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Risk factors for gastro-oesophageal reflux disease symptoms: a community study

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SUMMARY

Aim: To examine the prevalence of gastro-oesophageal reflux disease symptoms and potential risk factors among community subjects.

Methods: A questionnaire was sent to 4000 subjects, stratified by age, gender and ethnicity to be representative of the local population. Gastro-oesophageal reflux disease symptoms were defined as at least weekly heartburn or acid regurgitation.

Results: 2231 responded (59%), 691 refused to participate and seven were incomplete. 1533 (41%) were evaluable (637 male, mean age 51 years, range: 20–80). The prevalence of gastro-oesophageal reflux disease symptoms was 21%. Smoking, excess alcohol, irritable bowel syndrome, increasing body mass index, a family history of upper gastrointestinal disease, increasing Townsend deprivation index, anticholinergic drugs (all $P < 0.0001$), weight gain, antidepressant drugs, inhaled bronchodilators, no educational attainment (all $P < 0.01$), south Asian origin ($P = 0.02$) and manual work ($P < 0.05$) were associated with gastro-oesophageal reflux disease symptoms. Multivariate logistic regression revealed increasing body mass index, a family history of upper gastrointestinal disease, irritable bowel syndrome, south Asian origin (all $P < 0.0001$), smoking, excess alcohol, no educational attainment and anticholinergic drugs (all $P < 0.01$) were independently associated with gastro-oesophageal reflux disease symptoms.

Conclusions: Frequent gastro-oesophageal reflux disease symptoms affect 21% of the population. Increasing body mass index, a family history of upper gastrointestinal disease, irritable bowel syndrome, south Asian origin, smoking, excess alcohol, social deprivation and anticholinergic drugs are independently associated with gastro-oesophageal reflux disease symptoms.

INTRODUCTION

In the western world, symptoms of gastro-oesophageal reflux disease (GERD) are very common with 10–20% of the population reporting heartburn on a weekly basis in community studies.[1, 2] The most effective drug therapy for GERD is a proton-pump inhibitor (PPI).[3] In 1996, 5.7 million prescriptions were issued for PPIs in England, at a cost of £247 million.[4] GERD symptoms are also a major risk factor for the development of oesophageal adenocarcinoma,[5] the incidence of which is rising more rapidly than any other cancer.[6]

Population-based data on GERD are lacking in the UK. The only previous study failed to stratify patients according to whether they had frequent or infrequent GERD symptoms.[7] Frequent GERD symptoms are more strongly associated with oesophageal adenocarcinoma[5] and their aetiology may be different from infrequent GERD symptoms.

Previous community studies have identified associations between GERD symptoms and age,[8] smoking,[7–9]

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body mass index (BMI),[1, 2, 8] alcohol,[2] aspirin and non-steroidal anti-inflammatory drugs,[1, 10] social deprivation,[7] psychosomatism[1, 2] and a family history of upper gastrointestinal (GI) disease.[1, 2]

We have examined the prevalence of frequent GERD symptoms and the significance of a number of potential risk factors in an unselected community sample.

METHODS AND STUDY POPULATION

Study population

A random sample of 4000 adults stratified by age, gender and ethnicity to be representative of the Sandwell population at the 2001 Census was drawn from the Sandwell primary care trusts' database. This database contains information on all subjects registered with a general practitioner in Sandwell.

Questionnaire

Each subject was sent a 50-item questionnaire. The questionnaire records demographic details, symptoms of heartburn and acid regurgitation during the past year, health care utilization and potential risk factors for GERD [alcohol intake, BMI, drug therapy, a family history of upper GI disease in a first-degree relative, a spouse history of upper GI disease, parity, method of infant feeding, occupation, irritable bowel syndrome (IBS), educational attainment and current smoking]. The Townsend deprivation index was derived from the subjects' postcode.[11] The questionnaire has been validated in a hundred community subjects and has good validity for a diagnosis of GERD symptoms (based on at least weekly symptoms of heartburn or acid regurgitation) against an interview (κ: 0.68) and good reliability on re-test 4 weeks later in the 60 subjects who completed a second questionnaire (κ: 0.61).

The questionnaire was printed in English and the three most common ethnic minority languages in Sandwell (Urdu, Panjabi and Bengali). South Asian ethnic minority subjects were identified by their name and received an invitation letter, information sheet, and questionnaire in English and at least one other ethnic minority language based on their likely ethnic origin.[12]

Non-responders were sent a second questionnaire after 8 weeks and a reminder letter after 12 weeks if there was still no response. The study was approved by the Sandwell Local Research Ethics Committee.

Definitions

GERD symptoms were defined as at least weekly symptoms of heartburn or acid regurgitation. IBS was defined according to the Rome II criteria as at least 12 weeks in the preceding 12 months of abdominal pain or discomfort with at least two of: relief with defecation, change in stool frequency with pain or change in stool consistency with pain.[13]

Statistical analysis

Subjects' demographics and characteristics are reported as the mean and standard deviation for numerical factors and percentages and 95% confidence intervals (CI) for discrete characteristics. Categorical associations were analysed by the chi-squared test, continuous associations by the *t*-test. All *P*-values calculated were two-tailed and the α-level of significance was set at 5%. Multivariate forward stepwise logistic regression was performed with SPSS 10.0 software (SPSS Inc., Chicago, IL, USA). Effect sizes are expressed as odds ratios (OR) with 95% CIs. Associations between GERD symptoms and parity, method of infant feeding, oral contraceptive and hormone replacement therapy use were examined in women only.

RESULTS

Response

Following the first mailing, 212 people were identified by the postal service as no longer resident at the address recorded, eight were in nursing homes or too disabled to complete the questionnaire and 18 people had died. The eligible sample was therefore 3762 people. 2231 people responded (59%) of which 691 (18%) refused to participate and seven questionnaires were incomplete. The evaluable sample was therefore 1533 (41%) people with 637 males and a mean age of 51 years, s.d.: 16 (range: 20–80). Non-responders were more likely to be male (45% of men were non-responders cf 37% of women), younger (mean age 41, s.d.: 15 years cf responders 51 ± 16 years), of south Asian origin (62% of south Asians were non-responders cf 37% of whites) and resident in a deprived area (Townsend

deprivation index: 2.33 ± 2.74 cf responders 1.64 ± 2.75) (all $P < 0.0001$).

GERD symptom prevalence and health care utilization

The prevalence of GERD symptoms was 21% (95% CI: 19–23). 64% of subjects with GERD symptoms consumed antacids more than once a month. A quarter took prescription medication for their symptoms, mainly PPIs (17%). A third of the subjects with GERD symptoms had undergone either an endoscopy or a barium meal. 43% had consulted their general practitioner at least once in the past 12 months for GERD symptoms.

Univariate analysis of risk factors associated with GERD symptoms

The results of univariate analysis of risk factors associated with GERD symptoms are shown in Table 1. BMI data was not normally distributed and was therefore log-transformed prior to analysis. Log-BMI, IBS, anticholinergic drugs (antispasmodic drugs and tricyclic antidepressants), excess alcohol consumption (more than 30 units/week for men and more than 20 units/week for women), a family history of upper GI disease, current smoking and increasing Townsend deprivation index were associated with GERD symptoms (all $P < 0.0001$). Inhaled bronchodilators ($P = 0.005$), selective serotonin re-uptake inhibitor antidepressant drugs and weight gain as an adult ($P = 0.009$), no educational attainment ($P = 0.01$), south Asian origin ($P = 0.02$) and manual work ($P = 0.045$) were also associated with GERD symptoms. Risk factors not associated with GERD symptoms included age, gender, other prescription drugs (oral contraceptives, hormone replacement therapy, calcium-channel antagonists, benzodiazepines, aspirin or non-steroidal anti-inflammatory drugs and nitrates), parity, method of infant feeding and a spouse history of upper GI disease.

Table 1. Univariate analysis of risk factors associated with GERD symptoms

Risk factor	Odds ratio (95% CI)	*P*-value
Log-BMI*	23.16 (4.74–113.13)	<0.0001
IBS	4.21 (3.17–5.58)	<0.0001
Anticholinergic drugs	3.79 (2.16–6.66)	<0.0001
Excess alcohol†	2.87 (1.59–5.19)	<0.0001
Family history of upper GI disease	2.58 (1.97–3.37)	<0.0001
Current smoking	1.74 (1.29–2.36)	<0.0001
Townsend deprivation index	1.09 (1.05–1.15)	<0.0001
Inhaled bronchodilators	2.61 (1.34–5.09)	0.005
Antidepressant drugs	2.14 (1.21–3.80)	0.009
Weight gain as an adult	1.01 (1.00–1.02)	0.009
No educational attainment	1.38 (1.09–1.78)	0.01
South Asian	1.61 (1.08–2.39)	0.02
Manual work	1.57 (1.01–2.44)	0.045

* Odds ratio for log-BMI is for an increase of one in log-BMI, which is a 10-fold increase in BMI.
† Excess alcohol >30 units/week in men and >20 units/week in women.
GERD, gastro-oesophageal reflux disease; CI, confidence interval; BMI, body mass index; IBS, irritable bowel syndrome; GI, gastrointestinal.

Multivariate analysis of risk factors associated with GERD symptoms

All risk factors associated with GERD symptoms on univariate analysis were modelled using multivariate forward stepwise logistic regression analysis (Table 2). IBS, a family history of upper GI disease, log-BMI, south Asian origin (all $P < 0.0001$), no educational attainment ($P = 0.001$), excess alcohol consumption ($P = 0.003$), current smoking ($P = 0.004$) and anticholinergic drugs ($P = 0.004$) were independently associated with GERD symptoms.

Risk factors associated with GERD symptoms by gender

Univariate analysis of risk factors associated with GERD symptoms in women are shown in Table 3 and men in Table 4. Log-BMI, weight gain as an adult, inhaled bronchodilators and antidepressant drugs were only significantly associated with GERD symptoms in

Table 2. Multivariate analysis of risk factors associated with GERD symptoms

Risk factor	Odds ratio (95% CI)	*P*-value
Log-BMI	62.11 (9.87–390.98)	<0.0001
IBS	3.40 (2.45–4.70)	<0.0001
South Asian	2.66 (1.64–4.32)	<0.0001
Family history of upper GI disease	2.54 (1.86–3.47)	<0.0001
No educational attainment	1.69 (1.25–2.29)	0.001
Excess alcohol	2.96 (1.45–6.06)	0.003
Anticholinergic drugs	2.71 (1.38–5.33)	0.004
Current smoking	1.65 (1.17–2.33)	0.004

GERD, gastro-oesophageal reflux disease; CI, confidence interval; BMI, body mass index; IBS, irritable bowel syndrome; GI, gastrointestinal.

Table 3. Univariate analysis of risk factors associated with GERD symptoms in women

Risk factor	Odds ratio (95% CI)	*P*-value
Log-BMI	91.37 (13.62–613.04)	<0.0001
IBS	3.69 (2.58–5.27)	<0.0001
Family history of upper GI disease	2.15 (1.53–3.01)	<0.0001
Weight gain as an adult	1.03 (1.01–1.04)	<0.0001
Anticholinergic drugs	3.21 (1.66–6.21)	0.001
Antidepressant drugs	2.47 (1.32–4.62)	0.005
Inhaled bronchodilators	2.58 (1.23–5.45)	0.01
Townsend deprivation index	1.07 (1.01–1.14)	0.02
Current smoking	1.41 (1.02–1.96)	0.04

GERD, gastro-oesophageal reflux disease; CI, confidence interval; BMI, body mass index; IBS, irritable bowel syndrome; GI, gastrointestinal.

Table 4. Univariate analysis of risk factors associated with GERD symptoms in men

Risk factor	Odds ratio (95% CI)	*P*-value
IBS	5.53 (3.44–8.89)	<0.0001
Family history of upper GI disease	3.66 (2.35–5.71)	<0.0001
Excess alcohol	3.57 (1.80–7.08)	<0.0001
Townsend deprivation index	1.13 (1.05–1.21)	0.001
Anticholinergic drugs	6.25 (2.01–19.42)	0.002
Current smoking	1.97 (1.26–3.08)	0.003
Manual work	2.43 (1.20–4.90)	0.01
South Asian	1.76 (1.00–3.10)	0.05

GERD, gastro-oesophageal reflux disease; CI, confidence interval; IBS, irritable bowel syndrome; GI, gastrointestinal.

women. Excess alcohol consumption, south Asian origin and manual work were only positively associated with GERD symptoms in men. Associations with current smoking, IBS, a family history of upper GI disease, Townsend deprivation index and anticholinergic drugs were not gender-specific.

Risk factors independently associated with GERD symptoms in women included a family history of upper GI disease, IBS, anticholinergic drugs, current smoking and log-BMI (Table 5) and in men included a family history of upper GI disease, excess alcohol consumption, IBS and Townsend deprivation index (Table 6).

Risk factors associated with longstanding GERD symptoms

Univariate analysis of risk factors associated with a history of GERD symptoms for more than 10 years revealed associations with excess alcohol consumption OR 3.41 (95% CI: 1.35–8.62; $P < 0.01$), a family history of upper GI disease OR 1.89 (1.10–3.24; $P = 0.02$) and log-BMI 33.76 (1.16–982.21; $P = 0.04$).

Table 5. Multivariate analysis of risk factors associated with GERD symptoms in women

Risk factor	Odds ratio (95% CI)	*P*-value
Log-BMI	81.29 (9.43–700.73)	<0.0001
IBS	3.10 (2.08–4.62)	<0.0001
Family history of upper GI disease	1.90 (1.28–2.78)	0.001
Anticholinergic drugs	2.40 (1.10–5.24)	0.03
Current smoking	1.51 (1.04–2.18)	0.03

GERD, gastro-oesophageal reflux disease; CI, confidence interval; BMI, body mass index; IBS, irritable bowel syndrome; GI, gastrointestinal.

Table 6. Multivariate analysis of risk factors associated with GERD symptoms in men

Risk factor	Odds ratio (95% CI)	*P*-value
IBS	4.90 (2.95–8.15)	<0.0001
Family history of upper GI disease	3.74 (2.30–6.06)	<0.0001
Excess alcohol	3.23 (1.52–6.85)	0.002
Townsend deprivation index	1.10 (1.02–1.19)	0.02

GERD, gastro-oesophageal reflux disease; CI, confidence interval; IBS, irritable bowel syndrome; GI, gastrointestinal.

Multivariate analysis revealed that only excess alcohol consumption 3.15 (1.18–8.40; $P = 0.02$) and a family history of upper GI disease 1.89 (1.07–3.31; $P = 0.03$) were independently associated with a history of GERD symptoms for more than 10 years.

DISCUSSION

The prevalence of frequent GERD symptoms among this typical British urban population was 21%. Studies employing similar definitions of GERD symptoms have reported prevalences of 20% in the US,[2] 15% in Finland,[8] 9.8% in Spain[1] and only 2.5% in Chinese subjects in Hong Kong.[10] The increased prevalence in the UK and USA may relate to ethnic differences between the populations studied. Ethnicity has been shown to influence the prevalence of GERD symptoms,[1, 10] endoscopic oesophagitis[14, 15] and the complications of GERD – Barrett's oesophagus and oesophageal adenocarcinoma.[16–19] GERD symptoms, GERD and its complications are all more common among

whites.[15, 17, 19, 20] In the present study, GERD symptoms were more common among south Asian than white subjects. However, endoscopic oesophagitis has been noted to be much less common among south Asian and black patients than among whites.[15] The explanation for this apparent dichotomy may lie in a recent study which noted that although GERD symptoms were equally prevalent among white and black subjects, endoscopic oesophagitis was much more common among whites.[20] South Asian and black subjects may therefore be less prone to the complications of GERD or alternatively GERD symptoms may lack specificity for objective evidence of GERD among south Asians and blacks.

Increasing BMI was independently associated with GERD symptoms. This association has also been reported in the USA,[2] Finland[8] and Norway.[21] In the present study, the association between BMI and GERD symptoms was only found in women. The increased caloric intake of obese subjects and the hypothesized increased intragastric pressure because of obesity[22] are therefore unlikely to be responsible for this association. Similar findings were described in a case–control study in Sweden and an association between oestrogen replacement therapy and GERD was also noted.[23] Oestrogen has been reported to impair lower oesophageal sphincter (LOS) function[24] and it was suggested that increased plasma oestrogen levels in obese women were responsible for the increased prevalence of GERD.[23] However, in the present study, there was no association between oestrogen use as oral contraceptive or hormone replacement therapy and GERD symptoms. Further study of this association is clearly merited.

This study adds to the growing body of evidence implicating genetic factors in the aetiology of GERD. Case reports,[25] familial aggregation studies[26] and twin studies[27, 28] suggest a significant genetic contribution to the aetiology of GERD. A first-degree relative with GERD symptoms or upper GI disease was independently associated with GERD symptoms and furthermore this was one of two factors that distinguished subjects with GERD symptoms for longer than 10 years from those with a shorter history. This suggests that genetic factors may be particularly important in the aetiology of the complications of GERD (Barrett's oesophagus and oesophageal adenocarcinoma), as these conditions are associated with longstanding GERD symptoms.[5]

An association between IBS or psychosomatism and GERD symptoms has been reported by other authors.[1, 2, 7] There are two plausible explanations for this association. Patients with IBS frequently report other GI symptoms as a manifestation of their visceral hypersensitivity.[29] Patients with IBS are also more likely to report any given symptom, because of the association between IBS and psychosomatism.[30]

Epidemiological data consistently support an association between smoking and GERD symptoms.[1, 2, 7, 9, 10] Smoking may promote acid reflux by impairing LOS function,[31] slowing oesophageal acid clearance[32] or increasing the frequency of acid reflux episodes.[33]

Consumption of excess alcohol was independently associated with GERD symptoms. Two studies have described an association between alcohol intake and GERD symptoms[2, 10] but one study failed to find an association.[1] In the laboratory, alcohol impairs LOS function and increases acid reflux episodes.[34, 35] Excess alcohol consumption was also independently associated with longstanding GERD symptoms in the present study. It has been suggested that chronic excess alcohol may result in neuropathic damage resulting in impaired oesophageal motor function.[36]

Three measures were utilized to assess social deprivation – the Townsend deprivation index, occupation and lack of educational attainment. They were all positively associated with GERD symptoms on univariate analysis. Deprivation has been reported to be associated with oesophageal adenocarcinoma.[37, 38] The underlying causes of this association are uncertain but dietary differences are one possible explanation.[39]

Laboratory studies have revealed that a number of different drugs, including anitcholinergic drugs, benzodiazepines, calcium-channel antagonists and theophylline, decrease LOS pressure.[40] A community study of elderly subjects in Finland reported that GERD symptoms were associated with benzodiazepines and theophylline but not calcium-channel antagonists.[41] In the present study, anticholinergic drugs but not benzodiazepines or calcium-channel antagonists were independently associated with GERD symptoms. The most likely explanation for the differences between the laboratory and community studies is that anticholinergic drugs and benzodiazepines are prescribed for IBS or psychiatric disorders. IBS and psychiatric disorders are associated with psychosomatism and therefore increased reporting of GERD symptoms, as already discussed.

82% of the population of Sandwell is white and 18% non-white (mainly south Asian). Sandwell is therefore broadly comparable with the rest of England but has a

higher percentage of ethnic minority subjects than England as a whole, in which 92% of the population is white.[42] Our sample was drawn from a database of all subjects registered with a general practitioner in Sandwell. General practice registers offer the best means of sampling the general population in the UK.[43] However, studies such as this may be prone to response bias. The overall response rate was 59% and 41% took part in the study. The illiteracy rate in Sandwell has been reported to be 15%[44] and this may well have affected our response rate. Non-responders were more likely to be male, young, of south Asian origin and of deprived background, in common with previous community surveys,[7] and the results need to be interpreted in this context.

In conclusion, frequent GERD symptoms affected a fifth of this unselected community population. As in previous community studies of GERD symptoms, a family history of upper GI disease, IBS, smoking and excess alcohol intake was independently associated with GERD symptoms. In addition, increasing BMI in women, south Asian origin, social deprivation and anticholinergic drugs were found to be independently associated with GERD symptoms.

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