

Relationship between body mass and gastro-oesophageal reflux symptoms: The Bristol Helicobacter Project

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Objective	To examine the relationship between body mass and gastro-oesophageal reflux in a large population-representative sample from the UK.
Design and setting	Cross-sectional population-based study, as part of a randomized controlled trial of eradication of <i>Helicobacter pylori</i> infection, in Southwest England.
Subjects	In all, 10 537 subjects, aged 20–59 years, were recruited from seven general practices. Subjects provided data on frequency and severity of dyspeptic symptoms and anthropometric measurements were taken.
Main outcome measure	Relationship between overweight (body mass index [BMI] ≥ 25 kg/m ² and ≤ 30 kg/m ²) or obesity (BMI > 30 kg/m ²) and frequency and severity of heartburn and acid regurgitation.
Results	Body mass index was strongly positively related to the frequency of symptoms of gastro-oesophageal reflux. The adjusted odds ratios (OR) for frequency of heartburn and acid regurgitation occurring at least once a week in overweight participants compared with those of normal weight were 1.82 (95% CI: 1.33–2.50) and 1.50 (95% CI: 1.13–1.99) respectively. Corresponding OR (95% CI) relating to obese patients were 2.91 (95% CI: 2.07–4.08) and 2.23 (95% CI: 1.44–3.45) respectively. The OR for moderate to severe reflux symptoms were raised in overweight and obese subjects but not to the same extent as frequency of symptoms and only the relationship between obesity and severity of heartburn reached conventional statistical significance: OR = 1.19; 95% CI: 1.07–1.33.
Conclusions	Being above normal weight substantially increases the likelihood of suffering from heartburn and acid regurgitation and obese people are almost three times as likely to experience these symptoms as those of normal weight.
Keywords	Gastro-oesophageal reflux disease, heartburn, body mass index, obesity

A recent report has drawn attention to the lack of robust information on the relationship between body mass and

gastro-oesophageal reflux disease (GORD) and has highlighted the inconsistency in the findings of studies published in this field.¹ Clinical studies involving oesophageal pH monitoring show both positive² and negative³ associations between body mass and gastro-oesophageal reflux, and weight reduction is not consistently related to improvement in symptoms.^{4,5} Such studies have been conducted mainly in morbidly obese patients attending secondary or tertiary care, but evidence from population-based studies is also conflicting,^{1,6–8} which has led to claims that weight reduction may have no effect on the symptoms of GORD,¹ a view which is disputed.⁹

The relationship between weight and gastro-oesophageal reflux is an important one, not just because of the implications

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for treatment of symptomatic individuals, but also because both body mass^{10,11} and history of reflux^{12,13} have been shown to be important risk factors for oesophageal adenocarcinoma. The incidence of this cancer has been reported to have increased substantially in several developed countries in recent decades, mainly in white Caucasian populations.^{14,15} If high body mass is a causal risk factor for GORD, trends in overweight and obesity in these populations^{16,17} indicate that the incidence of this cancer may continue to rise.

To date no population-based study of the relationship between body mass and symptoms of GORD has been undertaken in the UK and only a few such studies have been performed in other countries.^{1,6–8,18,19} We examined this relationship within the population-based Bristol Helicobacter Project.

Methods

Survey methods

The Bristol Helicobacter Project is a large community-based randomized controlled trial of the effects of *Helicobacter pylori* eradication on dyspepsia, quality of life, and health services utilization. Between 1996 and 1998, all eligible patients, aged 20–59, registered with seven general practices in Southwest England (six located in a town north of Bristol and one within the city of Bristol) were invited to participate in the study.

Participants underwent ¹³C urea breath testing and their blood pressure and height and weight (after removing heavy outdoor garments) were measured. Subjects also completed a self-administered questionnaire that gathered information on the frequency and severity of dyspeptic symptoms (heartburn, acid regurgitation, epigastric pain/discomfort, a feeling of wind/fullness, belching and burping, and nausea) relating to the 3 months prior to examination. Heartburn was defined as 'a burning or ache behind the breast bone that is not due to heart trouble' and acid regurgitation as 'a very sour or acid tasting fluid at the back of your throat'. Data on self-medication and prescription-only medicines were also collected, including use of anti-dyspeptic medications, painkillers, aspirin, and non-steroidal anti-inflammatory drugs (NSAID). Lifestyle information was collected in the questionnaire and included smoking history (never smoker, ex smoker, current smoker <20 cigarettes a day, current smoker ≥20 cigarettes a day), alcohol intake (units of beer, wine and spirits per week, combined), coffee consumption (cups per day) and measures of adult socioeconomic status (occupation manual, or non-manual), highest educational qualification, tenure of accommodation (rented or owned), and number of cars in the household). This study includes data relating to all participants who tested positive for *H. pylori* infection and a computer-generated random sample of *H. pylori*-negative subjects to give an *H. pylori* negative to positive ratio of 2:1.

Statistical analysis

Frequency of heartburn and acid regurgitation were dichotomized into less than once a week and once a week or more frequently. Participants classified the severity of heartburn and acid regurgitation into (1) no problem at all, (2) a mild problem (could be ignored if not thinking about it), (3) a moderate problem (cannot be ignored but does not interfere with daily activities), (4) a severe problem (interferes with daily activities)

and (5) a very severe problem (interferes a lot with daily activities or have to rest when symptoms experienced). Categories 1 and 2 were grouped as mild symptoms and categories 3–5 as moderate or more severe symptoms. Body mass index (BMI) was calculated as body weight (kg) divided by the square of standing height (m). The BMI was categorized according to the World Health Organization classification of overweight and obesity:²⁰ normal weight—BMI <25 kg/m², overweight—BMI ≥25 kg/m² and ≤30 kg/m², obese—BMI >30 kg/m².

Bivariable relationships between BMI and frequency or severity of heartburn and acid regurgitation were assessed using χ^2 tests. In order to determine the specificity of the observed relationships between BMI and heartburn and acid regurgitation, the relationship between BMI and frequency of other dyspeptic symptoms were also assessed using χ^2 tests and these analyses were stratified by frequency of heartburn and acid regurgitation. Similarly, the bivariable tests of the relationships between frequency of heartburn and acid regurgitation were stratified by frequency of other dyspeptic symptoms.

The relationships between BMI and the frequency or severity of heartburn and acid regurgitation were further assessed using multivariate logistic regression modelling (Stata version 7, College Station, Texas, USA). Models were constructed with frequency or severity of reflux and acid regurgitation as the dependent variables and BMI as a categorical predictor variable, with adjustment for potential confounding by age group, sex, smoking, alcohol intake, coffee consumption, active *H. pylori* infection, measures of adult socioeconomic status, and the use of painkillers, aspirin, and NSAID. The clustered nature of the data (by general practice) was accounted for by defining the general practice at which participants were registered as the primary sampling unit in the logistic regression models. Weighted analyses were performed because of the increased sampling of *H. pylori* subjects (33% of subjects included in the database, but 15.5% of all subjects screened). The weights used were proportional to the inverse of the sampling fractions.

Results

A total of 27 536 subjects were eligible to participate in the study. The main reason for ineligibility to participate was known sensitivity to the constituents of the *H. pylori* eradication regime (ranitidine bismuth citrate and clarithromycin). Some 10 537 subjects (38.3%) consented to take part and underwent ¹³C-urea breath testing and completed the questionnaire. Overall, 1634 (15.5%) participants tested positive for *H. pylori* infection and 3268 of the negative subjects were randomly selected, providing a total study population of 4902 subjects. Of the study subjects, 2271 (46.3%) were male and 3.5%, 22.1%, 33.5%, and 40.9% were aged 20–29 years, 30–39 years, 40–49 years, and 50–59 years, respectively. Mean age was 45.8 years, with no difference between the sexes. Non-manual social classes were slightly over-represented, with 62.8% of participants from non-manual social classes compared with 52.3% for the general population in this Region of England (Office of National Statistics website, <http://www.statistics.gov.uk>). Of the participants, 20.6% were obese and a further 41.3% were overweight. The percentage obese was similar in females and males (20.9% versus 20.3%) but fewer women than men were overweight (34.5% versus 49.1%).

The frequency and severity of heartburn and acid regurgitation are shown in Table 1. Half of the participants had not experienced heartburn in the previous 3 months and almost 60% had not had acid regurgitation in the same period. Of all the participants, 13.4% had heartburn, and 8.2% acid regurgitation, at least once a week in the previous 3 months. Frequency of heartburn and acid regurgitation were associated: 97.0% of the 4002 participants who did not have heartburn at least once a week also did not have acid regurgitation this frequently, while 42.6% of the 643 participants who experienced heartburn at least once a week also had acid regurgitation at least once a week (χ^2 1112, d.f. 1, $P < 0.0001$).

The bivariable relationships between BMI and the frequency and severity of heartburn and acid regurgitation are shown in Table 2. A greater proportion of overweight and obese participants had more frequent and more severe heartburn compared with participants of normal weight. Overweight and obesity were also related to the frequency, but not to the severity of acid regurgitation. Frequency of heartburn increased from 11.0% to 15.5% between the youngest age group (<40 years) and the oldest age group (50–59 years) but this relationship was not statistically significant; adjusted P -value = 0.22 after weighting the analysis and adjusting for intraclass correlation in the primary sampling units. Heartburn was slightly less common in women than men (13.0% versus 14.8%, adjusted P -value = 0.03).

Table 1 Frequency and severity of heartburn and acid regurgitation among participants

Frequency of symptoms	Acid regurgitation	
	Heartburn No. (%)	regurgitation No. (%)
Not in the last 3 months	2453 (50)	2922 (59.6)
Less than once a month	1036 (21.1)	969 (19.8)
Between once a month and once a week	581 (11.9)	439 (9.0)
Between once a week and everyday	527 (10.8)	318 (6.5)
Every day	127 (2.6)	85 (1.7)
Missing data	178 (3.6)	169 (3.4)
Severity of symptoms^a		
Not a problem	369 (16.2)	434 (23.9)
A mild problem	954 (41.9)	818 (45.0)
A moderate problem	769 (33.8)	465 (25.6)
A severe problem	161 (7.1)	86 (4.7)
A very severe problem	24 (1.1)	13 (0.7)

^a Relates only to participants experiencing these symptoms in the last 3 months.

Table 2 Bivariable relationships between body mass index and symptoms of gastro-oesophageal reflux disease

Body mass index (kg/m ²)	Heartburn frequency		Heartburn severity ^a		Acid regurgitation frequency		Acid regurgitation severity ^a	
	< once a week	≥ once a week	a mild problem	a moderate or more severe problem	< once a week	≥ once a week	a mild problem	a moderate or more severe problem
<25	1638 (91.8)	146 (8.2)	442 (62.1)	270 (37.9)	1693 (94.4)	100 (5.6)	397 (71.9)	155 (28.1)
≥25 and ≤30	1642 (85.0)	291 (15.0)	551 (57.0)	416 (43.0)	1767 (91.1)	172 (8.9)	525 (68.9)	237 (31.1)
>30	765 (78.2)	213 (21.8)	320 (54.9)	263 (45.1)	847 (86.9)	128 (13.1)	325 (66.5)	164 (33.5)
Unadjusted P -value	<0.001		0.02		<0.001		0.16	
Adjusted P -value ^b	0.003		0.03		0.01		0.20	

^a Relates only to participants experiencing these symptoms in the last 3 months.

^b Weighted analysis and adjusted for intraclass correlation in the primary sampling units (primary care practices).

Current cigarette smoking was positively related to both frequency and severity of heartburn and acid regurgitation. Low and moderate alcohol intake (<20 units per week) appeared inversely related to the frequency and severity of these symptoms while coffee intake was inversely related to the severity of symptoms only. Use of painkillers, including aspirin and NSAID, at least once a week was strongly associated with more frequent and severe heartburn and acid regurgitation. Active *H. pylori* infection was not related to frequency or severity of heartburn or to severity of acid regurgitation. Frequency of acid regurgitation was slightly more common in participants with *H. pylori* infection but conventional statistical significance was not reached.

In the bivariable analyses, BMI was also associated with frequency of epigastric pain/discomfort, wind/fullness, and belching/burping but not with frequency of nausea. Statistically significant relationships between BMI and these variables were not seen when the analyses were stratified by frequency of heartburn and acid regurgitation. The relationships between BMI and frequency of heartburn and acid regurgitation were still significant after stratification for the other dyspeptic symptoms indicating that BMI is specifically associated with heartburn and acid regurgitation.

Table 3 shows the unadjusted and adjusted relationships between BMI category and frequency and severity of symptoms of gastro-oesophageal reflux. Following adjustment for potential confounders, BMI remained strongly and linearly positively related to frequency of symptoms of gastro-oesophageal reflux. The odds ratios (OR) for frequency of heartburn and acid regurgitation occurring at least once a week in overweight participants compared with those of normal weight were 1.82 (95% CI: 1.33–2.50) and 1.50 (95% CI: 1.13–1.99) respectively. Corresponding OR relating to obese patients were 2.91 (95% CI: 2.07–4.08) and 2.23 (95% CI: 1.44–3.45) respectively. The OR for moderate to severe reflux symptoms were raised in overweight and obese subjects but not to the same extent as frequency of symptoms and only the relationship between obesity and severity of heartburn reached conventional statistical significance: OR = 1.19; 95% CI: 1.07–1.33. In the multivariable models, age group, sex, social class (manual versus non-manual), and active *H. pylori* infection were not associated with frequency or severity of symptoms. Alcohol intake remained associated with frequency of heartburn but smoking and use of painkillers, aspirin, and NSAID remained consistently positively related to both frequency and severity of heartburn and acid regurgitation. However, the strongest relationships observed were for overweight and

Table 3 Multivariable analysis: unadjusted and adjusted analyses for relationships between body mass index and symptoms of gastro-oesophageal reflux disease

	Heartburn frequency		Heartburn severity		Acid regurgitation frequency		Acid regurgitation severity	
	Unadjusted OR ^a (95% CI)	Adjusted OR (95% CI) ^b	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^b	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^b	Unadjusted OR (95% CI) ^b	Adjusted OR (95% CI)
Body mass index (kg/m²)								
<25 (normal weight)	1.0 ^c	1.0 ^c	1.0 ^c	1.0 ^c	1.0 ^c	1.0 ^c	1.0 ^c	1.0 ^c
≥25 and ≤30 (overweight)	2.04 (1.55–2.69)	1.82 (1.33–2.50)	1.23 (0.96–1.57)	1.18 (0.84–1.66)	1.58 (1.19–2.10)	1.50 (1.13–1.99)	1.18 (0.86–1.61)	1.14 (0.91–1.45)
>30 (obese)	3.45 (2.31–5.16)	2.91 (2.07–4.08)	1.29 (1.10–1.52)	1.19 (1.07–1.33)	2.52 (1.67–3.80)	2.23 (1.44–3.45)	1.32 (0.97–1.79)	1.22 (0.91–1.64)

^a Odds ratio.

^b Adjusted for age group, sex, smoking, alcohol intake, coffee consumption, active *Helicobacter pylori* infection, measures of adult socioeconomic status and use of painkillers, aspirin, NSAID.

^c Reference category.

obesity. Sex-specific multivariate models were also constructed and the associations between overweight/obesity and frequency and severity of heartburn and acid regurgitation did not differ between the sexes.

Discussion

Important strengths of this study are its large size, its population basis, and the inclusion of data relating to the principal potential confounders of the relationship between body mass and symptoms of gastro-oesophageal reflux, with the exception of dietary data. As in all community-based studies, participants in this study were self-selected and cannot be assumed to be representative of the population. Some care must therefore be employed in generalizing the findings beyond the study population. The response rate seems low but it must be borne in mind that this study was designed as a randomized controlled trial of *H. pylori* eradication and the overall response rate was 12.5% higher than that of a comparable study recently undertaken in Leeds, UK.²¹ Also, the distribution of obesity and overweight seen among participants in this study is very similar to that seen in the nationally representative sample.¹⁷ It is difficult to compare the prevalence of symptoms of gastro-oesophageal reflux in this study with previous epidemiological research in the UK as different instruments were used. However, 34.7% of subjects in this study had experienced either heartburn or acid regurgitation at least once a month in the 3 months prior to participating in the study which is quite similar to the finding of a recent UK postal questionnaire that 28.7% of subjects had experienced these symptoms on at least six occasions in the previous year.²² We cannot, though, claim that the study participants are fully population-representative; undoubtedly they are self-selected and people with symptoms may have been more likely to have taken part than those without symptoms. However, for our findings to stem from selection bias, specifically those subjects who were overweight/obese with few symptoms or normal weight with frequent symptoms would have declined to participate.

In our study, being overweight or obese were strongly related to the frequency of heartburn and acid regurgitation, independently

of potential confounding variables (including other dyspeptic symptoms). Obese subjects had heartburn almost three times more frequently than had subjects of normal weight. This positive association between body mass and gastro-oesophageal reflux is clearly biologically plausible as there are several important pathophysiological mechanisms linking body mass and reflux. Oesophageal transit in obese reflux patients is slower than in their leaner counterparts,²³ BMI is associated with the development of a hiatal hernia^{24,25} (an important factor in delaying the clearance of acid from the oesophagus²⁶), and there is evidence that increasing BMI increases intra-abdominal pressure,²⁷ although this may be counteracted by equivalent increases in lower oesophageal sphincter pressure.²⁸

Our findings are in keeping with three other cross-sectional questionnaire/interview-based studies in this field.^{6–8} A recently published study involving Korean subjects undergoing upper gastro-intestinal endoscopy as part of a routine health check also demonstrated a positive relationship between BMI and reflux oesophagitis.¹⁸ Follow-up of 12 500 subjects in the First National Health and Nutrition Examination Survey (NHANES I) for almost 20 years also showed that hospitalization for gastro-oesophageal reflux disease was related to BMI.¹⁹ However, it is possible that overweight or obesity *per se* may have been a factor influencing admission to hospital with GORD. These population-based studies add to data from investigations in clinical populations undergoing upper gastrointestinal endoscopy. Although such studies may be open to selection and detection biases¹ they provide evidence, from a number of countries, that endoscopically-diagnosed oesophagitis is more common in overweight or obese patients.^{24,25,29}

The failure of Lagergren *et al.*¹ to find an association between body mass and gastro-oesophageal reflux is clearly at odds with most literature in this field. Their negative result was observed among the controls of a case-control study of oesophageal adenocarcinoma. These controls were frequency matched with cases and therefore represent a small section of the general population, principally elderly males. Furthermore, the calculated BMI was not concurrent with the period of reporting of gastro-oesophageal symptoms, which related to 5 years before the date of interview.

On the basis of our study and others it appears that being above normal weight substantially increases the likelihood of suffering gastro-oesophageal reflux symptoms. It may follow that weight reduction will decrease the occurrence of these symptoms^{30,31} but a more robust evidence base is required upon which to base clinical recommendations of weight loss in patients with GORD. The strong positive association we have demonstrated between body mass and symptoms of gastro-oesophageal reflux also has relevance for the general population. Trends in overweight and obesity in western populations,^{16,17} are set to substantially increase, in coming years, the proportion of the population experiencing gastro-oesophageal reflux disease. There are many reasons why an increase in the prevalence of overweight and obesity holds trouble in store for public health and the provision of health services. To these must be added the costs of managing symptoms of gastro-oesophageal reflux and given the association between body mass, symptoms

of reflux, and risk of oesophageal adenocarcinoma,^{10–13} further increase in this, once uncommon, cancer seems likely.

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KEY MESSAGES

- Being above normal weight substantially increases the likelihood of suffering from heartburn and acid regurgitation.
- Obese people are almost three times as likely to experience heartburn and acid regurgitation as those of normal weight.

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Commentary: The relation of obesity, reflux and its implications

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The relationship between gastro-oesophageal reflux disease (GORD) and obesity seems at first thought an obvious one. Indeed one of the foremost treatment strategies adopted is advice on lifestyle. Patients are usually advised to lose weight if they are obese, drink less alcohol and caffeine, and stop smoking. However, the evidence behind these instructions appears to be flawed when looked at in more detail. This paper¹ aids in understanding the link between obesity and GORD.

The prevalence of GORD and obesity both appear to be increasing throughout the Western world. Oesophagitis can occur at any age but is more common in men than women, at a ratio of 2:1.² The natural history is that of a chronic relapsing condition.³ The causation between the two is still not clearly known but factors such as increased sensitivity of the oesophagus to acid, increased prevalence of hiatus hernia, increased intra abdominal pressure, and vagal abnormalities in obese patients may cause higher bile and pancreatic enzyme output, so making the resulting refluxate more toxic.⁴ In one paper there was a strong correlation between obese females and GORD, and it appeared compounded by the use of oestrogen replacement therapies. It was suggested that there is an association between increased oestrogen activity and the symptoms of GORD in obese females.⁵ In the treatment of GORD the medications used seldom vary in dose despite the varying size of patients. Body composition affects the pharmacokinetics of

drugs taken in the treatment of GORD. There are few data about the efficacy of drug treatments in obese patients but poor absorption or a larger distribution of body mass may lead to the medications being less effective in their action. Less effective treatment can lead to further complications in the long term.

Obesity is rapidly becoming a major health issue in terms of its burden on health and health planning. We know obesity is increasing in prevalence and its relationship to GORD is shown in the Murray *et al.* paper.¹ Studies from the US have shown that 20% of the population had a body mass index of >30 kg/m²; this figure has almost doubled from that of 20 years ago.⁶ The implications for health are highlighted not only with regards to GORD but also diabetes, hypertension, hyperlipidaemia, and heart disease, as well as sleep apnoea and liver disease.

Inheritance of GORD has been explored in twin studies and these certainly show a degree of genetic determination in susceptibility to GORD. One study showed an increased concordance for reflux in monozygotic compared to dizygotic twins and heritability accounted for 31% of the liability to reflux disease within the study population. The study also showed the concordance for reflux was not caused by inherited obesity.⁷

One of the important things arising from the increasing prevalence of obesity and GORD is the planning of health services and what may lie ahead as a sequelae. The problems associated with obesity as described earlier will have many implications for the delivery of services throughout the majority of medical specialities. Within the gastroenterological specialty the