# Effects of *Helicobacter Pylori* Colonization/Infection on the Metabolic Profile of Obese Persons Undergoing Sleeve Gastrectomy Surgery for Weight Reduction

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**ABSTRACT:** **Background:** *Helicobacter pylori* (HP) infection of the gastric mucosa may be involved in the development of insulin resistance (IR).

**Objectives:** To investigate the association between HP status in stomach biopsies and weight reduction in patients who underwent laparoscopic sleeve gastrectomy (LSG).

**Methods:** In this retrospective analysis of medical charts, all patients who underwent LSG for weight reduction and had at least 1 year of follow-up were included. HP status was ascertained by two to four biopsies of the removed stomach.

**Results:** The study group comprised 70 patients; their mean age was 45.9 ± 11.9 years and 31.9% were males. Fourteen patients (20%) tested positive for HP colonization in gastric mucosa. HP status was not associated with age or smoking status. No difference was noted in the rate of diabetes mellitus (DM) or hypertension, but patients with HP had lower rates of hyperlipidemia (0 vs. 29 patients, 52%, $P < 0.001$). Patients lost an average of 10.5 kg/m$^2$ after 12 months of follow-up, and no difference was noted between HP-positive and HP-negative patients. The rate of DM control was also similar between HP-positive and HP-negative patients at baseline (33.3 vs. 29.4, $P$ = NS) and at 12 months of follow-up (70% vs. 50%, $P$ = NS).

**Conclusions:** HP status was not associated with changes in metabolic profiles and co-morbidity status, or in the efficacy of LSG.

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**KEY WORDS:** laparoscopic sleeve gastrectomy (LSG), diabetes mellitus (DM), insulin resistance (IR), *Helicobacter pylori* (HP)

Diabetes mellitus type 2 (DMT2) is a condition of imbalance between insulin secretion and abnormally elevated blood glucose levels. This disease is believed to occur following the development of insulin resistance (IR) and an inability to reduce glucose levels.

It is well established that increased levels of insulin, which are the result of increased food intake and weight gain, are a serious risk factor for the development of DMT2. These increased levels of insulin lead, over time, to desensitization to insulin on the one hand and enhanced apoptosis of insulin-secreting pancreatic beta cells on the other. However, among obese individuals, IR can occur even without elevated glucose levels [1] and is associated with waist circumference and the amount of visceral fat [2].

An interesting question recently discussed in the literature is the association of IR, diabetes mellitus and gastric diseases, particularly *Helicobacter pylori* (HP) infection. Despite contradicting data, some studies showed higher rates of HP infection among diabetes mellitus patients [3-5]. HP infection was also associated with IR without diabetes in some patients [6,7] in whom the eradication of HP led to improved insulin sensitivity [8]. However, despite the mounting evidence, this question is still under debate.

It was recently shown that non-diabetic morbidly obese patients undergoing bariatric surgery exhibit improved insulin sensitivity soon after the surgery and before any weight loss is achieved [9]. These results raise the intriguing possibility that IR is influenced by other factors, not necessarily weight reduction and loss of fat mass. It is possible that the gastric/intestinal mucosa play a role in the development of IR. As such, HP infection of the gastric mucosa may be involved in the development of IR. Therefore, by removing a large portion of the stomach, and potentially a reduction of HP load, patients may show improved insulin sensitivity following surgery. We therefore sought to investigate the association between HP status in stomach biopsies and weight reduction among patients undergoing laparoscopic sleeve gastrectomy (LSG).

## PATIENTS AND METHODS

This retrospective non-randomized study was reviewed by the local institution review board and was approved as an observational study, precluding the need for written informed consent.

We reviewed the medical charts of obese individuals with a body mass index (BMI) > 35 kg/m² who had undergone LSG for weight reduction and had completed at least 1 year of follow-up. We excluded from the analysis patients who were younger than 18 years old at the time of surgery. In addition, given the effect of steroids on metabolic parameters such as glucose, patients who received prolonged systemic steroid treatment (> 3 weeks) within the 12 months preceding the surgery were also excluded from the analysis.

### DATA ACQUISITION

Electronic medical records were reviewed for patients undergoing LSG during the period 1 July 2009 to 30 June 2012. The information that was extracted from the records included demographics (age, gender), co-morbidities (presence of hypertension, hyperlipidemia, DM, ischemic heart disease, smoking, high blood pressure levels) as well as laboratory information (including full lipid profile, glucose and HbA1c levels for diabetics) before and at least 12 months following surgery. Information regarding HP status was extracted from the pathology reports. Data were recorded on paper and uploaded to Excel Spreadsheet (Microsoft Inc., USA) for storage.

### PATHOLOGY REPORTS FOR *H. PYLORI*

Routine tests for HP are performed in all patients undergoing LSG in our center. For each patient, a biopsy is taken from the antrum during the pathology examination before the cutting of the stomach. In addition, two representative sections that sample gastric corpus and antrum are examined from the gastric tissue removed. In case of visible gastritis in the removed stomach, one of the biopsies is taken from the inflamed gastric tissue. All sections are paraffin-embedded, sectioned at 4 μm, and subsequently stained with Giemsa stain.

In general, *H. pylori* density is graded as none, mild (when few microorganisms are present), moderate (when bacteria are present in separate foci), and severe (when near complete or complete surface layering with HP was observed). For the purpose of this study, patients were categorized into two groups according to the presence or absence of HP in the stomach.

### STATISTICAL ANALYSIS

SPSS v. 21.0 (IBM Inc., USA) was used for all statistical analyses. Distributions of continuous variables were assessed for normality using the Kolmogorov-Smirnov test (cutoff $P < 0.01$). Continuous variables were described using mean ± standard deviation. Categorical variables such as gender and co-morbidities were described using frequency counts and expressed as a percentage. Continuous variables were compared by HP status using the *t*-test for independent samples or the Mann-Whitney U test as appropriate. Associations between categorical variables were assessed using the chi-square test. All tests were two-sided and considered significant at $P < 0.05$.

## RESULTS

Included were 70 patients who met the inclusion criteria. Mean age was 45.9 ± 11.9 years, and 22 patients (31%) were males. Twenty-nine patients (42%) had hyperlipidemia, 26 (37%) had hypertension, 23 (33%) had diabetes mellitus, and 5 patients (7%) had a positive history of ischemic heart disease. In addition, 6 (9%) patients were smokers.

At 12 months follow-up all patients exhibited significant changes in their metabolic profile. Patients lost an average of 10.7 units of BMI, and their blood pressure, triglyceride and high density lipoprotein (HDL) levels were improved. In addition, 15 DM patients (65%) achieved diabetes control (HbA1c levels < 7%), compared to 7 (30%) at baseline ($P = 0.05$). Changes in metabolic profile are specified in Table 1.

Of the examined gastric tissue, 14 samples (20%) stained positive for *H. pylori*. *H. pylori* status was not associated with age. When comparing co-morbidities, patients who tested positive for HP in the gastric mucosa had lower rates of hyperlipidemia, but no other association was noted.

Efficacy of the LSG for weight reduction and improvement in metabolic profile was similar in both HP-positive and negative patients [Table 2]. In addition, the rate of diabetes control (HbA1c < 7%) did not vary across HP status groups at baseline

**Table 1.** Baseline and 12 month follow-up laboratory results for all patients

| | Baseline | Follow-up | *P* value |
|---|---|---|---|
| BMI (kg/m²) | 41.8 ± 6.0 | 31.0 ± 6.1 | < 0.001 |
| Triglycerides (mg/dl) | 167 ± 81 | 124 ± 46 | < 0.001 |
| LDL-cholesterol (mg/dl) | 109 ± 25 | 112 ± 34 | 0.219 |
| HDL-cholesterol (mg/dl) | 42 ± 11 | 49 ± 11 | < 0.001 |
| Total cholesterol (mg/dl) | 183 ± 31 | 184 ± 34 | 0.746 |
| Systolic blood pressure (mmHg) | 145 ± 17 | 129 ± 17 | 0.001 |
| Diastolic blood pressure (mmHg) | 85 ± 13 | 74 ± 10 | 0.001 |

BMI = body mass index, LDL= low density lipoprotein, HDL = high density lipoprotein

**Table 2.** Demographic parameters and co-morbidities in the study population and across HP colonization status

| | No colonization | HP colonization | *P* value |
|---|---|---|---|
| Age (years) | 45.6 ± 11.9 | 43.9 ± 11.5 | 0.477 |
| Male gender (n, %) | 18 (32%) | 4 (29%) | 0.928 |
| Hyperlipidemia (n, %) | 36 (54% | 0 | < 0.001 |
| Hypertension (n, %) | 23 (41%) | 3 (21%) | 0.340 |
| Diabetes mellitus (n, %) | 21 (38%) | 2 (14%) | 0.191 |
| Smoking (n, %) | 6 (11%) | 0 | 0.463 |
| Ischemic heart disease (%) | 3 (5%) | 1 (7%) | 0.783 |

**Table 3.** Laboratory and blood pressure values of the study population at baseline and follow-up across HP colonization status

| | No colonization | HP colonization | *P* value |
|---|---|---|---|
| Baseline BMI (kg/m2) | 41.9 ± 6.2 | 41.9 ± 5.7 | 0.992 |
| BMI reduction (kg/m2) | 10.7 ± 5.3 | 10.5 ± 3.7 | 0.871 |
| Baseline triglycerides (mg/dl) | 174 ± 85 | 144 ± 68 | 0.251 |
| Follow-up triglycerides (mg/dl) | 123 ± 42 | 120 ± 51 | 0.911 |
| Baseline LDL-cholesterol (mg/dl) | 108 ± 25 | 111 ± 23 | 0.763 |
| Follow-up LDL-cholesterol (mg/dl) | 106 ± 35 | 131 ± 25 | 0.142 |
| Baseline HDL-cholesterol (mg/dl) | 41.7 ± 10.5 | 42.3 ± 12.8 | 0.855 |
| Follow-up HDL-cholesterol (mg/dl) | 47.8 ± 11.8 | 48.8 ± 5.6 | 0.857 |
| Baseline systolic BP (mmHg) | 144 ± 17 | 150 ± 21 | 0.309 |
| Follow-up systolic BP (mmHg) | 129 ± 17 | 129 ± 21 | 0.952 |
| Baseline diastolic BP (mmHg) | 85 ± 12 | 87 ± 17 | 0.578 |
| Follow-up diastolic BP (mmHg) | 74 ± 11 | 73 ± 7 | 0.839 |

BMI = body mass index, LDL = low density lipoprotein, HDL = high density lipoprotein, BP = blood pressure

(50% in the HP-positive group and 30% in the HP-negative group, $P = 0.86$), nor at follow-up (50% in the HP-positive group and 70% in the HP-negative group, $P = 0.927$) [Table 3].

## DISCUSSION

Bariatric surgery is associated with high rates of gastropathies, most predominantly gastritis [10]. It was recently shown that more than 70% of patients undergoing LSG had gastritis [11]. Among these patients, the rate of positive-HP staining varies, ranging from as high as 44% in one study [12] to less than 10% in another [13]. However, depending on the population assessed, the rates are still similar to that of the general population [14]. In our study, almost 20% of the patients were HP-positive, and rates were not associated with age or with smoking status.

Despite the possible association discussed in the literature, we did not find any association between HP colonization and IR status or a detrimental co-morbidity profile. Patients with positive DMT2 status had similar rates of positive HP status as those in non-diabetic obese individuals. In addition, rates of hypertension were similar across HP status groups, as were laboratory values, indicating a lack of association. In addition, HP status was not associated with changes in surgical efficacy after 12 months of follow-up.

Our study should be viewed within the context of its limitations. The sample size of the study was small and therefore our general negative results, including the documented lower rates of hyperlipidemia among HP-positive patients, may be due to a type 2 error. Despite the statistical significance, the lower rates of hyperlipidemia are contradictory to our baseline hypothesis and should be examined in larger studies. In addition, the fact that HP status was ascertained by biopsy of the removed tissue alone may result in underestimating the frequency of HP colonization. This as well may interfere with the true interpretation of our results.

## CONCLUSIONS

The prevalence of HP, as examined in biopsies of patients undergoing LSG for weight reduction, was similar to that of the general population. In addition, HP status had no association with changes in metabolic profile and co-morbidity status, and was not associated with the efficacy of the surgery.

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