Original Article

Helicobacter pylori infection prevalence: Is it different in diabetics and nondiabetics?

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ABSTRACT

Background: *Helicobacter pylori* (HP) infection plays a significant role in the development of gastrointestinal complications and has a significant role in systemic inflammation. It has some extragastrointestinal manifestations like endocrine diseases. In this study, we aimed to compare the prevalence of HP infection in diabetic and nondiabetic individuals. **Materials and Methods:** In this cross-sectional study, 218 nondiabetic and 211 diabetic patients referring to Shahid Beheshti Hospital of Qom between March 2013 and 2014 were studied. The patients were divided into two HP^+ and HP^- groups based on serological immunoglobulin G antibody against HP and the association between diabetes, and HP infection was evaluated. Data were analyzed using independent *t*-tests, Chi-square, Fisher's exact and Mann–Whitney tests. **Results:** The prevalence of HP seropositive was 65.9% versus 50.5% in diabetic and nondiabetics, respectively, and the difference was statistically significant ($P = 0.001$). **Conclusions:** This study showed a higher prevalence of HP infection in diabetic patients.

Key words: Diabetic, *Helicobacter pylori,* nondiabetic, prevalence

Introduction

Helicobacter pylori (HP) infection is one of the most common bacterial infections round the world, which is more prevalent in developing countries.[1] Initially, it was proposed that this organism causes local inflammation in the gastric epithelium and various and severe gastric diseases such as gastritis, gastric ulcer, adenocarcinoma and lymphoma but it is now clear that it is associated with many extragastrointestinal manifestations.[2] HP infection causes polymorphonuclear infiltration in gastric mucosa, which is gradually replaced by mononuclear cellular infiltration.[3] These mononuclear cells in the gastric mucosa lead to local production and release of inflammatory cytokines.[4] These cytokines, which include interleukin-6 (IL-6), C-reactive protein and tumor necrosis factor alpha (TNF-α), will cause systemic inflammation. It seems that some extragastrointestinal manifestations of HP occur as a result of this systemic inflammation, which is mentioned in some studies[5] and includes coronary artery disease, sideroblastic anemia, idiopathic thrombocytopenic purpura, some neurological diseases such as Alzheimer and Parkinson's diseases and biliary system diseases.[1,6-11]

Recent studies have proposed the association between this infection and certain endocrine diseases such as autoimmune thyroid disease, hyperparathyroidism and diabetes mellitus.[12] It has also been suggested that HP infection may be more prevalent among people with diabetes.[3] This association was first introduced in 1989 and had been proposed that the prevalence of HP is significantly higher among diabetics (62% vs. 21%).[13] In contrast, some studies have shown no such relationship. In Anastasios *et al*.'s study, the difference of HP prevalence between diabetics and nondiabetics was not significant.[14]

Furthermore, it is shown that diabetic patients are at high risk for coronary artery disease and the point that HP infection predisposes people to vascular events, makes the relationship between diabetes and HP infection important because the

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proof of this association may be a reason to discuss about the treatment of the infection in diabetic patients to reduce the risk of cardiovascular events in these patients.[1] Hence, in this study we aimed to compare the prevalence of HP infection in diabetic and nondiabetic individuals.

Materials and Methods

In this cross-sectional study, diabetic patients referring to Shahid Beheshti Hospital of Qom between March 2013 and 2014 were studied. Nondiabetics referring to the hospital were enrolled as a control group. Smokers, pregnant women, patients treated with insulin, patients with a history of HP and consumers of proton pump inhibitors, H2 blockers, and bismuth, individuals with a known history of gastric cancer, upper gastrointestinal surgery and inflammatory bowel disease were excluded. Demographic characteristics such as age, gender, body mass index (BMI), abdominal circumference, exercise, symptoms of dyspepsia, nausea and vomiting, and history of gastrointestinal bleeding were recorded and biochemical markers including low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), fasting blood sugar (FBS), and fasting insulin levels were checked.

The subjects were tested for the presence of HP infection. After 8 h of fasting, blood samples were obtained and stored at 4°C. Serum was obtained by centrifugation at 2000 rpm for 15 min, immediately after sampling. Anti-HP immunoglobulin G antibody was measured using enzyme-linked immunosorbent assay (ELISA) kit, Padtan Company, Iran. If the serum titer was >30 AU/mL, it was considered positive. BMI was calculated by body dividing weight (kg) by squared height (m). Serum insulin was measured using ELISA kit, DiaMetra Co, Italy. We calculated and compared homeostatic model assessment of insulin resistance (HOMA-IR) in this study multiplying the fasting glucose value (mg/dL) by serum insulin value in each person and then dividing it by 405.

Results

In this study, 429 cases (218 nondiabetic and 211 diabetic patients) were studied. Initially, the two groups were compared for age, gender and body mass index [Table 1].

The prevalence of HP infection was 65.9% among diabetics while it was 50.5% among nondiabetic subjects. Hence, HP infection is markedly more prevalent among individuals with diabetes ($P = 0.001$).

Regarding the relationship between variables affecting HP infection, after entering the variables including diabetes, HDL, LDL, FBS, TG, IR and insulin in the regression model, only diabetes affected HP and hence that it increased the chance of developing HP infection up to 88% (odds ratio [OR] = 1.88, confidence interval = 1.27–2.78). Notably, hemoglobin A1c variables were removed from the regression model because of its destructive effect on the model (R^2 coefficient = 0.032) [Table 2].

Table 1: Some characteristics of the patients in diabetic and nondiabetic groups

Parameter	Diabetics (*n*=211) (%)	Nondiabetic (*n*=218) (%)	*P*
Age	52.84±8.82	39.52±12.45	0.000
Gender female/male	135 (64)/76 (36)	109 (50)/109 (50)	0.003
BMI	28.97±4.78	26.11±4.69	0.000
HP seropositivity	139 (65.9)	110 (50.5)	0.001

BMI: Body mass index, HP: *Helicobacter pylori*

Regarding the relationship between variables affecting diabetes, after entering the variables including HDL, LDL, FBS, TG, IR and insulin in the model, LDL and TG increased the chance of developing diabetes up to 0.016 and 0.004, respectively (R^2 coefficient = 0.83).

Discussion

In this study, the prevalence of HP infection was 65.9% among diabetics while it was 50.5% among nondiabetic subjects, and it was more prevalent among patients with diabetes. It was confirmed in other studies. For example, in Talebi-Taher *et al*.'s study, its prevalence among diabetic and nondiabetic patients were 60% and 26.66%, respectively ($P = 0.001$)[15] or in Bener *et al*.'s study,[16] it has been reported 76.7% versus 64.8% in diabetic and nondiabetic subjects ($P = 0.009$). This finding was confirmed in a study by Candelli *et al*. The strength point of this study was that in 3 years follow-up, the reinfection rate was higher in diabetic patients.[17] On the other hand, on the previous study, we found that HP eradication in patients with diabetes was lower than nondiabetic subjects.[18] Although, some studies have not supported this association.[19] In Anastasios *et al*.'s study, the difference of HP prevalence between diabetics and nondiabetics was not significant (37.3% vs. 35.2%).[14] In Mallecki *et al*.'s study, the rate of HP infection in Hong Kong Chinese subjects with type 2 diabetes was around 50%, which is similar to control subjects. No association was found between HP infection, glycemic status, and diabetes duration with upper gastrointestinal symptoms in these diabetic subjects.[20]

The prevalence of endoscopically detectable gastro-intestinal complications were higher in HP infected diabetics (OR = 4:2; $P < 0.05$).[21]

Table 2: Comparison of laboratory parameters in HP⁺ and HP⁻ groups

Parameter	Diabetic		*P*	95% CI	Nondiabetic		*P*	95% CI
	HP⁺	HP⁻			HP⁺	HP⁻		
LDL	116.0±51.7	107.1±43.2	0.212	−22.94-5.13	85.96±32.67	83.26±29.75	0.525	−11.04-5.65
HDL	60.7±26.7	69.2±29.2	0.037	0.51-16.32	56.55±20.05	54.23±19.79	0.390	−7.64-2.99
TG	229.3±114.6	224.2±100.2	0.747	−36.65-26.35	140.81±95.20	142.63±112.27	0.897	−25.95-29.59
Cholesterol	207.3±67.4	205.1±63.2	0.820	−21.10-16.74	157.50±38.86	161.16±42.68	0.509	−7.23-14.55
FBS	180.12±64.27	173.43±61.32	0.468	−24.82-11.45	92.58±14.92	92.75±11.70	0.926	−3.41-3.75
HOMA-IR	4.48±2.78	3.16±2.32	0.013	−2.36-0.28	3.01±2.12	2.74±2.18	0.704	−1.64-1.11

LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglyceride, FBS: Fasting blood sugar, HOMA-IR: Homeostatic model assessment of insulin resistance, HP: *Helicobacter pylori*, CI: Confidence interval

It is interesting that in Yang *et al*.'s study, HP infection was positively associated with diabetes, but no positive correlation was found between HP infection and prediabetes.[22]

These findings raise the question whether a person's diabetes makes him susceptible to HP infection or the chance, of developing diabetes, is greater in patients with HP infection? There are studies that have shown that diabetics are at risk for HP.[23] It was confirmed in our study too.

In some studies, the reason, why diabetics are more prone to HP infection has been explained. It is reported that the prevalence of HP in diabetic patients has a significant association with autonomic neuropathy. In Gentile *et al*.'s study, a significant concordance was found between the presence of autonomic neuropathy and HP infection.[24]

It is likely that autonomic neuropathy in diabetic patients will delay gastric emptying, which causes an imbalance between the absorption of carbohydrates and insulin secretion that will result in tighter control of blood sugar. On the other side, a decrease in gastric acid secretion in diabetic patients may facilitate bacterial colonization of the gastrointestinal tract. Theoretically, it is believed that diabetics are more susceptible to colonize HP due to elevated blood glucose level and subsequently, gastric mucosal change and increased glucose concentration in it. Another reason for the higher HP infection in diabetic patients is a higher rate of hospital admission in these patients.[25] These reasons raise the hypothesize that people with diabetes are more prone to HP infection. In addition, it is reported that HP infection is significantly associated with coronary artery disease. On the other hand, the increased risk of coronary artery disease in diabetic patients makes the HP infection in diabetics important.[1] In Agrawal *et al*.'s study, coronary heart disease was more prevalent in diabetics with HP infection than those without it (57%).[21]

In contrast, some researchers believe that HP infection increases the risk of diabetes. In the prospective study of Jeon *et al*. on Latino elderly over 10 years, HP⁺ patients experienced a greater rate of incident diabetes than HP- ones.[26] Some researchers believe that HP infection causes chronic inflammation, which increases insulin resistance as a major cause of diabetes.[27] Results of a large study in Japan in 2009 on 1,107 asymptomatic subjects showed that HP infection is significantly associated with insulin resistance.[28]

It has also been demonstrated in other studies. However, other studies revealed no association between HP infection, the prevalence of diabetes and insulin resistance.[29,30] Impaired insulin secretion is another reason that makes HP infected patients prone to diabetes. Some studies reported that chronic exposure to IL-1 β, TNF-α, and interferon gamma, which are secreted in HP⁺ patients, inhibits insulin secretion from pancreatic beta cells and induction of apoptosis in these cells.[31,32] Others believe that HP caused diabetes due to systemic inflammation and increased production of proinflammatory cytokines.[33] The finding that increased IL-1 β causes inflammation in adipose tissue and leads to insulin resistance, which plays a key role in developing diabetes, in addition to the fact that secretion of IL-1 β increases in HP⁺ patients, helped the researchers in addressing this hypothesis.[34]

However, some studies reject this hypothesis and have suggested no association between inflammatory factors and HP infection with diabetes.[35,36] We did not find any association between adiponectin level among diabetic patients with and without HP infection in our previous study.[37] On the other hand, it is stated that HP infection gastritis causes susceptibility to diabetes by affecting gastric hormones such as leptin, ghrelin, gastrin, and somatostatin.[25] In addition, some studies showed that HP infection increases the risk factors of type 2 diabetes. For example, Cohen *et al*. demonstrated a higher BMI in patients with HP infection.[38] In addition, HP infection has been shown to interfere with the serum lipid profile of and it can be a risk factor for diabetes by this way.[39,40] However, regardless of the fact, which one causes the other, the association between diabetes and HP is undeniable and needs to be reviewed in different studies. In a previous

study on diabetic patients, we found that serum insulin ($HP^- = 6.97 \pm 5.64$ vs. $HP^+ = 10.12 \pm 7.72$, $P = 0.002$) and insulin resistance degree ($HP^- = 3.16 \pm 3.32$ vs. $HP^+ = 4.48 \pm 3.78$, $P = 0.013$) are significantly higher in HP^+ group. It seems that the HP^+ diabetic patients require higher levels of serum insulin to reach the same degree of glycemic control compared to the HP-ones.[41]

It is more interesting to know that there is an association between diabetic complications, especially microvascular complications and HP infection.[42] For example, in Agrawal *et al*.'s study,[21] the association between nephropathy, retinopathy and neuropathy with HP infection was also observed and a strong association was seen with diabetic retinopathy, diabetic neuropathy and nephropathy.

Conclusion

This study showed a higher prevalence of HP infection in diabetic patients, and it is said that HP and diabetes can affect each other. Therefore, prospective studies should be conducted to better determine the causal relationship between them.

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