellitus patients and healthy non-diabetics were 46% and 39% respectively. Hyperglycemia, BMI and gender were not shown to be *H. pylori*-related risk factors in type 2 diabetes patients. We recommend further studies that would address the molecular epidemiologic basis of *H. pylori* infection in the study population.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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