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Is There Any Association Between Overweight, Obesity and Symptoms of Reflux Disease?

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Abstract: The present study was aimed to identify the association of overweight and obesity with gastroesophageal reflux disease (GERD). This age- and sex-matched case-control study was carried out in a sample of subjects referred to the specialized clinic of Tabriz University of Medical Sciences from November 2006 to March 2007. Data were collected using a demographic questionnaire and a checklist to determine reflux symptoms. Weight and height were measured and Body Mass Index (BMI) was calculated. Logistic regression was used to examine the association between overweight, obesity and reflux symptoms. The study population included 106 cases (with reflux symptoms) and 111 controls with a mean age of 35.2±12.9 years. The mean BMI was 2.4 units greater in cases than controls (p = 0.0001). In unadjusted model, overweight (OR = 3.41, CI: 1.8-6.44) and obesity (OR = 2.84, CI: 1.38-5.82) were significantly associated with GERD. Results of multivariate logistic regression revealed significant association between overweight and GERD after adjusting for confounders (OR = 2.87, CI: 1.49-5.53). Given the increasing prevalence of patients with both overweight/obesity and GERD, Serious dietary intervention studies for weight loss as a therapeutic strategy should be carried out in GERD patients complicated with obesity.

Key words: BMI, obesity, overweight, reflux, GERD

INTRODUCTION

Obesity is becoming more and more prevalent across the world. It is well associated with several chronic diseases, such as cardiovascular disease, diabetes mellitus type II and gastrointestinal diseases including gastroesophageal reflux disease (GERD), gallbladder stone and cancer, colon cancer (Kang *et al*., 2006).

GERD is a pathologic condition of the esophagus caused by regurgitation of gastric or gastroduodenal contents into the lumen of the esophagus (Wetscher *et al*., 1993). Epidemiologic studies showed that the prevalence of GERD is between 10 to 48% in western countries and up to 5% in Asia (Dent *et al*., 1999). In Iran, according to a population-based study (Khoshbaten, 2003), it is estimated to be 2.7%, similar to other Asian countries. It has been reported that lower BMI, genetic factors and less fat consumption account for low prevalence of GERD in Asian countries (Szarka *et al*., 2001). Subjects with long-standing GERD are at increased risk for esophageal adenocarcinoma (Farrow *et al*., 2000). Mechanisms of GERD have been poorly understood. However, obesity has been postulated as one of the risk factors for GERD. Studies conducted on the association between BMI and GERD have conflicting results (El-Serag *et al*., 2005a; Locke *et al*., 1994; Murray *et al*., 2003; Nandurkar *et al*., 2004; Nilsson *et al*., 2003; Ruigomez *et al*., 2004; Talley *et al*., 2004; Wang *et al*., 2004). Of these, three found a modest positive association (Chang *et al*., 1997; Ruhl and Everhart, 1999; Wilson *et al*., 1999), one reported no association (Furukawa *et al*., 1999) and another detected a positive association in women but not in men (Nilsson *et al*., 2002). Therefore, the present study was aimed to identify the association between overweight, obesity and GERD.

MATERIALS AND METHODS

Subjects: A total of 217 subjects consented to participate in our case-control study. The sample frame was selected among patients who visited the specialized clinic of Tabriz University of Medical Sciences for different purposes from November 2006 to March 2007. This clinic is the

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major provider of medical care in Tabriz, Northwest of Iran. Enrolled subjects were all 14 years or older.

Study protocol: Subjects were asked whether they had recurrent heartburn, acid regurgitation, or both at least monthly in prior 12 months; if so, all being suspected of having GERD were referred to an experienced gastroentrologist for GERD diagnosis. After the disease confirmation, patients were assigned to case group. Subjects who had not experienced any of the mentioned symptoms during the last 12 months were selected as controls, matched for sex and age. The following exclusion criteria were applied at baseline: gastric surgery, esophageal or gastric cancer, history of vagotomy, confirmed peptic ulcer disease, dieting such as weight loss diet, use of LES-motility changing drugs such as calcium-channel blockers and nitrates, Proton Pump Inhibitors (PPIs), H_2 Receptors Antagonists (H_2-RA) and contraceptive/hormonal medications. As heartburn and acid regurgitation are the two main symptoms of GERD, therefore assessing these symptoms can be reliable to measure the true occurrence of reflux and to allow appropriate treatment (Klauser *et al*., 1990; Locke *et al*., 1994; Revicki *et al*., 1998; Ter and Castell, 1997). Therefore, GERD diagnosis was based on a GERD symptom checklist. This included specific questions about the type and frequency (at least weekly or monthly) of symptoms. It is noteworthy that endoscopy, being invasiveness, was offered only to patients who did not respond to GERD treatment or lifestyle modifications. Data including age, marital status, education level, occupation, smoking and post-menopausal status were gathered. Weight and height of subjects were measured in light clothing and without shoes by a trained person, respectively. Measurement of height and weight were taken both standing. Weight was measured with a calibrated seca scale (made in Germany) to the nearest 0.1 kg and height with a wall-mounted stadiometer to the nearest 0.1 cm. BMI was calculated as body weight (kg) divided by the square of height (m^2). The standard for BMI, based on WHO classification, was as follow: BMI<25 kg m^{-2} as normal; 25-29.9 as being overweight and ≥30 as obesity.

Statistical analysis: Statistical analysis of the data was carried out using SPSS software (Version 11.5). For continuous variables, mean and standard deviation were presented. χ^2-tests were performed to test associations for categorical variables and t-tests were used for continuous variables. BMI measurement was analyzed as continuous as well as categorical variables categorized by tertiles in which lowest tertile served as the reference group. The association of GERD with BMI was assessed using a logistic regression model that no reflux was the reference category. Univariate logistic regression was performed to calculate odds ratios and 95% confidence intervals. Furthermore, the associations were assessed based on fitting multiple logistic regression models adjusted for education level. All calculated p-values were two-sided and p-values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Of 217 participants, 106 (48.8%) had experienced GERD symptoms (case group) and 111 (51.2%) were controls. Of 106 cases, 69 (65.1%) had at least weekly symptoms while 37 (34.9%) complained of monthly symptoms. The mean age (±standard deviation) of cases and controls were 35.3±12.6 and 35.1±13.2 years, respectively and 73.7% were females (Table 1). As shown in Table 1, only education level differed markedly between cases and controls ($p<0.001$). Mean BMI was 26.5±5.32 kg m^{-2}. More than half of the patient population was overweight (44.3%) or obese (26.4%) (Table 1).

Table 1: BMI and demographics between participants with and without GERD symptoms

Variables	GERD symptoms (n = 106) n (%)	No GERD symptoms (n = 111) n (%)	p-values
Age (year)			
Mean±SD	35.3±12.6	35.1±13.2	0.9
<35 year	55 (51.9)	64 (57.7)	
≥35 year	51 (48.1)	47 (42.3)	
BMI (kg m^{-2})			
Mean±SD	27.7±5.6	25.3±4.7	0.0001
<25	31 (29.2)	63 (56.8)	
25-29.9	47 (44.4)	28 (25.2)	
≥30	28 (26.4)	20 (18.0)	
Gender			
Male	27 (12.4)	30 (13.8)	0.4
Female	79 (36.4)	81 (37.3)	
Occupation			
Unemployed	89 (84)	91 (82)	0.1
Non-governmental	10 (9.4)	13 (11.7)	
Retired	3 (2.8)	8 (7.2)	
Housewife	62 (58.5)	46 (41.4)	
Student	14 (13.2)	24 (21.6)	
Employed	17 (16)	20 (18)	
Education			
Illiterate	20 (9.2)	8 (3.7)	0.007
Literate	67 (31)	64 (29.5)	
Higher education	19 (8.8)	39 (18.8)	
Marital status			
Single	25 (11.5)	34 (15.7)	0.4
Married	81 (37.3)	77 (35.5)	
Smoking			
None-smoker	103 (47.5)	110 (50.7)	0.2
Menopausal status			
Yes	14 (8.9)	9 (5.7)	0.1
No	64 (40.8)	70 (44.6)	

Table 2: Results of logistic regression analyses examining the probability of GERD

Variables	OR (95% CI)
Unadjusted (continuous variables)	
BMI (per 1 unit)	1.03 (1.00-1.06)
Unadjusted (categorical variables)	
BMI	
>30	2.84 (1.38-5.82)
25-30	3.41 (1.80-6.44)
<25	
Adjusted model[†]	
BMI	
>30	2.04 (0.94-4.42)
25-30	2.87 (1.49-5.53)
<25	

OR: Odd Ratio, CI: Confidence Interval, BMI: Body Mass Index, [†]: Adjusted for education level

Cases had significantly higher BMI than controls (Table 1). The mean BMI was 2.4 units greater in cases than controls ($p = 0.0001$). More importantly, the proportion of overweight and obese patients with BMI>25 kg m^{-2} was 1.6 fold higher in cases, compared to controls (70.7% vs 43.2%). In univariate logistic regression, higher BMI as continuous variable was significantly associated with GERD (OR = 1.03, CI: 1.00-1.06) (Table 2). In unadjusted model, obesity increased the risk of GERD to approximately 3 fold (OR = 2.84, CI: 1.38-5.82), but being overweight increased it to 3.5 fold (OR = 3.41, CI: 1.8-6.44).

Results of multivariate logistic regression revealed significant association between BMI and GERD after adjusting for education level as a confounding factor (OR = 1.06, CI: 1.00-1.13). Only overweight was significantly associated with GERD after adjusting for confounders (OR = 2.87, CI: 1.49-5.53).

In this study, the association of overweight and obesity with GERD was investigated. More than half of the population was overweight or obese. We found a significant difference in BMI between the two groups. We also detected a strong association between BMI and GERD as have others (Nilsson *et al*., 2002, 2003; Locke *et al*., 1999; Wilson *et al*., 1999), but not all studies agree (Lagergren *et al*., 2000; Shapiro *et al*., 2007). The inconsistency in studies could be due to specific cut-offs for BMI, the study population and the absence of association (Van Oijen *et al*., 2006). However, the results of a meta-analysis showed that obesity is associated with statistically significant increase in the risk for GERD symptoms, erosive esophagitis and esophageal adenocarcinoma (Hampel *et al*., 2005).

Present study also demonstrated that overweight affects GERD more than obesity, i.e., overweight is associated with approximately 3 fold GERD development, whereas obesity increases the risk of GERD 3.5 times. That is because obese patients were fewer than overweight patients in the present study. Jacobson *et al*. (2006) performed a study on women and indicated that BMI was associated with symptoms of GERD in both normal weight and overweight women. In a population-based study (Ruhl and Everhart, 1999), a total of 12,349 subjects who participated in the first National Health and Nutrition Examination Survey were followed for about 18.5 years. The results revealed GERD hospitalization is due to higher BMI; according to this study, overweight but not high dietary fat intake can trigger GERD.

The mechanisms through which obesity affects GERD are not completely understood. However, obesity can trigger GERD by mechanical, hormonal and dietary intake. Among mechanical factors, abdominal obesity can increase the risk of GERD by increasing intragastric pressure and consequently, provoking transient Lower Esophageal Sphincter (LES) relaxations, considered as one of the most important mechanisms for reflux, especially in patients with normal resting LES pressure (Xing and Chen, 2004). It has been reported ~ 55 to 80% of reflux episodes result from transient LES relaxations in GERD patients (Mittal *et al*., 1995; Dodds *et al*., 1982). Other factors such as hiatus? hernia that leads to decreased esophageal clearance capacity (Mittal *et al*., 1987) and impaired esophageal motility (Xing and Chen, 2004) may trigger GERD.

Hormonal factors seem to be an effect modifier of the association between BMI and reflux (Nilsson *et al*., 2003). According to Nilsson *et al*. (2002, 2003), estrogen may play an important role in the etiology of GERD. Mechanisms for observed effect are due to lower concentration of sex-hormone binding globulin and consequently, higher unbound, active stradiol in obese women, increased synthesis of estrone in fatty tissues of obese women (Hautanen, 2000), occurrence of reflux symptoms in the first trimester of pregnancy (Day and Richter, 1990), reduced LES tone by contraceptive medication (Van Thiel *et al*., 1976) and increased synthesis of nitric oxide (LES relaxing agent) as a result of estrogen (Hirsch *et al*., 1998; Konturek *et al*., 1997) in animal (Nuedling *et al*., 1999) and human (El-Serag *et al*., 2005b) studies.

Dietary intake, as another mechanism, is postulated to affect GERD. However, results of studies on the effect of diet (most notably fat) on GERD are inconsistent (El-Serag *et al*., 2005a; Nandurkar *et al*., 2004; Shapiro *et al*., 2007). Therefore, dietary intake can not be a good explanation for the effect of obesity on GERD (Hampel *et al*., 2005).

This study owns some advantages. First, it is a case-control study consisting of both genders. Second, it has

adequate power to detect the differences between BMI and GERD. Third, weight and height were not self-reported, but measured by a trained person.

We acknowledge some limitations. This is a clinical-based but not a population-based study. Meanwhile, misclassification might exist since endoscopy was not offered to all patients, however, suspected cases were excluded and only those who had at least monthly symptoms of GERD were selected.

CONCLUSION

The increasing prevalence of patients with both overweight/obesity and GERD requires evaluation of the appropriate dietary intervention for GERD and its symptoms. Serious dietary intervention studies for weight loss as a therapeutic strategy should be carried out in GERD patients complicated with obesity.

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