## ORIGINAL ARTICLE

# Insulin Sensitivity, β Cell Function and Serum Lipid Levels in Helicobacter Pylori Positive, Non-Obese, Young Adult Males

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**Abstract:** It is not clear whether Helicobacter pylori (Hp) infection affects insulin levels and insulin sensitivity. We aimed to determine insulin sensitivity and beta cell function, and to evaluate serum lipids in subjects with and without Hp infection. Eighty non-obese young adult males, 40 of whom were Hp positive and 40 were negative, were included in the study. Two endoscopic biopsy specimens were obtained from each subject. Height, weight and waist-hip circumference were measured, and body mass index (BMI) was calculated. Serum glucose, total, HDL, LDL and VLDL-cholesterol and triglyceride levels were determined. Body fat mass and percentage were determined by bioelectric impedance. Serum insulin levels were measured by the RIA method. HOMA was used as an index of pancreatic beta cell function and insulin sensitivity. The independent-t test was used in the comparison of results. Age, BMI, waist and hip circumferences, and fat percentages did not exhibit any statistical differences. Mean HOMA-B [111.7, in Hp(+) and 112.0 in Hp(-) subjects] and HOMA-S [67.7 in Hp(+) and 60.7 Hp(-) subjects] did not differ amoung the groups. The lipid and aminotransferase levels of the 2 groups were also similar.

Conclusion: Hp infection is not associated with impairment of insulin sensitivity and deterioration of the glucose metabolism. It seems to be metabolically neutral in terms of serum lipids and aminotransferase levels.

**Key Words:** Helicobacter pylori, insulin sensitivity

## Introduction

In patients with diabetes mellitus, chronic infections are frequent and severe, due to the impairment of their immune status. However, data on the prevalence of Helicobacter pylori (Hp) infection in diabetics are scanty and contradictory (1). Due to the fact that diabetes mellitus may be associated with a variety of upper gastrointestinal tract complaints, investigators sought to determine whether Hp infection is linked to different forms of diabetes (2). The relationship between diabetes and Hp infection is still controversial. Some authors have claimed that there is no association between Hp infection, glycemic status, and duration of diabetes and upper gastrointestinal symptoms in diabetic subjects (1-4). On the other hand some authors have pointed out that a higher prevalence of Hp infection was seen in diabetic patients with dyspepsia. The Hp infection was also found to be significantly associated with the presence of endoscopic lesions and chronic gastritis in diabetic patients, but not in the controls (5). Alterations in the glucose metabolism in diabetes have been suggested as promoting Hp colonization, but the probable relationship between Hp and insulin resistance has not been carefully investigated. Although some studies showed no association between Hp status and levels of total cholesterol, triglyceride, or glucose (6-8), the data in the literature have not clarified whether Hp affects insulin plasma levels and therefore insulin sensitivity. Peach and Barnett (9) showed that women infected with Hp had a lower mean fasting plasma glucose concentration than did non-infected women. The aims of this study are to determine insulin sensitivity and beta cell function, and to evaluate serum lipids in subjects with and without Hp infection.

## Materials and Methods

**Subjects:** Eighty non-obese young adult males, 40 of whom were Hp positive and 40 negative (aged 20-45 ) who complained of dyspeptic problems were included in the study. Subjects were selected from patients admitted to the endoscopy unit for 6 months. Exclusion criteria were: Men younger than 20 and older than 45, female gender, obesity (BMI > 25 kg/m$^2$), diabetes mellitus, hypertension and coronary heart disease. Individuals using drugs that affect insulin sensitivity were also excluded from the study.

**Methods:** The patients' heights, weights, waist and hip circumferences were measured, and body mass indexes (BMI) were calculated. Weight was measured without shoes and in light clothing, and was recorded to the nearest 0.5 kg. Subjects were measured barefooted and bareheaded, and were recorded to the nearest centimeter. BMI was expressed as weight (kg) by height (meters) squared. Waist circumference was taken as the maximum abdominal girth and was recorded to the nearest centimeter. Hip circumference was taken as the maximum circumference at the level of the greater trochanter and was also recorded to the nearest centimeter. Endoscopic examination was performed by an Olympus GIF XQ type 30 device in all subjects. Two biopsies were taken from each patient using Olympus FB-25K biopsy forceps: one from the greater curvature of the mid-antrum, the other from the incisura angularis. Each biopsy specimen was processed by urease test. Group - 1 (patients, n = 40) consisted of subjects with positive urease tests, and group - 2 (control, n = 40) composed subjects with negative urease tests. Trained hospital staff measured blood pressure. Informed and written consent was obtained from all participants.

**Biochemistry:** Blood samples were obtained at 08:00 after a 12 hour fasting period, and were centrifuged and separated immediately. After collection, serum samples were stored at -80 $^0$C until assayed. Serum glucose, total, HDL and VLDL-cholesterol and triglyceride levels were determined by the use of an Abbott Aeroset autoanalyzer. LDL-cholesterol was calculated by Friedwald's equation (LDL chol = Total chol - (HDL + TG / 5). Serum insulin levels were measured by the Radioimmunoassay method (RIA, Diagnostic System Laboratories, Webster, Texas, USA, Berthold LB 2111). The intra-assay coeffeicents of variation (CVs) were 8.2%, 4.8% and 6.3%, at serum concentrations of 4.75, 17.62 and 54.60 µU/ml,

respectively. The interassay CVs were 11.2%, 7.5% and 4.7%, at serum concentrations of 4.92, 16.23, and 52.92 µU/ml, respectively. Body fat percentage and fat mass were determined by bioelectric impedance (Body composition analyzer, TANITA Corporation, Tokyo, Japan).

**Evaluation of beta cell function and tissue insulin sensitivity:** Since the measurement of insulin sensitivity in vivo involves techniques that are not readily available to most investigators and requires significant amounts of both physician and patient time, Turner et all (10, 11) developed a mathematical model that predicted insulin sensitivity from simple measurement of fasting plasma glucose and insulin concentrations. This approach was called homeostasis model assessment (HOMA). If the simultaneous fasting plasma glucose and insulin levels are known, the model will generate estimates of the ß-cell secretory capacity and insulin sensitivity required to produce the measured glucose and insulin concentrations. The euglycemic insulin clamp technique provides the most direct measure of tissue sensitivity to insulin and has become the gold standard for measuring insulin action in vivo (12). Authors found that assessment of insulin by HOMA sensitivity correlated well with that determined by the euglycemic insulin clamp technique (r = 0.88, p < 0.0001) (10). In our study mathematical modelling of the fasting glucose and insulin pairs HOMA was used as an index of pancreatic beta cell function [HOMA-(%B)] and tissue insulin sensitivity [HOMA-(%S)]. HOMA-(%S) and HOMA-(%B) were determined by the use of HOMA and a CIGMA – computer program application (Dr. Jonathan C Lewy, Diabetes Research Laboratories, Radcliffe Infirmary, Oxford, UK)

**Statistical analysis:** All results were given as mean ± standard deviation. Results were stored and an independent-t test was used in the comparison of results.

## Results

The all metabolic and anthropometrical results of both Hp(+) subjects and the healthy control group are shown in the table. Ages, BMIs, waist and hip circumferences, fat percentages and fat masses of the groups did not exhibit any statistical differences. The mean HOMA-B(%) value of subjects with Hp infection was 111.7 ± 38.5 and 112.0 ± 36.9 in the control group. On the other hand, the mean HOMA-S(%) value was 67.7 ± 38.6 in Hp(+)

Table. All anthropometrical and metabolic parameters of both groups (helicobacter (+) and (-) subjects).

|  | Group-1 | Group-2 |
| --- | --- | --- |
|  | (Helicobacter pylori +) | (Helicobacter Pylori -) |
| Age (yr) | 35.3 ± 8.6 | 35.7 ± 6.9 |
| BMI (kg/m$^2$) | 24.7 ± 4.3 | 24.0 ± 3.8 |
| Waist circ. (cm) | 86.8 ± 12.6 | 89.1 ± 15.6 |
| Hip circum. (cm) | 102.1 ± 9.5 | 101.3 ± 9.4 |
| Fat percent (%) | %20.5 ± 9.03 | %21.0 ± 9.3 |
| Fat mass (kg) | 14.1 ± 6.2 | 15.4 ± 6.6 |
| T.cholesterol (mg/dl) | 180.3 ± 36.9 | 202.3 ± 38.0 |
| Triglyceride (mg/dl) | 120.0 ± 53.3 | 171.3 ± 125.7 |
| LDL-chol (mg/dl) | 108.6 ± 29.4 | 117.4 ± 37.2 |
| HDL-chol (mg/dl) | 41.8 ± 9.9 | 43.2 ± 8.9 |
| VLDL-chol (mg/dl) | 25.7 ± 20.2 | 29.7 ± 23.5 |
| AST (mU/L) | 22.3 ± 8.3 | 21.3 ± 6.1 |
| ALT (mU/L) | 26.0 ± 16.7 | 23.0 ± 12.7 |
| ALP (mU/L) | 85.6 ± 18.1 | 82.3 ± 26.0 |
| Insulin /IU/ml | 8.1 ± 5.2 | 7.8 ± 3.3 |
| Glucose(mmol/L) | 4.93 ± 0.4 | 5.16 ± 0.6 |
| HOMA-B(%) | 111.7 ± 38.5 | 112.0 ± 36.9 |
| HOMA-S(%) | 67.7 ± 38.6 | 60.7 ± 34.1 |

subjects, and 60.7 ± 34.1 in control subjects. Not only the HOMA-B values, but also the HOMA-S results in both groups (Hp positive and negative) were similar. The lipid profile (total cholesterol, LDL-cholesterol, VLDL-cholesterol, HDL-cholesterol, triglyceride), and transaminase (ALT and AST) levels in the 2 groups were also similar.

## Discussion

Little information about the prevalence of Hp infection in diabetics is available in the literature (1). The best evidence of an association between Hp infection and diabetes comes from case control studies. There are, however, inconsistencies among different studies. There is no substantial evidence that Hp infection affects diabetic control or insulin requirements. The data in the literature have not clarified whether Hp affects insulin plasma levels and therefore insulin sensitivity. We showed that there is no relationship between insulin sensitivity and Hp infection. Although some studies showed that there is no association between Hp status and levels of total cholesterol, triglyceride or glucose, we could not find any data about Hp infection and insulin sensitivity. Many factors affect glucose metabolism and insulin sensitivity, such as obesity, gender and aging. Obesity significantly affects insulin senstivity and beta cell function. It leads to insulin resistance by a variety of mechanisms, for example glucotoxicity, tumor necrosis factor-alpha and resistin (13). The menstrual cycle also affects insulin sensitivity, which is higher in the follicular phase than the luteal phase (14). Knowledge of the variations in insulin sensitivity that occur during the normal menstrual cycle provides a basis for comparison for studies of other clinical conditions. In addition, this phenomenon should be considered if the determination of insulin resistance is the purpose of particular epidemiological studies (8). It has been suggested that postmenopausal women taking oral estrogen or those taking a combination of estrogen and HRT are more insulin-resistant than women not on HRT, even when women are of comparable total and abdominal adiposity (15). It has been pointed out that glycemic control deteriorates with age in healthy, non-diabetic individuals,

and age related rises in fasting plasma glucose result from a small but steady decline in pancreatic beta cell function (16). Aging is also associated with an increased incidence of hypertension, macrovascular disease and type 2 diabetes. The elderly are more glucose intolerant and insulin resistant. However, insulin secretion appears to decrease with age even after adjustments for differences in adiposity, fat distribution and physical activity. The glucose intolerance of aging may be due, in part, to decreased insulin sensitivity of pancreatic cells to insulinotropic gut hormones (GLP1/GIP) and in part to alterations in hepatic glucose production (17). In addition it has been reported that glycemia and insulinemia increase with age and that a small deterioration occurs in insulin sensitivity with age in animals (18). In order to eliminate the effects of aging, obesity, gender, menstrual cycle and HRT on glucose metabolism and insulin sensitivity, we carried out this study only in non-obese young adult males aged between 20 and 45. Peach and Barnett (9) showed that women infected with Hp had a lower mean fasting plasma glucose concentration than did non-infected women. However our study does not support this finding. We do not think that there is any association between Hp positivity and insulin sensitivity / glucose metabolism.

We also found that there is no relationship between Hp infection and serum levels of total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, triglyceride and transaminases (AST and ALT). Our study groups consisted of healthy subjects apart from Hp infection and/or gastrointestinal complaints. Therefore the subjects included in the study form a homogeneous group in terms of gender, age, body weight, waist circumference, fat percentage and fat mass. We therefore suggest that Hp infection does not lead to deterioration in lipid metabolism and serum transaminases in addition to insulin sensitivity and glucose metabolism in homogeneous groups from the point of view of gender, body weight and age. Scragg et al. (6) studied a large group of asymptomatic, non-diabetic workers in New Zealand and found no association between Hp infection and total cholesterol, triglyceride, or glucose. It was also shown that there was no association between Hp status and hypercholesterolemia and/or diabetes in other studies (2,7,8).

We concluded that : 1-Hp infection is not associated with impairment of insulin sensitivity, beta cell function or deterioration in glucose metabolism; 2- Hp infection seems to be metabolically neutral in terms of serum lipids (total-cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride) and serum transaminases in non-obese young adult males.

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