www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 3(11): 68-71

www.thepharmajournal.com
Received: 09-12-2014
Accepted: 19-12-2014

Haala M. Gabra
Department of laboratory, Fedail Hospital, Khartoum, State ZIP: 11111, Sudan.

Mohammed E. Tageldin
Department of laboratory, Elfatih Hospital, Khartoum State, ZIP: 11111, Sudan.

Elmutuz H. Elssaig
Department of medical laboratory sciences, Alzaim Alazhari University. Khartoum, State ZIP: 11111, Sudan.

Hani K. Fahmi
Department of medical laboratory sciences, Alzaim Alazhari University, Khartoum, State ZIP: 11111, Sudan.

Nour M. Abdelateif
Department of medical laboratory sciences, Alneelein University, Khartoum, State ZIP: 11111, Sudan.

Sharif A. Elgoul
Department of laboratory, Fedail Hospital, Khartoum, State ZIP: 11111, Sudan.

Correspondence:
Haala M. Gabra
Department of laboratory, Fedail Hospital, Khartoum, State ZIP: 11111, Sudan.

Effect of *Helicobacter pylori* infection on insulin resistance in Asymptomatic Sudanese Patients

Haala M. Gabra, Mohammed E. Tageldin, Elmutuz H. Elssaig, Hani K. Fahmi, Nour M. Abdelateif, Sharif A. Elgoul

Abstract
Introduction: *Helicobacter pylori* is associated with severe gastrointestinal pathologies. Moreover, it may cause an extra gastrointestinal disease such as atherosclerosis, insulin resistance, diabetes mellitus and some autoimmune diseases.
Aim To investigate the relation between *Helicobacter pylori* infection and Insulin Resistance in Sudanese healthily subjects.
Methods: In a case control study conducted in the period from May 2013 to May 2014, a total of a hundred and twenty patients were enrolled in this study; these patients were divided into two groups by matching age, sex. Group (A) patients were *Helicobacter pylori* positive. Group (B) subjects were *Helicobacter pylori* negative. The homeostasis model assessment (HOMA) was used to assess insulin resistance.
Results: In the present study, there was a statistically significant association between *Helicobacter pylori* positive patients (80/120; 66.67%) and insulin resistance (IR) compared to *Helicobacter pylori* negative patients (40/120; 33.33%) (P value <0.001). The mean value of IR was 3.21 ± 1.26, 2.05 ± 1.20 respectively, for *Helicobacter pylori* positive and *Helicobacter pylori* negative patients.
There was no statistical significant difference between Helicobacter pylori positive and *Helicobacter Pylori* negative patients as regard to other investigations (P value >0.05).
Conclusion: The findings confirm the existence of an association between infection with *Helicobacter pylori* and insulin resistance.

Keywords: Helicobacter pylori; Insulin resistance; gastrointestinal disorders; diabetes Mellitus.

1. Introduction
Helicobacter pylori (*H. pylori*) is a gram negative, noninvasive, non-spore forming, spiral shaped bacteria. *H. pylori* infection is one of the most prevalent chronic infections worldwide [1]. *H. pylori* was cultivated first from human gastric mucosa in 1982 and has since emerged as one of the most common chronic bacterial infections in the world, affecting about 40% and 80% of the general population in developed and developing countries, respectively [2]. Infection with this bacterium induces gastric inflammation in most subjects and has been associated with an increased production of cytokines [3]. Also, gastric parietal cell auto-antibodies have been identified more frequently in diabetic patients with concomitant H pylori infection compared with uninfected patients [4]. Moreover, it is associated with non-gastrointestinal tract conditions such as atherosclerosis, insulin resistance, diabetes mellitus and some autoimmune diseases [5, 6, 7].
The Insulin Resistance (IR) is a pathologic state in which normal insulin concentrations produce a subnormal response in the peripheral tissues, the association of *H. pylori* infection with insulin resistance has been reported [8, 9].
H. pylori infection increases insulin resistance (IR) since it causes a chronic inflammation and affects gastrointestinal hormones function in insulin regulation [10]. The prevalence of IR syndrome, and its component is rapidly increasing worldwide as a consequence of the ongoing obesity epidemic that significantly increases with age [11]. IR syndrome is included in degenerative conditions that have an increasingly high impact on aged population and their association with *H. pylori* infection, which affect more than half of the world population has only been addressed [12]. The present study was, therefore, to evaluate the relationship between the seropositivity for *H. pylori* and the HOMA-IR in Sudanese healthy subjects.

2. Material and methods

2.1. Subjects

The study was conducted from May 2013 to May 2014 at Fedail Hospital and Khartoum Teaching Hospital. A total of a hundred and twenty subjects were enrolled in this study. The participants were divided into two groups according to the presence of H pylori infection. Eighty Patients were H pylori positive and forty patients were H pylori negative.

The local ethics committee approved the study. Before participation, volunteers were fully informed of the nature and purpose of the study and written consent was obtained from each.

2.2. Samples

Blood samples were obtained following an overnight fasting, samples were withdrawn from a cubital vein into blood tubes, then the serum was separated from the cells by centrifugation at 3000 r/min for 10 min and immediately stored on ice at 4 ℃.

2.3. Diagnosis of *H. pylori* infection

H. pylori infection was determined using a serologic test with a reported sensitivity and specificity of 99.9% and 97%, respectively. 2 mL of blood was collected, and sera were separated for the determination of H pylori-specific immunoglobulin G antibodies using chromatographic immunoassay (Bio Trancer ^{TM}; *H. pylori* Rapid Card). Using control sera, the specimens were tested in duplicate according to the manufacturer's specifications.

2.4. Exclusion criteria

Exclusion criteria included recent gastrointestinal by-pass surgery, pregnancy, and usage of supplemental vitamins several months prior to the study, *H. pylori* eradication therapy, and H2 receptor antagonist or proton pump inhibitor within the last 4 weeks or nonsteroidal anti-inflammatory drugs (NSAIDs) within the last 2 weeks prior to study, existence of diabetes mellitus, hyperlipidemia, hypertension, coronary artery disease, rheumatoid arthritis, renal disease, smoking, cancer, systemic or local infection.

2.5. Biochemical measurements

2.5.1. Measurement of glucose, lipid profile and Insulin

Serum glucose concentration was measured by enzymatic glucose oxidase-peroxidase [GOD-POD] using commercial kits in an auto-analyser (C311 -Roche).

Triglyceride, total cholesterol, and high-density lipoprotein cholesterol (HDL-cholesterol) concentrations were measured by enzymatic methods on C311 –Roche). Levels of low-density lipoprotein cholesterol (LDL-cholesterol) were calculated by Friedewald formula.

LDL-cholesterol = [total cholesterol-(TG/5)-HDL-cholesterol].

Serum insulin levels were measured using an automated chemiluminescence autoanalyzer (Cobas e 411 Roche®).

2.5.2. Insulin resistance

The insulin resistance index was calculated on the basis of fasting values for glycaemia and insulinemia, according to the homeostasis model assessment (HOMA) [13]:

Insulin resistance (HOMA-IR) = fasting insulinaemia (μU/mL) × fasting glycaemia (mmol/L)/22.5.

2.6. Statistical evaluation

Data were expressed as mean ± standard deviation (SD). The means were compared using Independent sample t. test and a p-value ≤ 0.05 was considered as statistically significant.

3. Results

In the present study the patients with *H. pylori* positive was 66.7% and patients with *H. pylori* negative was 33.3%. The overall mean age was 51.63 ± 10.07 years. The mean of age was 50.29 ± 10.14 and 53.52 ± 9.75 years old in female and male patients respectively. Demographic characteristic of the subjects are shown in Table 1. There were no statistically significant differences between the two groups with regard to age and gender (P> 0.05) (Table 1). As shown in Table 1.

Table 1: Demographic data for *H. pylori* positive and negative group.

	***H. pylori* [Positive][n=80] Mean±SD**	***H. pylori* [negative][n=40] Mean±SD**	**P value**
Age [Years]	51.09 ± 10.0	50.29 ± 10.14	0.08
Sex [Female / Male]	42/38	28/12	NA

NA: not Significant, *P* value ≤ 0.05 considered significance

There was no statistical significant difference between *H. pylori* positive group and negative group for the investigations as regard the Hb, PCV, Platelet, Creatinine and lipid profile. P value >0.05.

Table 2: Laboratory findings by Mean ± SD for the studied groups (Hb, PCV, Platelet, serum creatinine and lipid profile.

	***H. pylori* [Positive] [n= 80] Mean±SD**	***H. pylori* [negative] [n= 40] Mean±SD**	**P value**
Hb [g/dl]	13.29 ± 1.5	13.08 ± 1.4	0.46
PCV [%]	40.66 ± 4.32	39.48 ± 4.13	0.33
Platelet [c/mm^3]	259.69 ± 53.14	267.07 ± 62.43	0.50
S. Creatinine [mg/dl]	0.80 ± 0.18	0.92 ± 0.25	0.41
S. Cholesterol [mg/dl]	170.95 ± 15.75	169.77 ± 14.67	0.69
S. Triglyceride [mg/dl]	127.56 ± 25.80	119.72 ± 30.19	0.14
S. HDL-C [mg/dl]	46.44 ± 8.20	44.08 ± 8.14	0.13
S. LDL-C [mg/dl]	99.80 ± 16.77	101.18 ± 17.80	0.67

P value ≤ 0.05 considered significance

There was a statistical significant association between the groups as regard to IR (3.21±1.26 ng/ml), (2.05±1.20 ng/ml) respectively, p value <0.001 (Table 3)

Table 3: Laboratory findings by Mean ± SD for the studied groups (Fasting Blood Glucose, Insulin and insulin resistance

	***H. pylori* [Positive] [n= 80] Mean±SD**	***H. pylori* [negative] [n= 40] Mean±SD**	**P value**
Fasting Blood Glucose [mmol/l]	5.56 ± 0.71	5.57 ± 0.46	0.54
Insulin [IU/ml]	12.87 ± 4.52	8.38 ± 4.46	0.00*
HOMA- IR	3.21 ± 1.26	2.05 ± 1.20	0.00*

P value ≤ 0.05 considered significance

4. Discussion

Information about the association of insulin resistance with H pylori infection is scarcity available [14, 15]. Aydemir *et al* [8] reported that insulin resistance is significantly related with H pylori infection. However, Park *et al* [15] reported that no improvement in the metabolic parameters including insulin resistance could be observed following eradication of H pylori. The results of this study are in consistent with those of Aydemir *et al.* [14], as this study did not investigate the effect of *H. pylori* eradication on insulin resistance, we were not able to compare these results with those of Park *et al* [15].

HOMA -IR in *H. pylori* positive cases were 3.21 ± 1.26 while it was 2.05 ± 1.20 in *H. pylori* negative cases with a high statistical significant difference between the two groups (P value <0.001)this is consistent with Gen R. *et al*, Ozdem S. *et al* and Gunji T. *et al.* [12, 16, 17]. The explanation for that could be chronic inflammation and an alteration in counter regulatory hormones are deemed responsible for IR pathogenesis. Although the pathogenic link between *H. pylori* infection and IR remains elusive, this infection may influence the pathophysiology of IR [18]. A significant association between increased oxidative stress and IR was studied with *H. pylori* infection. It has been reported that *H. pylori* infection is associated with increased tissue and systemic oxidative stress that were proposed as the main cause for the development of IR, B cell dysfunction, impaired glucose tolerance and type 2 diabetes mellitus [19] However, others reported that decreased somatostatin and increased gastrin hormone levels in patients with *H. pylori* infection may have a role in the development of IR as somatostatin regulates pancreatic insulin secretion and has an inhibitory effect on insulin release [8, 20]. Moreover, other researchers reported that chronic inflammation promotes platelets activation and platelets – leucocyte aggregations, which were involved in IR [21]. In contrary, others stated that there is no association between *H. pylori* infection and IR [16, 22]. The explanations of this difference were due to selection of diabetic and dyslipidemic patients in the study. In addition, the diagnosis of *H. pylori* infection was done by serum *H. pylori* immunoglobulin G antibody and not by histopathological examination of antral biopsies, which is considered as the gold standard diagnostic tool.

5. Conclusion

There was a strong association between *H. pylori* positive and insulin resistant.

Further studies on a large number of patients to prove the association between *H. pylori* and IR and to explore the benefit of *H. pylori* eradication in reduction of IR and vice versa.

6. Acknowledgment

The authors would like to thank all participants who cooperated during the study and Dr. Osman Hassan Musa for his excellent assistance and for allowing the performance of the test in his laboratory.

7. Conflict of interest

No potential conflicts of interest relevant to this article were reported.

8. References

1. Cave DR. Transmission and epidemiology of Helicobacter pylori. Am J Med 1996; 100:12-17.
2. Blaser MJ. Helicobacter pylori: its role in disease. Clin Infect Dis 1992; 15:386–393.
3. Genta RM. The immunobiology of Helicobacter pylori gastritis. Semin Gastroenterol Dis 1997; 8:2–11.
4. Barrio R, Roldan MB, Alonso M, Canton R, Camarero C. Helicobacter pylori infection with parietal cell antibodies in children and adolescents with insulin dependent diabetes mellitus. J Pediatr Endocrinol Metab 1997; 10:511–516.
5. Naito Y, Yoshikawa T. Molecular and cellular mechanisms involved in Helicobacter pylori-induced inflammation and oxidative stress. Free Radic Biol Med 2002; 33:323-336.
6. Leontiadis GI, Sharma VK, Howden CW. Non-gastrointestinal tract associations of Helicobacter pylori infection. Arch Intern Med 1999; 159:925-940.
7. Gasbarrini A, Ojetti V, Pitocco D, De Luca A, Franceschi F, Candelli M *et al.* Helicobacter pylori infection in patients affected by insulin dependent diabetes mellitus. Eur J Gastroenterol Hepatol 1998; 10:469-472.
8. Aydemir S, Bayraktaroglu T, Sert M, Sokmen C, Atmaca H, Mungan G, Gun BD, Borazan A, Ustundag Y. The effect of Helicobacter pylori on insulin resistance. Dig Dis Sci 2005; 50:2090-2093.
9. Gillum RF. Infection with Helicobacter pylori, coronary heart disease, cardiovascular risk factors, and systemic inflammation: the Third National Health and Nutrition Examination Survey. J Natl Med Assoc 2004; 96:1470-1476.
10. Aydemir S, Bayraktaroglu T, Sert M *et al.* The effect of Helicobacter pylori on insulin resistance. Dig Dis Sci 2005; 50:2090-3.
11. Razzouk L, Muntner P. Ethnic, gender and age – related differences in patients with the metabolic syndrome. Curr Hypertens Rep 2009; 11:127–32.
12. Gen R, Demir M, Atasseven H. Effect of H-pylori eradication on insulin resistance, serum lipids and low grade inflammation. South Med J 2010; 103:190-6.
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985; 28:412-419.
14. Mungan G, Gun BD, Borazan A, Ustundag Y. The effect of Helicobacter pylori on insulin resistance. Dig Dis Sci 2005; 50:2090-2093.
15. Park SH, Jeon WK, Kim SH, Kim HJ, Park DI, Cho YK *et al.* Helicobacter pylori eradication has no effect on

metabolic and inflammatory parameters. J Natl Med Assoc 2005; 97:508-513.
16. Ozdem S, Akcam M, Yilmaz A, Artan R. Insulin resistance in children with Helicobacter pylori infection. J Endocrinol Invest 2007; 30:236-40.
17. Gunji T, Matsuhashi N, Sato H *et al.* Helicobacter pylori infection significantly increases insulin resistance in the asymptomatic Japanese population. Helicobacter 2009; 14:144-50.
18. Polyzos SA, Kountouras J, Zavos C. Nonalcoholic fatty liver disease: the pathogenic roles of insulin resistance and adipocytokines. Curr Mol Med 2009; 72:299-314.
19. Aslan M, Horoz M, Nazligul Y *et al.* Insulin resistance in H pylori infection and its association with oxidative stress. World J Gastroenterol 2006; 12:6865-8.
20. Basso D, Plebani M, Kusters JG. Pathogenesis of Helicobacter pylori infection. Helicobacter 2010; 15:14-20.
21. Hsieh MJ, Chen CC, Lee TH *et al.* Metabolic syndrome and homocysteine level as predictors of the severity of coronary artery disease in patients with carotid stenosis. Am J Med Sci 2009; 338:447-52.
22. Gao XY, Kuang HY, Liu XM *et al.* Circulating ghrelin/obestatin ratio in subjects with Helicobacter pylori infection. Nutrition 2009; 25:506-11.

9. Author contributor

H.M.G. and M.H.E. conceived the specific aims of the article, designed, collected data, and prepared the data for analysis. H.K.F., M.E.T. and N.M.A. conducted the analysis and wrote the initial draft. S.A.E and M.E.T. contributed to the interpretation of the results. All authors contributed to the final draft of the manuscript. H.M.G. is guarantor of this work, and takes responsibility for the integrity of the data and the accuracy of the data analysis.