Section: General Medicine

Research

ASSOCIATION OF THE IMPACT OF H. PYLORI INFECTION ON DIABETIC AND LIPID PROFILE IN PRE-DIABETIC PATIENTS

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Abstract

Background: Helicobacter pylori (H. pylori) is one of the most prevalent human bacterial infections, and infection with H. pylori causes various stomach diseases, including simple gastritis, peptic ulcers, and gastric cancer. In addition, globally, type 2 diabetes mellitus (T2DM) is increasing and is a severe public health concern. Consequently, the objective of the present investigation was to evaluate the impact of H. pylori infection on the Diabetic and Lipid profiles of pre-Diabetic patients. **Materials and Methods:** An observational cross-sectional investigation was performed on pre-diabetic patients (HbA1c; 5.7-6.4%) from October 2021 to August 2022. The study was carried out at a single centre in a site tertiary care centre in East Delhi. The study comprised 120 patients, categorised into two groups depending on whether their H. pylori test findings were positive (group A) or negative (group B). **Result:** One hundred two patients (mean age 46.8 years) out of 120 completed the present study. There was 62 (60.78%) male and 40 (39.21%) female. 55 (53.92%) patients were positive for H. Pylori colonisation. Compared to the non-infected group, the HbA1c levels of H. pylori-infected patients (group A) increased significantly faster (p=0.042) (group B). In addition, group A exhibited statistically-significant increases in LDL cholesterol (p=0.038) and decreases in HDL cholesterol (p=0.02) compared to group B. **Conclusion:** An increase in HbA1c levels is associated with H. pylori infection in pre-diabetics. Additionally, it is linked to a rise in LDL cholesterol and a fall in HDL cholesterol.

INTRODUCTION

H. pylori is a common spiral gram-negative bacterium found in the stomach. More than fifty percent of the world's population is infected with H. pylori, making it one of the most widespread chronic diseases in the world.[1] H. pylori is now recognised to be responsible for most instances of peptic ulcer disease.[2] In addition, other studies have shown that it is associated with other severe gastro-intestinal problems, such as chronic gastritis, gastric adenocarcinoma, and MALT lymphoma, which are major worldwide public health issues. In addition to its influence on gastro-intestinal disorders, H. pylori may have a role in developing non-gastrointestinal ailments, such as cardiovascular disease and metabolic syndrome, notably diabetes.[3] Diabetes is the most widespread metabolic disease in the world and is responsible for around 4 million fatalities each year. In 2010, the prevalence of diabetes globally was 4.6%, or 285 million people; this number climbed to 371 million in 2012 and is anticipated to reach 545 million by 2030.[4] The pre-diabetic state is a phase of impaired glucose tolerance characterised as impaired fasting glucose levels between 100 mg/dL and 125 mg/dL and HbA1c levels between 5.7% and 6.4% in 75 g oral glucose tolerance test findings.[5] Pre-diabetes has pathophysiological similarities with Type II Diabetes, with insulin resistance and early beta cell loss as its fundamental defects. In pre-diabetes, the size of insulin's strong pulses and quick release are lessened.[6] In pre-diabetes, the glycemic excursions are normally below normal, and the second phase of insulin production is delayed and protracted. Recent research has shown that H. pylori colonisation is linked to an increased risk of developing diabetes mellitus.[7,8]

Dyslipidemia is a complicated condition that significantly contributes to unfavourable cardiovascular outcomes.[9] Myocardial infarction and stroke incidence correlate with high LDL and low HDL levels. In addition, dyslipidemia contributes significantly to the macrovascular effects of diabetes.[10] Stronger evidence implicates H. pylori infection with the onset, progression, or

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persistence of atherosclerosis and coronary heart disease. In order to stop the development of dyslipidemia and its negative consequences, it may be helpful to investigate the involvement of curable causes of dyslipidemia, such as H. pylori.[11,12]
The current study was carried out to examine the possible association of H. pylori infection on diabetes and lipid profile in pre-diabetic patients.

MATERIALS AND METHODS

The present study was carried out at a single centre at a site Tertiary care centre in North Delhi, India, from October 2021 to August 2022. Participants were recruited from the patients attending the outpatient department of the onsite tertiary care centre during the study. Before the start of the study, approval from the institution's ethics committee and patients' signed consent was obtained.
All study participants were instructed to have routine follow-ups and report any changes to their lifestyle, use of drugs, or the emergence of any co-morbid diseases. One hundred twenty individuals were included in the research; however, 12 acquired co-morbid diseases (DM, hypertension, and hyperlipidemia) and were started on medicines during the study period, excluding them from the analysis. In addition, two patients did not return for the follow-up, and four received lifestyle adjustments, such as food management, yoga treatment, and physical activity, and were thus omitted from the research. A total of 102 patients finally finished the research.

Inclusion Criteria
Patients with HbA1c values between 5.7% and 6.2% and glucose levels between 100 and 125 mg/dL 5. Patients with high borderline cholesterol levels (as determined by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP)) were included in the research13.

Exclusion Criteria
Patients who have previously used antacids, antibiotics, proton pump inhibitors, or H2 receptor blockers (within the past four weeks). Patients diagnosed with diabetes, hyperlipidaemia, or hypertension. Patients with prior or current symptoms of gastro-intestinal bleeding, jaundice, or post-gastric surgery, as well as pregnant or breastfeeding women, should be closely monitored.
All trial participants were screened for pre-diabetes, lipid profile, and H. pylori infection. Glycosylated haemoglobin (HbA1c) was used to assess the diabetic profile at the beginning of the trial, after six months, and after the 12-month study period with high-performance liquid chromatography.[14] LDL was evaluated using the Friedewald formula, while HDL was measured directly using the precipitation technique.[15,16] H. pylori infection was identified using an H. pylori IgG Enzyme-Linked Immunosorbent Assay (ELISA) test kit to detect IgG antibodies.[17]
55 of the 102 patients in Group A tested positive for H. pylori infection. The remaining 47 individuals comprised Group B.

Statistical Analysis
Data was compiled and organised in Microsoft Excel spreadsheets, and SSPE Software, version 22, was used to analyse the data. The results were reported as Mean± SD. Statistically sound techniques were used to examine the data. Using a student t-test, the various studied parameters were compared between groups. Statistical significance was defined as 0.05 or lower P-values.

RESULTS

Of 120 subjects total of 102 patients completed the study, of which 62 (60.78%) were male and 40 (39.21%) were female, with a mean age of 46.8 years. A total of 55 (53.92%) patients of all participating subjects were found to be positive for H. Pylori infection and categorised as Group A. In comparison, 47 (46.07%) patients were observed without H. Pylori infections were classified as Group B. The mean age of Group A (45.8 years) was lower than that of Group B (50.2 years) [Table 1].
Group A: H. pylori-positive patients, consisted of 34 men (61.81%) and 21 females (38.18%), while Group B: H. pylori-negative patients, consisting of 27 males (57.44%) and 20 females (42.55%).
At the beginning of the study, there was no significant difference between Group A and Group B in terms of mean HbA1c, mean LDL, and mean HDL (p-value > 0.05) [Table 2].
H. pylori infection may play a role in the diabetic profile of pre-diabetic patients. It may speed up the progression of pre-diabetes to diabetes. A comparison of the HbA1c readings in Group A at the start and end of the trial revealed a significant difference with a p-value of 0.042. In Group B, the difference in HbA1c values was not statistically significant. Group A, LDL and HDL values before and after the research likewise showed statistically-significant differences (p-value > 0.05) [Table 4].

Table 1: Gender distribution among both group

Gender	Group A, n (%)	Group B, n (%)
Male	34 (61.81%)	27 (57.44%)
Female	21 (38.18%)	20 (42.55%)
Total n (%)	55 (100%)	47 (100%)

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Table 2: Age distribution of patients in both groups

Age(Years)	Group A Mean± SD	Group B Mean± SD	Total Mean± SD	p-value
Male	45.08±4.5	51.69±6.7	48.39±6.6	0.14
Female	46.54±3.8	48.87±5.8	47.71±5.9	0.22
Mean	45.8 ±5.9	50.2±7.1	48.05±7.2	0.41

Table 3: Group A and Group B mean HbA1c, LDL, and HDL values at the start of the trial (0 months), after 6 months, and after 12 months.

Parameters	Group A	Group B	p-value
Hb1AC			
Baseline (%)	7.23±0.14	7.09±0.22	0.72
6 Months (%)	7.68±0.12	7.25±0.19	0.058
12 Months (%)	7.85±0.38	7.28±0.33	0.42
LDL			
Baseline (%)	146.6±8.1	144.2±7.1	0.52
6 Months (%)	147.3±7.9	146.5±6.8	0.56
12 Months (%)	148.2±7.2	146.8±6.4	0.48
HDL			
Baseline (%)	48.1±5.9	43.3±4.4	0.25
6 Months (%)	46.0±4.8	44.0±4.3	0.28
12 Months (%)	49.3±5.1	46.1±3.7	0.31

Table 4: Comparison of Group A and Group B HbA1c, LDL, and HDL values during the 12-month study

Parameters after 12 Months	Group A		Group B	
	Mean difference ±SD	p-Value	Mean difference ±SD	p-Value
Hb1Ac (%)	0.122± 0.318	0.045	0.08±0.31	0.067
LDL (mg/dL)	2.65±6.87	0.036	1.82± 6.1	0.06
HDL (mg/dL)	-1.67±3.15	0.021	-0.52±2.01	0.11

DISCUSSION

Since Barry J. Marshall and Robin Warren first identified Helicobacter pylori in 1984, most studies have focused on how the bacteria affect the gastro-intestinal system. They concluded that it might be a substantial etiological factor of these diseases after discovering that the bacterium was present in virtually all people with active chronic gastritis, duodenal ulcer, or stomach ulcer.[18] In addition, H. pylori may have extra-gastric functions, and there is evidence that infection with the bacteria increases the likelihood of developing Type-2 diabetes. However, other studies have shown no link between the two conditions. Lack of information makes it impossible to say whether immune-compromised diabetics are more prone to the disease or if infection leads to diabetes mellitus.[19]

Diabetes-related cellular and humoral immunity impairment may enhance a person's vulnerability to H. pylori infection.[20] Diabetes is also associated with decreased gastro-intestinal motility and acid production, facilitating pathogen colonisation and infection.[19] In order to prevent confounding variables associated with diabetes, the current research was done on pre-diabetic individuals to examine the connection between H. pylori infection and the development of pre-diabetes.

The current investigation revealed a substantial effect of H. pylori on HbA1c, confirming the organism's function in establishing type 1 diabetes. This resembles the research undertaken by Polyzos et al.[21] In a Japanese study with 1 077 asymptomatic patients, Gunji et al. found that H. pylori independently leads to insulin resistance, which validates the findings of the current investigation.[22] However, Park et al. found that eradicating H. pylori had no impact on insulin resistance.[23]

A study by Oshima et al. suggests that H. pylori may have a role in the development of type 2 diabetes by promoting the production of pro-inflammatory cytokines such as IL-6, CRP, and TNF-α, which causes insulin resistance24. The colonisation of the stomach's submucosa and mucosa by the organism results in the invasion of acute and chronic inflammatory cells, including neutrophils and monocytes, as well as the production of many pro-inflammatory cytokines that help diabetes mellitus develop. Few studies, nonetheless, dispute the contribution of pro-inflammatory cytokines to the development of insulin resistance.[19] In socioeconomically comparable American men, Ridker et al. observed no statistically significant link between H. pylori seropositivity and cytokine secretion.[25]

Gastritis brought on by H. pylori interferes with the release of hormones such as ghrelin, leptin, gastrin, and somatostatin. These hormones support the maintenance of insulin sensitivity and glucose homeostasis. H. pylori also reduces the production of ghrelin, which results in insulin resistance.[26] Additionally, it promotes the release of leptin, which is directly related to insulin resistance. Greater baseline amounts of gastrin, known to play a part in food-induced insulin release, were seen in H. pylori-infected patients.[27] Somatostatin, a hormone that regulates pancreatic insulin synthesis and regulates insulin release, is reduced in H. pylori-positive

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people. Brown and Dunmore identified conflicting evidence pointing to a role for leptin in avoiding the loss of pancreatic cells and, consequently, the onset of diabetes.[28]

H. pylori is associated with many extra-gastrointestinal symptoms and may have a role in developing several cardiovascular risk factors. In Type 2 diabetes, H. pylori infection is associated with dyslipidemia and higher levels of oxidised LDL, according to a study by Mukhtar et al.[29] The current investigation shows that H. pylori colonisation influences the lipid profile of pre-diabetic individuals. It raises LDL levels while lowering HDL levels. The findings of this study are supported by research by Chimienti et al. and Takashima et al. that suggests a link between H. pylori and dyslipidemia.[30,31] However, the results of this study conflict with the findings of the Ando et al. study, which showed that lipid profiles remained unchanged even after H. pylori was eradicated.[32] Since both conditions include the generation of ghrelin and pro-inflammatory cytokines by the stomach mucosa, the severity of gastritis and gastric mucosal atrophy may affect lipid metabolisms.[33]

Pro-inflammatory cytokines such as IL-6, interferon, and TNF are released due to chronic H. pylori infection. These pro-inflammatory cytokines act on fatty tissues, setting off a cascade of circumstances that activate lipoprotein lipase.[30] These lipases regulate lipolysis by acting on adipose tissue. In addition, they stimulate the production of hepatic fatty acids. The results of the Kim et al. study showed that individuals with H. pylori infection had higher total cholesterol, LDL cholesterol, and lower HDL cholesterol, despite other potentially confounding factors like age, sex, socioeconomic status, Body Mass Index (BMI), smoking status, alcohol consumption, and amount of exercise.[34]

Limitations of the study

1. The research may not accurately reflect the total population since it only included patients who attended the OPD and were willing to participate.
2. Since diabetes and dyslipidemia are chronic conditions, the follow-up duration was insufficient to draw specific results.
3. In addition, the severity of gastritis and mucosal atrophy, which may be associated with the rate of diabetes development and lipid profile, were not evaluated.

CONCLUSION

According to the current study, pre-diabetic individuals with H. pylori infection had statistically significant increases in HbA1C levels. Furthermore, compared to the control group, H. pylori colonisation was also associated with increased LDL cholesterol and reduced HDL cholesterol levels.

H. pylori infection is associated with a statistically significant increase in HbA1c levels in pre-diabetic individuals. It is also associated with higher LDL cholesterol and lower levels of HDL cholesterol when compared to the control group. The results of our study conclude that H. pylori may be very important in the emergence and development of DM. Raising the levels of LDL cholesterol could potentially contribute to the development of dyslipidemia. But to prove the connection and correlation between H. pylori and diabetes and lipid profile, bigger Randomised cross-sectional studies are required.

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