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ORIGINAL ARTICLE



Trends in gastro-oesophageal reflux in a Norwegian general population: the Tromsø Study 1979–2016

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ARSTRACT

Background: The prevalence of overweight and smoking has changed over time. However, whether the changes in the risk factors are reflected in the prevalence of gastro-oesophageal reflux disease (GORD) is unknown. The aims of this study were to assess the changes in prevalence of GORD and the associated risk factors over time in a general population.

Methods: This was a population-based study using repeated surveys of the Tromsø Study: Tromsø2 (1979–1980, n=14,279), Tromsø6 (2007–2008, n=11,460) and Tromsø7 (2015–2016, n=20,664). Complaints of heartburn and acid regurgitation and common risk factors were reported, and height and weight were measured. The prevalence of GORD was calculated and the association with risk factors was assessed at each time point by odds ratios (OR) and 95% confidence intervals (CI) using multivariable logistic regression.

Results: The prevalence of GORD was 13% in 1979–1980, 6% in 2007–2008 and 11% in 2015–2016. In all three surveys, the risk of GORD was consistently increased with overweight and smoking. However, overweight was a weaker risk factor in the first (OR 1.58, 95% CI 1.42–1.76) compared to the last (OR 2.16, 95% CI 1.94–2.41) survey. Smoking was a stronger risk factor in the first (OR 1.45, 95% CI 1.31–1.60) than at the last (OR 1.14, 95% CI 1.01–2.29) survey.

Conclusion: During four decades of follow-up of the same population, no clear change in prevalence of GORD was found. GORD was clearly and consistently associated with overweight and smoking. However, overweight has become a more important risk factor than smoking over time.

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KEYWORDS

Esophageal-disorders; cohort study; body mass index: tobacco: adults

Introduction

Gastro-oesophageal reflux disease (GORD) is due to pathological reflux of acidic gastric content to the oesophagus, leading to complaints of heartburn and acid regurgitations or complications [1]. Complications include mucosal erosions (oesophagitis), strictures, premalignant metaplasia of the mucosa (Barrett's oesophagus) and malignancy (adenocarcinoma). According to the current Montreal definition of GORD, the presence of GORD is defined as at least weekly reflux symptoms in most population-based studies [2].

The prevalence of GORD show great geographical variation, from 10% to 20% depending on the population [3]. A recent meta-analysis of the global prevalence of GORD found a pooled prevalence of 13.3% (95% confidence interval (CI) 12.0%–14.6%) [4]. The prevalence seems to be increasing, as studies conducted after 1995 report higher prevalence than those conducted before 1995 [3]. However, whether there is changing prevalence over time in the same population is uncertain. In addition to genetic factors, the main modifiable

risk factors of GORD are high body mass index (BMI) and tobacco smoking [4,5]. In most Western populations, BMI has increased considerable while smoking has decreased during the recent decades [6,7]. However, as high BMI is a stronger risk factor for GORD than smoking, the expected net effect is an increase in the prevalence of GORD over time.

The aim of the present study was to assess time-trends in the prevalence and risk factors of GORD in a general Norwegian population. Our hypothesis was that the prevalence of GORD has increased as the prevalence of overweight has increased in the general population.

Methods

The Tromsø study

The Tromsø Study is a population-based study where 45,000 inhabitants of Tromsø municipality, Norway, have participated in one or several of the seven surveys between 1974 and 2016 (Tromsø1-Tromsø7) [8–10]. In the present study, data from

Tromsø2 (1979–1980, n = 16,620,78%), Tromsø6 (2007–2008, n = 12,984, 66%) and Tromsø7 (2015–2016, n = 21,083, 65%) were used. In Tromsø2, all men aged 20-54 years and women aged 20-49 years were invited. In Tromsø6, all participants of Tromsø4 part 2, a random selection of 10% aged 30-39 years, all aged 40-42 years and 60-87 years and a random selection of 40% age 43-59 years were invited. In Tromsø7, all aged above 40 years were invited. Data collection included questionnaires, interviews, biological samples and clinical examinations.

Reflux symptoms and use of acid suppressive medication

Reflux symptoms were assessed through questionnaires using the following questions: "Do you have much complaints with acid regurgitation or heartburn?" with response alternatives "Yes" or "No" (Tromsø2), "To what degree have you had complaints with heartburn/acid regurgitations the last 12 months?" with response alternatives "Never", "A little" or "Much" (Tromsø6) and "How often have you had complaints with heartburn and/or acid regurgitation during the last 3 months?" with response alternatives "Never", "Monthly", "Weekly" or "Daily", where those reporting at least monthly complaints, received two follow-up questions: "To what degree have you had complaints with heartburn/acid regurgitations"" with response alternatives "None", "Some" or "Much", and "How long have you been bothered with heartburn and/or acid regurgitation?" with response alternatives "Less than a week", "Less than 3 months", "3-5 months", "6-12 months" or "More than 1 year" (Tromsø7). Use of acid suppressive medication was assessed by a questionnaire using the following question: "How often have you used acid suppressive medication during the last 4 weeks?" with response alternatives "Not used the last 4 weeks", "Less than weekly", "Every week, but not daily" or "Daily" (Tromsø7 only). Prevalent GORD was defined by the following responses to the reflux questions: "Yes" (Tromsø2), "Much" (Tromsø6) and "Weekly" or "Daily" (Tromsø7), corresponding to the current definition of GORD' [2].

Risk factors

Anthropometrical measurements were performed by trained personnel in all surveys. BMI was calculated as weight in kilograms (kg) divided by height in meters (m) squared (kg/m²) and defined as overweight if BMI >25 kg/m² according to the World Health Organization (WHO)'s definition [11]. Tobacco smoking was assessed through self-reported guestionnaires using the following questions: "Do you smoke ciqarettes daily?" with response alternatives "Yes" or "No" (Tromsø2) and "Do you smoke/have you been smoking daily?" with the response alternatives "Yes, now", "Yes, previously" or "Never" (Tromsø6 and Tromsø7), of which "Yes" (Tromsø2) or "Yes, now" (Tromsø6 and Tromsø7) was defined as current daily smoking'.

Statistical analyses

The prevalence of GORD was assessed for each survey by sex and 10-year age groups: 20–29 years (Tromsø2), 30–39 years (Tromsø2 and Tromsø6), 40-49 years (Tromsø2, Tromsø6 and Tromsø7), 50–59 years, 60–69 years, 70–79 years or above 80 years (Tromsø6 and Tromsø7). Further, multivariable logistic regression models were used to examine the association between sex (women; men), age (10-year age groups), overweight (BMI $<25 \text{ kg/m}^2$; BMI $\ge 25 \text{ kg/m}^2$) and smoking (never/previous; current) (exposures) and GORD (no; yes) (outcome), reporting odds ratios (ORs) and 95% CIs. All analyses were performed in Stata version 15.1 (StataCorp, College Station, Texas, USA).

Ethical approval

Tromsø6 (reference 121/2006) and Tromsø7 (reference 2014/940) were approved by the Regional Ethical Committee for Medical and Health Research Ethics North.

Results

Characteristics

In total, 14,279 (Tromsø2), 11,460 (Tromsø6) and 20,664 (Tromsø7) participants responded to the reflux questions (Table 1). The mean BMI of the population and the

Table 1. Characteristics of the study population. The Tromsø Study 1979–2016.

	Tromsø2 1979–1980	Tromsø6 2007–2008	Tromsø7 2015–2016
Destining the total are (0/)			
Participants total, no. (%)	16,621 (77.5)	12,984 (65.7)	21,083 (64.7)
Participants reporting on GORD, no.	14,279	11,460	20,664
Age in years, median (range)	34 (20–54)	58 (30–80)	57 (40–99)
Women, no. (%)	8,120 (49.0)	6,928 (53.4)	11,074 (52.5)
Women, in age groups, no. (%)			
20–29 years	3,112 (38.3)		•
30–39 years	3,147 (38.8)	297 (4.3)	•
40–49 years	1,860 (22.9)	1,912 (27.6)	3,378 (30.5)
50–59 years		1,289 (18.6)	3,245 (29.3)
60–69 years		2,107 (30.4)	2,677 (24.2)
70–79 years		988 (14.3)	1,361 (12.3)
80+ years		335 (4.8)	411 (3.7)
Body mass index (kg/m²), mean (sd)	23.5 (3.2)	26.9 (4.3)	27.3 (4.5)
Overweight, no. (%)	4,420 (27.3)	8,440 (65.1)	14,269 (67.9)
Smoking, no. (%)			
Current	8,457 (51.0)	2,610 (20.4)	2,904 (13.9)
Previous		5,407 (42.3)	9,250 (44.3)
Never		4,767 (37.3)	8,733 (41.8)

GORD: gastro-oesophageal reflux disease; Overweight: body mass index >25 kg/m²; sd: standard deviation.

prevalence of overweight increased with time and among those 40-49 years, the proportion of overweight was 27% in 1979-1980, 65% in 2007-2008 and 68% in 2015-2016. The prevalence of smoking decreased with time and among those 40-49 years, the proportion was 51% in 1979-1980, 20% in 2007-2008 and 14% in 2015-2016.

Prevalence

The overall prevalence of GORD was 13% in 1979-1980, 6% in 2007-2008 and 11% i 2015-2016 (Table 2). In the age group 40-49 years, the prevalence was 15% in 1979-1980, 5% in 2007–2008 and 9% i 2015–2016 for both sexes combined.

Risk factors

The risk of GORD over time was consistently higher with overweight and current daily tobacco smoking (Table 3). Overweight was a weaker risk factor in the first (OR 1.58, 95% CI 1.42-1.76) compared to the last (OR 2.16, 95% CI 1.94–2.41) survey, while smoking was a stronger risk factor in the first (OR 1.45, 95% CI 1.31-1.60) compared to the last (OR 1.14, 95% CI 1.01-2.29) survey.

Table 2. The prevalence of gastro-oesophageal reflux disease, by survey, sex and age. The Tromsø Study 1979-2016.

	Tromsø2 1979–1980	Tromsø6 2007–2008	Tromsø7 2015–2016
	(N = 14,279)	(N = 11,460)	(N = 20,664)
In total, no. (%)	1,883 (13.2)	650 (5.7)	2,326 (11.3)
Women, no. (%)	714 (10.1)	343 (5.7)	1,268 (11.7)
20-29 years	250 (9.2)	•	•
30-29 years	272 (9.9)	10 (3.7)	
40-49 years	192 (12.2)	90 (5.1)	286 (8.6)
50–59 years		58 (5.0)	351 (11.0)
60–69 years		127 (7.0)	366 (14.0)
70-79 years		41 (5.3)	198 (15.1)
80+ years		17 (7.8)	67 (17.7)
Men, no. (%)	1,169 (16.2)	307 (5.6)	1,058 (10.8)
20-29 years	291 (13.8)	•	
30–39 years	444 (16.5)	8 (4.6)	
40-49 years	291 (17.7)	89 (5.8)	307 (10.2)
50–59 years	143 (18.5)	70 (6.6)	283 (10.3)
60–69 years		90 (5.0)	290 (11.8)
70–79 years		43 (6.0)	137 (10.7)
80+ years	•	7 (4.6)	41 (12.7)

Table 3. The risk (odds ratio and 95% confidence interval) of gastro-oesophageal reflux disease, by survey and risk factor. The Tromsø Study 1979–2016.

	Tromsø2 1979–1980 (N = 14,279)	Tromsø6 2007–2008 (N = 11,460)	Tromsø7 2015–2016 (N = 20,664)
Men ^a	1.53 (1.38-1.70)	0.91 (0.77-1.08)	0.82 (0.75-0.89)
Age, per 10 years increase ^b	1.12 (1.06–1.19)	1.04 (0.98–1.11)	1.16 (1.11–1.20)
Overweight ^c	1.58 (1.42-1.76)	2.30 (1.89-2.81)	2.16 (1.94-2.41)
Smoking ^d	1.45 (1.31–1.60)	1.40 (1.16–1.69)	1.14 (1.01–2.29)

Overweight: body mass index (BMI) >25 kg/m^b.

Acid suppressive medication

In Tromsø7, 17% of the participants reported using acid suppressive medication during the last four weeks (Table 4). Among participants reporting GORD, 70% used acid suppressive medication during the last four weeks, compared to 10% among those not reporting GORD.

Discussion

During four decades of follow-up, no clear trend in the prevalence of GORD was found in this general Norwegian population of adult women and men. Throughout, GORD was clearly and consistently associated with overweight and smoking. However, overweight became a stronger risk factor than smoking over time.

The prevalence of GORD found in the present study is in line with the prevalence found in comparable Western populations [3,4,12]. However, the present study could not find a clear increase in the prevalence over time as expected. In the population-based Trøndelag Health Study (HUNT), Norway, the overall prevalence of GORD increased by 47% from 11.6% in 1995-1997 to 17.1% in 2006-2009 [12]. This increase was found for both sexes and all age groups. However, direct comparison between the HUNT Study and the Tromsø Study is limited, as the HUNT Study has shorter follow-up time and only covers the decennium before Tromsø6.

The increased risk of GORD with overweight and smoking is in line with previous studies [4,5,13-15]. Probably, the increased mean BMI seen over time in the population made overweight a stronger risk factor in the later surveys. The opposite is probably true for smoking. Globally, the pooled OR of GORD in obese (BMI $>30 \text{ kg/m}^2$) compared to nonobese was 1.73 (95% CI 1.46-2.06) and the pooled OR of GORD in smokers compared to non-smokers was 1.26 (95% CI 1.04-1.52) [4]. In the HUNT Study, BMI was dose-dependently associated with new-onset GORD during 11 years follow-up (OR 1.30, 95% CI 1.25-1.35, per unit increase in BMI), irrespective of baseline BMI [5]. Moreover, current smoking was associated with new-onset GORD (OR 1.29, 95% CI 1.00-1.67). Interestingly, smoking cessation was also associated with new-onset GORD, due to weight gain associated with smoking cessation (OR 2.03, 95% CI 1.31-3.16, among

Table 4. Use of acid suppressive medication during the last four weeks, by gastro-oesophageal reflux disease (GORD), sex and age. The Tromsø Study 2015–2016.

GORD	Not GORD
1,595 (70.0)	1,821 (10.4)
901 (73.3)	953 (10.6)
201 (71.5)	199 (6.7)
254 (73.4)	264 (9.6)
265 (74.9)	282 (13.3)
140 (74.9)	160 (16.8)
41 (66.1)	48 (20.3)
694 (67.8)	876 (10.3)
189 (62.4)	189 (7.1)
193 (70.4)	228 (9.5)
200 (71.4)	256 (12.2)
88 (68.8)	165 (15.3)
24 (63.2)	38 (15.0)
	1,595 (70.0) 901 (73.3) 201 (71.5) 254 (73.4) 265 (74.9) 140 (74.9) 41 (66.1) 694 (67.8) 189 (62.4) 193 (70.4) 200 (71.4) 88 (68.8)

Adjusted for age, BMI and smoking; women as reference.

^bAdjusted for sex, BMI and smoking; youngest age group as reference.

^cAdjusted for sex, age and smoking; normal weight (BMI <25 kg/m^b) as reference.

^dAdjusted for sex, age and BMI; never or previous smoking as reference.

smoking guitters with >3.5 units increase in BMI). As in the present study, the HUNT Study showed that overweight was a stronger risk factor for GORD than tobacco smoking.

In the present study, despite the considerable increased prevalence of overweight in the general population over time and the clear association with GORD, this has not translated in an increased prevalence of GORD. This could not be explained by increase in age nor increased use of acid suppressive medication.

The major strength of the present study is the use of a population-based sample with almost 40 years of follow-up to study the prevalence of GORD during a time-period of considerable changes in two main risk factors, smoking and overweight. The use of objectively measured height and weight reduces the risk of misclassification of the most important risk factor.

A limitation of the study is the lack of objective assessment of GORD. However, in comparable epidemiologic studies, GORD is defined by self-reported questionnaires. Another limitation is that different questions were used to assess GORD in each survey of the Tromsø Study i.e., the three surveys are not directly comparable. However, all questions used are in line with the current Montreal definition where GORD is defined as the presence of at least weekly reflux symptoms. A general limitation is that participants in population-based studies tend to be healthier than non-participants [16]. Although not all age-groups were represented in all surveys, the result of the age group 40-49 years corresponds well with the main result and argues for a valid conclusion. The rate of surgical management of GORD (fundoplication) has generally been reduced over time, but information on this in the Tromsø population is not available over the 37year time span of the present study, thus could not be assessed.

In conclusion, no clear change in prevalence of GORD was found in this general population followed for 37 years. GORD was clearly and consistently associated with overweight and smoking. However, overweight has become a more important risk factor than smoking over time.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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