

## Association between Helicobacter Pylori Eradication and Weight Gain

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### ABSTRACT

**BACKGROUND:** Helicobacter Pylori is a common infection highly prevalent globally causing chronic gastritis, duodenal ulcer and gastric carcinoma. It is observed clinically that patients who underwent therapy for eradication of H Pylori developed weight gain.

Objective of this study was to evaluate the association between weight gain and eradication of H pylori infection.

**METHOD:** For this observational cross sectional study, 137 patients were studied after confirmation of diagnosis of H pylori. Base line data at the beginning of the study and comparison between pre- treatment and post treatment outcomes were assessed after 3 months of follow up.

**RESULT:** After eradication therapy, a difference in body weight was evident from pre-treatment mean body weight of  $61.7 \pm 12.3$  kg to  $62.5 \pm 11.2$  Kg ( $P=0.011$ ). An increase in BMI was recorded from pretreatment BMI of  $23.24 \pm 2.1$  Kg/m<sup>2</sup> to  $26.4 \pm 3.8$  Kg/m<sup>2</sup> ( $P=0.028$ ). The assessment of symptoms was performed by applying Mann-Whitney U test of significance; score of symptoms showed a decline in intensity after eradication therapy. Mean score of dyspepsia decreased from 2.65 to 1.02 with a P value of 0.024, mean score of epigastric pain from 2.73 to 1.14 ( $P=0.041$ ), mean upper abdomen fullness from 2.49 to 0.35 ( $P=0.021$ ). A decrease in heart burn was noted 3.46 vs 0.92 ( $P=0.003$ ) and loss of appetite was less severe; 2.89 vs 0.58 ( $P=0.011$ )

**CONCLUSION:** The eradication of H Pylori, after 3 months of treatment, is associated with mild weight gain.

**KEY WORDS:** Helicobacter pylori, weight gain, BMI, eradication therapy.

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### INTRODUCTION

H. Pylori is one of the most common infection inflicting about half of the population worldwide<sup>1</sup>, infection is commonly acquired in earlier years of life, once infected individuals remains asymptomatic for decades, sometimes causing transit infections, the pathogenesis depends on the host environment factors<sup>2</sup>. It is the major etiologic agent causing chronic active gastritis, gastric ulcer, duodenal ulcer and it is associated as causative factor for gastric cancer, more so ever it is cited as an attributed factor for gastric Mucosa Associated Lymphoid Tissue (MALT) Lymphoma<sup>3</sup>. The estimated prevalence of developing peptic ulcer is 10 - 15% and 3% for gastric carcinoma<sup>4</sup>. Helicobacter P infection persists for several years and spontaneous eradication is quite low. The association between with eradication of Helicobacter Pylori and weight gain has been studied in various parts of world<sup>4,5</sup>. It is postulated that appetite and satiety are regulated

by ghrelin and Leptin which are secreted by gastric mucosa. Level of ghrelin and leptin are affected by H pylori infection, when H pylori is eradicated, an increase in ghrelin level leads to enhanced appetite causing weight gain<sup>6</sup>. More ever in addition to ghrelin and leptin level, dyspepsia; a common symptom in gastric and duodenal ulcer also plays a contributing factor which is eliminated after cure of H pylori infection and improving food intake. An increase in weight gain has been recorded after H. pylori eradication; however, controversy remains elucidative about confirmed explanation for this gain of weight. Various explanations have been given for increased weight in these patients after eradication of H Pylori; effects may be mediated through hormonal derangement which is observed in H pylori infection. The peptide hormones, ghrelin and leptin which regulate food intake and appetite, are located in the stomach wall<sup>7,8</sup>. Ghrelin is a 28 amino acid, it was discovered in 1999

and it is an acrylate endogenous ligand for the growth hormone secretagogue receptor. It is also named as "Hunger Hormone" which plays a vital role in increasing appetite and increase in weight gain.

A low Level of ghrelin in patients infected with H pylori has been reported. The mechanism of ghrelin on appetite is well documented<sup>9</sup>. Ghrelin is secreted by the oxyntic glands and the cells located in stomach. Functions of ghrelin are multiple in nature and it is responsible as a regulatory peptide for growth hormone releasing agent and it effects appetite, energy balance and also regulate acid secretion as well. But relation of ghrelin level with presence of H pylori infection remains controversial<sup>10</sup>.

Anorexia, dyspepsia and loss of weight are the major symptoms in patients suffering from acute or chronic gastritis. Dyspepsia which is also a causative factor in poor intake of food and loss of weight which improves after eradication by increasing appetite so ultimately leads to weight gain. Osawa et al<sup>11</sup> revealed a decreased plasma level of ghrelin after eradication of H pylori but level of ghrelin remained high in the stomach while weight gain was also noted. Dyspepsia which is one of the major symptoms of chronic gastritis, causes decrease in food intake in patients of gastritis caused by H pylori infection, these patients when treated and become symptom free, an increase in dietary intake could cause weight gain. Some studies have focused their research on this aspect but conclusive evidence has not been documented. Nishi Y et al<sup>12</sup> also dismiss this argument for increase in body weight after eradication of H pylori. Isomoto et al and Shiotani A<sup>13,14</sup> concluded from their studies that plasma ghrelin level was lower in patients infected with H pylori. Various laboratory tests are available for diagnosis of H Pylori infection. Most reliable and confirmatory test is stool antigen but this is not a cost effective method in developing countries like Pakistan.<sup>15</sup> The association between BMI and H Pylori infection has been evaluated and a reverse correlation is recorded, this inverse correlation provides an indirect evidence of possibility of higher BMI and increased body weight after H Pylori eradication<sup>15</sup>. The inverse relationship between BMI and seropositivity of H pylori exists particularly in developed countries; this inverse relation is attributed to the impact of H pylori infection<sup>16</sup>.

This study was planned to evaluate the impact of eradication of H pylori infection on weight gain, as very limited literature is available in Pakistan on this aspect.

## METHODS

This was a prospective longitudinal study carried out at Department Of Medicine, LUMHS, Jamshoro. Sample size was calculated by applying formula for comparison of 2 proportions. A total of 137 patients diagnosed as H. Pylori positive with symptoms of H Pylori associated gastric/ duodenal ulcer were selected. After approval from ethical committee and taking informed written consent from the patients. Patients above age of 18 years with symptoms of chronic gastritis were include while patients below age of 18 years, patients with history of pregnancy, diabetes mellitus, cancer, systemic infection, thyroid and liver and renal diseases, use of medications effective against H. pylori during the preceding 6 months were excluded. Diagnosis of H pylori was confirmed by laboratory-based, ELISA antibody. Informed consents were taken before inclusion in the study. A structured questionnaire was used to recode demographic, presence and severity of symptoms. Symptoms were scored as graded score; score 1 for mild, score 2 for moderate and score 3 for severe. Height and weight were taken by using standard measuring tools. Eradication therapy included proton pump inhibitor; omeprazole 40 mg, amoxicillin 1000 mg twice a day and clathromycin 500 mg twice a day for 14 days. Statistical analysis was performed, comparing continuous variables like BMI and weight were calculated by using t-test and paired data was calculated by using non-parametric Mann-Whitney U test. A follow up after 3 months was undertaken and end study parameters were recorded and analyzed by SPSS version 21.

## RESULT

From medical OPD 137 patients were included in this study, 132 completed follow-up successfully. Among these 74 were male and 58 were female patients, having mean age 53.3(±7.4) years. Pretreatment mean Body weight was 61.7(±12.3) and mean BMI was 22.21 (±2.1) Kg/m<sup>2</sup>. The results of this study showed an increase in body weight after 3 months, from 61.7±12.3 kg to 62.5±11.2 Kg with statistically significant difference (p=0.011). An increase in BMI was also statistically significant (p=0.028) with an increase of pretreatment BMI from 23.24 ±2.1Kg/m<sup>2</sup> to 26.4±3.8 Kg/m<sup>2</sup>. The analysis of symptoms score after eradication therapy done using Mann-Whitney test, and showed a decline in intensity. Mean score of dyspepsia decreased from 2.65 to 1.02 (p=0.024), mean score of epigastric pain from 2.73 to 1.14(p=0.041), mean upper abdomen fullness from 2.49 to 0.35 (p=0.021). A decrease in heart burn was noted 3.46 vs 0.92 (p=0.003) and decline in symptom of loss of appetite was recorded; 2.89 vs 0.58 (p=0.011).

**TABLE I:**

Variable	Pretreatment		Post treatment	
	Mean	St .D	Mean	St.D
Body weight (Kg)	61.7	±12.3	62.5	±11.2 <sup>α</sup>
BMI (kg/m <sup>2</sup> )	22.24	±2.1	23.4	±2.8 <sup>β</sup>
Age (Years)	53.3	±7.4		

( $\alpha p= 0.011, \beta P=0.028$ )

**TABLE II:**

Symptoms	Pre treatment (Mean score)	Post treatment (Mean score)	P – Value*
Dyspepsia	2.65	1.02	0.024
Epigastric pain	2.73	1.14	0.041
Heart burn	3.46	0.92	0.003
Upper abdomen fullness	2.49	0.35	0.021
Regurgitation	2.69	0.56	0.032
Loss of appétit	2.89	0.58	0.011

\* *Mann-Whitney U test.*

## DISCUSSION

Weight gain documented in our study showed an increase from 61.7±12.3 kg to 62.5±11.2 Kg (p=0.01), Suto et al<sup>17</sup> evaluated weight gain after eradication of H Pylori, reported increased in mean body weight from 68.07 Kg to 69.38 Kg; a finding identical to our study. Azuma et al<sup>18</sup> from Japan, in a case control study evaluated correlation of BMI with H Pylori Infection eradication. The pretreatment base line BMI and total cholesterol levels were noted and in H pylori seropositive patient's and compared with data taken after cure of the infection. The analysis showed a significant increase in BMI in H pylori seropositive patients after 12 months of treatment when compared to unchanged BMI of control who were seronegative for H pylori. These finding are in accordance to our study results which indicate a positive correlation of cure of H pylori and increase weight gain.

A plenty of evidence exists showing a positive correlation of increased level of ghrelin after eradication of H pylori which plays a vital role in appetite stimulation, which is secreted by gastric mucosa, ghrelin de-

creased significantly after acquiring H pylori infection which causes destruction of these cells. Nwokolo et al<sup>19</sup> noted an increase in ghrelin level after eradication of H pylori but this study was carried out in H pylori positive asymptomatic patients but objective of our study was not identical to that study where correlation of ghrelin was sought, however this study provides an indirect evidence where increase level of ghrelin in subjects with H pylori showed an enhanced value of ghrelin level after eradication of H pylori, which is linked to increase in body weight and increase in appetite.

Macadam RC et al<sup>20</sup> reviewed the changes in ghrelin level returned to normal after eradication of H pylori which, in opinion of the author has no relevance to BMI. In fact ghrelin levels have been found low in obese persons in comparison to non-obese persons as concluded by Cummings DE et al<sup>21</sup> in their study but the same authors agree that total resection of gastric mucosa leads to reduction in hunger is an indirect evidence that obesity is related to presence of ghrelin level.

Wu JT et al<sup>22</sup> assessed the relation of weight gain and prevalence of H Pylori infection; a negative correlation was observed between H Pylori infection and weight gain. These findings are in accordance to our study. The results of their studies are comparable to our study but the sample population being different in terms of age group depicts a non-identical inference. Zullo A et al<sup>24</sup> determined the effect of eradication of H pylori on weight gain and BMI, in this randomized control trial, a significant increase in BMI was observed and an increase of 0.7 was observed in intervention group where as in control group an increase of 0.5 kg was seen. In the conclusion of this study explanation cited for increase in weight after eradication of H pylori was disappearance of dyspepsia. This study also support results of our study.

However further research at bimolecular level is required for direct evidence of association between eradication of H Pylori infection and weight gain.

## REFERENCES

- Ioannou GN, Weiss NS, Kearney DJ. Is Helicobacter pylori seropositivity related to body mass index in the United States? *Aliment Pharmacol Ther.* 2005;21:765–72.

2. Testerman TL, Morris J. Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. *World J Gastroenterol.* 2014;20(36):12781-808.
3. Peura D.A. Should (or could) we have a Stomach without Helicobacter pylori? *Rev Gastroenterol Mex.* 2010;75(2):25-30.
4. Boltin D, Niv Y. Ghrelin, Helicobacter pylori and body mass: is there an association? *Isr Med Assoc J.* 2012;14(2):130-2.
5. Osawa H, Kita H, Ohnishi H, Nakazato M, Date Y, Bowlus CL, et al. Changes in plasma ghrelin levels, gastric ghrelin production, and body weight after Helicobacter pylori cure. *J Gastroenterol* 2006;41(10):954-61.
6. Tschop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. *Diabetes* 2001;50(4):707-9.
7. Kamada T, Haruma K, Hata J, Kusunoki H, Sasaki A, Ito M, et al. The long-term effect of Helicobacter pylori eradication therapy on symptoms in dyspeptic patients with fundic atrophic gastritis. *Aliment Pharmacol Ther* 2003; 18 (2):245-52.
8. Kamada T, Hata J, Kusunoki H, Ito M, Tanaka S, Kawamura Y, et al. Eradication of Helicobacter pylori increases the incidence of hyperlipidaemia and obesity in peptic ulcer patients. *Dig Liver Dis.* 2005 Jan;37(1):39-43.
9. Salles N, Menard A, Georges A, Salzmann M, de Ledinghen V, de Marcarel A, et al. Effects of Helicobacter pylori Infection on Gut Appetite Peptide (Leptin, Ghrelin) Expression in Elderly Inpatients. *J Gerontol A Biol Sci Med Sci.* 2006; 61(11):1144-50.
10. Furuta T, Shirai N, Xiao F, Takashima M, Hanai H. Effect of Helicobacter pylori infection and its eradication on nutrition. *Aliment Pharmacol Ther.* 2002;16:799-806.
11. Osawa H. Ghrelin and Helicobacter pylori infection. *World J Gastroenterol.* 2008; 14 (41):6327-6333.
12. Nishi Y, Isomoto H, Uotani S, Wen CY, Shikuwa S, Ohnita K et al. Enhanced production of leptin in gastric fundic mucosa with Helicobacter pylori infection. *World J Gastroenterol.* 2005;11(5):695-9.
13. Kamangar F, Dawsey SM, Blaser MJ, Perez-Perez GI, Pietinen P, Newschaffer CJ, et al. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with Helicobacter pylori seropositivity. *J Natl Cancer Inst.* 2006; 98(20):1445-52.
14. Pacifico L, Anania C, Osborn JF, Ferrara E, Ferrara E, Schiavo E, et al. Long-term effects of Helicobacter pylori eradication on circulating ghrelin and leptin concentrations and body composition in pre pubertal children. *Eur J Endocrinol.* 2008; 158:323-32.
15. Gisbert JP, Pajares JM. Stool antigen test for the diagnosis of Helicobacter pylori infection: a systematic review. *Helicobacter.* 2004;9(4):347-68.
16. Jang EJ, Park SW, Park JS, Park SJ, Hahm KB, Paik SY, et al. The influence of the eradication of Helicobacter pylori on gastric ghrelin, appetite, and body mass index in patients with peptic ulcer disease. *J Gastroenterol Hepatol.* 2008 ;23 (2):S278-85.
17. Suto H, Ito Y, Yamazaki Y, Kato T, Azuma T. An increase in body weight after eradication of Helicobacter pylori, *Nihon Shokakibyō Gakkai Zasshi* 2007;104(3):339-43.
18. Azuma T, Suto H, Ito Y, Ohtani M, Dojo M, Kuriyama M, et al. Gastric leptin and Helicobacter pylori infection. *Gut* 2001;49:324-329.
19. Nwokolo CU, Freshwater DA, O'Hare P, Randeva HS: Plasma ghrelin following cure of Helicobacter pylori. *Gut* 2003, 52(5):637-40.
20. Macadam RC, Borse V, Dodo I, Pollard SG. Helicobacter pylori, ghrelin, and obesity. *Gut* 2004; 53(2):315-16.
21. Cummings DE. Helicobacter pylori and ghrelin: interrelated players in body-weight regulation? *Am J Med.* 2004;117(6):436-39.
22. Wu JT, Kral JG. Ghrelin: integrative neuroendocrine peptide in health and disease. *Annals of Surgery* 2004;239(4):464-74.
23. Wu MS, Lee WJ, Wang HH, Huang SP, Lin JT. A case-control study of association of Helicobacter pylori infection with morbid obesity in Taiwan. *Arch Intern Med.* 2005;165(13):1552-5.

24. Zullo A, Hassan C, Cristofari F, Andriani A, De Francesco V, Lerardi E, et al. Effects of Helicobacter pylori eradication on early stage gastric

mucosa-associated lymphoid tissue lymphoma. Clin Gastroenterol Hepatol. 2010;8(2):105-10.



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