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## **Regular post dinner walk; can be a useful lifestyle modification for gastroesophageal reflux**

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### **Abstract**

**Objectives:** To evaluate the correlation of gastroesophageal reflux disease (GERD) symptoms with routine post dinner physical activity and time interval before going to bed, in multiethnic South Asian population.

**Methods:** Prospective, cross sectional analytical, multicenter study was conducted from February 2009 to March 2010. Patient's relative sitting in outpatient clinics with no comorbidities, nonsmoker and non alcoholic were included. They were asked to fill a validated GERD questionnaire and were also inquired about routine post dinner physical activity (lying, sitting, walking) and dinner-bed time interval. Odds Ratios (OR) and their 95% Confidence Intervals (CI) were estimated using Logistic Regression, with gastroesophageal reflux (GER) symptoms as an outcome.

**Results:** Subjects analyzed were 1875. Mean age was  $35.37 \pm 12.69$  years of which 689 (36.74%) had GERD symptoms. GERD symptoms were 42.08% in routine post dinner recumbency position. While 35.17% and 30.52% had the symptoms in post dinner sitting and walking before going to bed [OR for walking 0.66(95% CI 0.5-0.88) when compared with lying posture]. GERD symptoms were 45.86 % among those with dinner-bed time of one hour, progressively decreasing to 41.68 %, 31.45 % and 29.88 % in the second, third and fourth hour respectively. Odds ratio was significant only at 3rd [0.55(0.41-0.74)] and  $\geq$  4th hr [0.51(0.37-0.71)] when compared with first hour.

**Conclusion:** Regular post dinner walk and > 3 hour dinner-bed time interval were less associated with GERD symptoms.

**Keywords:** GERD, Routine post dinner activity, Dinner-bed time interval (JPMA 61:526; 2011).

### **Introduction**

Gastroesophageal reflux disease (GERD) is one of the common disorders of upper gastrointestinal tract.<sup>1</sup> The prevalence of GERD worldwide ranges from less than 5% in Asia to 10-20 % in Western world and is more prevalent in North America as compared to Europe.<sup>2-4</sup> It is also common in urban population of Pakistan.<sup>5</sup> GERD is characterized by the reflux of acidic contents across the lax or incompetent gastroesophageal junction. This reflux results in mucosal injury and inflammation in the distal esophagus.<sup>6</sup> Several factors, alone or in combination contribute to the development of GERD. It may include decreased basal tone of lower esophageal sphincter, impaired esophageal clearance, delay in gastric emptying, hiatal hernia and failure of esophageal mucosal resistance (mucus layer and surface bicarbonate ion concentration).<sup>3</sup> Reflux symptoms can also be triggered by dietary and lifestyle habits including positioning, physical activity, lying down, food, drink and drugs.<sup>7</sup> Gastroesophageal reflux disease has a range of manifestations from common symptoms of retrosternal burning, regurgitation, heartburn to alarming features like dysphagia, odynophagia, weight loss and anaemia. If

untreated, the persistent exposure of acidic reflux may result in complications like erosive esophagitis, Barrett's esophagus and distal esophageal adenocarcinoma.<sup>8-10</sup> Commonly applied diagnostic tools are endoscopy, pH monitoring and response to proton pump inhibitor (PPI). Therapy is aimed to relieve symptoms, improve quality of life and prevent complications. Treatment options for GERD include lifestyle modifications, PPI course in patients without alarming features to surgical intervention in patients with alarming features and persistent symptoms.<sup>1</sup>

Lifestyle measures have an important bearing on GERD symptoms. Different body postures, smoking, alcohol intake, high dietary fat, lack of physical activity, and post meal early recumbency modifications have been suggested for GERD therapy, including avoiding early post meal recumbency but concrete evidence is lacking for its efficacy in GERD. Most of the literature is from western world where GERD has a high incidence. South Asian population differs from the West in many aspects by dietary habits, anthropometric scale, physique, climate and GERD prevalence.<sup>1,11-15</sup> It may be possible that the result of this study may be contrary to the West. The focus of this study is

to evaluate the impact of lifestyle behaviour in relation with routine post dinner physical activity and dinner to bed time interval on classic GERD manifestation, including post meal retrosternal burning, regurgitation and heartburn.

## Methods

This multicenter, prospective, cross sectional study was conducted from Feb 2009 to March 2010. Study population was 18 years and above relatives of the patients in the outpatient clinics of different section/center of tertiary care hospitals, with no prior history of any comorbid (i.e. diabetes, hypertension, ischaemic heart disease, chronic renal disease and stroke). They were randomly selected by computer generated chart and screened as potential study subjects after taking informed consent. Subjects with history of acid peptic disease, chronic liver disease, smoking, alcohol, history of drugs (i.e. Aspirin, NSAIDS, Beta-blocker or any other drugs during last 6 months) or with any of the above mentioned comorbid were excluded. Sample size was calculated with GERD prevalence of 24% from one of the local studies.<sup>6</sup> With power of 80%, level of significance of 0.05 and error of 2% sample size was calculated as 1750 and due to non-responder sample size was inflated by 7-10%. Study subjects were provided with a validated modified "Ritcher Acid Scale" questionnaire.<sup>5</sup> This questionnaire has already been validated and translated in local language with reverse translation for one of the studies conducted at gastroenterology, department of medicine Aga Khan University hospital in 2005.<sup>5</sup> Team of trained volunteer administered the questionnaire to the study participant who then filled it out on their own and if the study subjects had any query, that was explained by the volunteers. In questionnaire they were asked about GERD screening questions such as presence of retrosternal burning or discomfort from epigastrium to mouth, burning at back of throat, sour / bitter taste, post meal GERD symptoms, GERD symptoms two or more than two times per week. Two or more than two "Yes" for questions was indication of presence of GERD symptoms. They were splitted into two groups on the basis of presence or absence of gastroesophageal reflux symptoms. Additionally, they were asked about time duration from dinner to bed on most of the days in a week. Time duration was divided into four categories i.e. 1 hour, 2 hour, 3 hour and  $\geq 4$  hour post dinner to bed. They were asked about meals they eat most of the days in a week. Moreover, they were asked about physical activity after dinner and before going to bed or recumbency. Physical activity was assessed as their habit that included direct post dinner recumbency and sitting or walking before going to bed on most of the days in a week. Questionnaire included age, gender, cultural background (from all provinces of Pakistan), and education level (i.e. from illiterate, 5th level, 8th level, 10th level, 12th level to

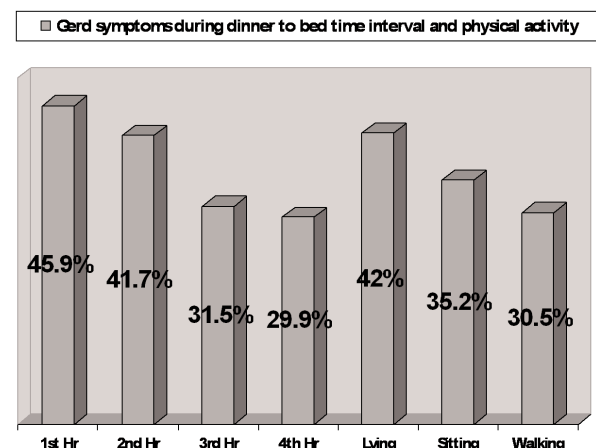
graduates). Age of study subjects was divided into three groups to observe the association of GERD symptoms with increase in age i.e. A:  $\leq 30$  years, B: 31-50 years and C:  $> 50$ years. Investigator calculated the body mass index (ratio of weight in kg to height in  $m^2$ ). The protocol of this study was approved by Ethical Board Review Committee at Aga Khan University Hospital Karachi, Pakistan.

A descriptive analysis was performed for demographic, clinical features and results are presented as mean  $\pm$  standard deviation for quantitative variables like age and BMI; number (Percentage) for qualitative variables like gender, GERD symptoms. Differences in proportions for GERD symptoms present and absent were assessed by using the Chi-square test or Fisher exact test where appropriate. For contrasts of continuous variables, independent sample t-test was used to assess the difference of means.

Odds Ratios (OR) and their 95% Confidence Intervals (CI) were estimated using Logistic Regression, with GERD symptoms as an outcome. Univariate Analysis was performed to examine the effect of each variable on the risk GERD symptoms present. In Univariate Analysis  $p < 0.25$  was used as the level of significance in order not to exclude important variables from the model. Multivariable models were constructed, including variables that showed an effect in the prediction of GERD symptoms present in the Univariate Analyses. All p-values were based on two-sided tests and significance was set at a p-value less than 0.05. The analysis was performed using SPSS (Statistical Package of Social Sciences) version 16.

## Results

Total 2383 subjects were approached to participate;



\*GERD symptoms were maximum (45.9%) when dinner to bed time is one hour and during fourth hour GERD symptoms were minimum (29.9%). GERD symptoms were maximum during dinner to bed lying activity (42%) as compared to dinner to bed sitting (35.2%) and walking activity (30.5%).

Figure: Gastroesophageal reflux disease symptoms during Dinner- bed time interval and physical activity.

**Table-1: Association of gastroesophageal reflux disease symptoms with different Variables.**

Variables	GERD symptoms Present N=689/1875(%)	GERD symptoms Absent N=1186/1875 (%)	Total (1875)
<b>Sex</b>			
◆ Male	420 (41.2%)	599(58.8%)	1019
◆ Female	269 (31.4%)	587(68.6%)	856
<b>Age groups</b>			
Mean	37.8(± 12.1)	34.0(±12.8)	
◆ <31 years	224 (27.8%)	582 (72.2%)	806
◆ 31-50 years	362 (44.8%)	446 (52.2%)	808
◆ >50 years	103 (39.5%)	158 (60.5%)	261
<b>Ethnicity</b>			
◆ Punjabi Speaking	110 (36.7%)	190 (63.3%)	300
◆ Sindhi Speaking	119 (42.8%)	159 (57.2%)	278
◆ Pashto Speaking	95 (41.9%)	132 (58.2%)	227
◆ Baluchi Speaking	60 (62.5%)	36 (37.5%)	96
◆ Urdu speaking	305 (31.3%)	669 (68.7%)	974
<b>GERD symptoms</b>			
◆ Retrosternal burning and Regurgitation	72%	28%	
◆ Burning in back of throat	85.70%	14.30%	
◆ Bitter or sour taste in mouth	81.50%	18.50%	
◆ Symptoms after meal	78%	22%	
◆ Symptoms 2 times per week	90.60%	9.40%	
<b>Dinner-bed time Interval</b>			
◆ 1Hr	133 (45.9%)	157 (54.1%)	290
◆ 2Hr	254 (41.7%)	353 (58.3%)	607
◆ 3Hr	195 (31.5%)	425 (68.5%)	620
◆ 4Hr	107 (29.9%)	251 (70.1%)	358
<b>Routine post dinner physical activity</b>			
◆ Lying	287(42.1%)	395(57.9%)	682
◆ Sitting	527(64.8%)	813	
◆ Walking	116(30.5%)	264(69.5%)	380
BMI	24.5(± 4.5)	24.(± 4.3)	

2109 gave consent for study and 274 refused. Two hundred eighty four subjects were excluded (150 were smokers, 54 were diabetic, 34 had acid peptic disease and 46 history of drugs (i.e. NSAIDs, Aspirin, Beta blockers) during last six month. Total of 1875 subjects fulfilled the inclusion criteria and their data was collected and analyzed.

GERD symptoms were present in 689/1875 subjects (36.7%). The percentages of different GERD manifestations between two groups are summarized in Table-1. Overall, males were predominant in number 1019 (54.3%) as well as in GERD symptoms, 420/689 (41.2%). Odd ratio was significant in females when compared to males (Table-2).

In age group of "≤ 30 years", "30-50 years" and "≥ 51years" number of subjects were 806/1875 (43.0%), 08/1875 (43.1%) and 261/1875 (13.9%) respectively. Odd ratios for GERD symptoms in group of "30-50 years" and "≤ 51years" when compared with group of "≤ 30 years "are given in Table-2.

**Table-2: Factors associated with Gastroesophageal reflux disease symptoms in Univariate and Multivariate analysis.**

Variables	Univariate Analysis Odd ratio(95% CI)	p-value	Multivariate Analysis Odd ratio(95% CI)	p-value
<b>Sex</b>				
◆ Male	1		1	
◆ Female	0.64(0.53-0.78)	0.001	0.65(0.53-0.79)	0.001
<b>Age groups</b>				
◆ <31 years	1		1	
◆ 31-50 years	2.24(1.82-2.76)	0.001	2.09(1.66-2.63)	0.001
◆ >50 years	1.79(1.34-2.40)	0.001	1.82(1.34-2.48)	0.001
<b>Ethnicity</b>				
◆ Punjab	1		1	
◆ Sindh	1.25(0.89-1.75)	0.18	1.26(0.89-1.79)	0.18
◆ NWFP	1.26(0.88-1.79)	0.19	1.30(0.90-1.88)	0.15
◆ Baluchistan	2.67(1.66-4.28)	0.001	2.58(1.58-4.21)	0.001
◆ Urdu speakers (Karachi)	0.81(0.62-1.06)	0.13	0.79(0.59-1.05)	0.1
<b>Dinner to recumbency time</b>				
◆ 1 Hr	1		1	
◆ 2 Hr	0.87(0.65-1.15)	0.34	0.92(0.68-1.24)	0.59
◆ 3 Hr	0.55(0.41-0.74)	0.001	0.60(0.44-0.81)	0.001
◆ 4 Hr	0.51(0.37-0.71)	0.001	0.61(0.43-0.86)	0.005
<b>Routine post dinner physical activity</b>				
◆ Lying	1		1	
◆ Sitting	0.75(0.61-0.93)	0.009	0.80(0.64-1.0)	0.05
◆ Walking	0.61(0.46-0.79)	0.001	0.66(0.50-0.88)	0.005

The frequency of subjects coming into the hospital from different provinces of Pakistan speaking Punjabi, Sindhi, Pashto, Baluchi and Urdu were 16%, 14.8%, 12.1%, 5.1%, and 51.9% respectively. GERD symptoms in different ethnic groups are given in Table-1.

Reflux symptoms were 42.1%, 35.2% and 30.5% in subjects with routine post dinner lying, sitting and walking physical activity before going to bed. The Odd ratios of GERD symptoms in subjects with post dinner walking were significant when compared to those with post dinner lying postural habits (Table-2, Figure).

From dinner to recumbency GERD symptoms were 45.9%, 41.7%, 31.5%, and 29.9% during first, second, third and fourth hour respectively (Figure). The Odd ratios of GERD symptoms at 2nd, 3rd and at ≥ 4th hour when compared with those who had 1hour dinner to recumbency time are given in Table-2.

Age, gender, routine post dinner physical activity and dinner to bed time interval were significantly associated with GERD symptoms in univariate as well as in multivariate analysis (Table-2).

## Discussion

Life style behaviours are considered as potential aggravating factors for GERD.<sup>7,13,14</sup> Recommendations for life style modifications are made to assist the GERD therapy.

However, these recommendations are based on conflicting evidences and mostly from high prevalent western areas. Our study highlights the impact of lifestyle behaviour on gastroesophageal reflux symptoms in South Asian population.<sup>2,3</sup>

Recumbency and lying down especially after meals are known precipitating factors of GERD symptoms.<sup>11,16</sup> Strenuous exercises have proven to be a risk factor for GERD. However evidence also highlights the protective effect of normal physical activity in GERD. It has been demonstrated that higher prevalence of GERD symptoms are associated in physically inactive subjects and exercise session of approximately 30 minutes reduces the risk of GERD symptoms (OR 0.5 95% CI, 0.4-0.7).<sup>17,18</sup>

In our study, approximately one fifth of the subject population had routine post dinner walking, while one third of study population had adopted recumbent posture after dinner before going to bed on most of the days of the week. The results of our study signify the importance of physical activity with GERD symptoms as subjects with post dinner recumbency had more symptoms comparatively. While subjects with post dinner walking had less frequent GERD symptoms. The current study demonstrates the significance of post dinner regular walk OR 0.61(95% CI, 0.46-0.79, p-value 0.001); which is supported by the available literature.<sup>17,18</sup>

Clinical evidences suggested that nocturnal reflux plays an important role in progression of gastroesophageal reflux disease and have a negative impact on sleep and work productivity.<sup>19</sup> Late evening meal has been one of the precipitating factors for nocturnal reflux.<sup>20</sup> One study from Japan demonstrated the association of shorter dinner to bed time with gastroesophageal reflux disease. In that matched case-control study, 147 GERD patients mostly smokers (p-value 0.001), with drinking habits (p-value 0.02), and mean age of 54.5± 10 years had significant association with dinner to bed time of less than 3 hours.<sup>15</sup> Smoking and alcohol drinking habits are the additional risk factors for gastroesophageal reflux disease so both can be significant confounders and need to be excluded.<sup>21,22</sup>

Our study was carried out with comparatively larger sample size, with mean age of 35.4±12.7 years, without smoking and drinking habits. Gastroesophageal reflux symptoms decreased as the time from dinner to recumbency increased and were experienced maximally when time from bed to dinner was one hour or less. There was no significant difference of reflux symptoms between 1st and 2nd hour and between 3rd and 4th hour. On the other hand, significant difference was found between 1st and ≥ 4th hour, with an odd ratio of 0.51(95% CI, 0.37-0.71). With comparatively younger subjects, without drinking and smoking habits and with narrow range odd ratio, our findings supported the guidelines of American College of Gastroenterology.<sup>1</sup>

In this study, the questionnaire (available on American college of gastroenterology website)<sup>5</sup> contained classic GERD screening questions sufficient for clinical diagnosis of possible GERD. An earlier questionnaire based study from this region, in the urban population, demonstrated GERD symptoms 24% with mean age of 24 ± 9.3 years and from different educational institutions.<sup>5,23,24</sup> In our study the target population was the attendants or relatives of the patients visiting outpatients department of tertiary care centers, affiliated with Aga Khan University Hospital (AKUH). The subjects were selected from urban as well as rural areas of Pakistan belonging to various cultural groups to get a generalized picture. In this study, the frequency of gastroesophageal reflux symptoms was 36.7% in comparison to previously reported 24% in 2005.<sup>5</sup> However, the previous study was conducted in educational institutions with younger subjects and mainly included urban population. This difference of questionnaire based GERD can be explained by a relatively higher mean age as well as by inclusion of all ethnic groups and subjects from both urban and rural areas. Furthermore, association of GERD with increasing age is documented in literature but with the existence of conflict in clinical evidence. Our study also highlights that GERD symptoms were significantly associated with increasing age. In the current study, male gender was significantly associated with GERD which is in accordance with other studies.<sup>5,9</sup> We had male dominance in this study which can be explained by the accompanying male attendants of our majority of patients. Also, as the gender based difference or association was not our objective. Hence, we did not match for gender.

Ethnicity as a risk factor of gastroesophageal reflux has been studied widely but data is contradictory. In a questionnaire based study the prevalence of gastroesophageal reflux symptoms among blacks and whites was 27% and 23%, respectively.<sup>25</sup> The results of the current study showed increased frequency of GERD in subjects from rural Baluchistan than urban Karachi, however, it is beyond the domain of this study to comment on rural and urban frequencies of GERD. This needs further studies to clarify the association of urban and rural localities with GERD.

The limitations of this study include that it was a questionnaire based GERD diagnosis and oesophago-gastroscopy and/ or ambulatory pH monitoring was not done. Furthermore, the severity of disease at the mucosal level could not be assessed. Time interval from dinner to bed and routine post dinner physical activities with its association and reflux symptoms could be varied and a recall bias could play a potential role.

## Conclusion

Routine post dinner walking and post dinner to bed time interval of more than three hours are associated with less



gastroesophageal reflux disease symptoms. Interventional studies testing the role of these factors in control of symptoms, improvement in quality of life and their impact on the need for acid suppressing therapy are needed.

## References

1. DeVault KR, Castell DO, American College of Gastroenterology. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 2005; 100: 190-200.
2. Fock KM, Talley N, Hunt R, Fass R, Nandurkar S, Lam SK, et al. Report of the Asia-Pacific consensus on the management of gastroesophageal reflux disease. *J Gastroenterol Hepatol* 2004; 19: 357-67.
3. Goh KL, Chang CS, Fock KM, Ke M, Park HJ, Lam SK. Gastro-oesophageal reflux disease in Asia. *J Gastroenterol Hepatol* 2000; 15: 230-8.
4. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005; 54: 710-7.
5. Jafri N, Jafri W, Yakoob J, Islam M, Manzoor S, Jalil A, et al. Perception of gastroesophageal reflux disease in urban population in Pakistan. *J Coll Physicians Surg Pak* 2005; 15: 532-4.
6. Knipschild P. Symptoms in gastro-oesophageal reflux. *Lancet* 1990; 335: 971.
7. Festi D, Scafoli E, Baldi F, Vestito A, Pasqui F, Di Biase AR, et al. Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. *World J Gastroenterol* 2009; 15: 1690-701.
8. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; 101: 1900-20.
9. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Prevalence of gastro-oesophageal reflux symptoms and the influence of age and sex. *Scand J Gastroenterol* 2004; 39: 1040-5.
10. Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet* 2006; 367: 2086-100.
11. Katz LC, Just R, Castell DO. Body position affects recumbent postprandial reflux. *J Clin Gastroenterol* 1994; 18: 280-3.
12. Pehl C, Wendl B, Pfeiffer A, Schmidt T, Kaess H. Low-proof alcoholic beverages and gastroesophageal reflux. *Dig Dis Sci* 1993; 38: 93-6.
13. Heading RC. Review article: diagnosis and clinical investigation of gastro-oesophageal reflux disease: a European view. *Aliment Pharmacol Ther* 2004; 20 (Suppl 8): 9-13.
14. Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology* 1997; 112: 1448-56.
15. Fujiwara Y, Machida A, Watanabe Y, Shiba M, Tominaga K, Watanabe T, et al. Association between dinner-to-bed time and gastro-oesophageal reflux disease. *Am J Gastroenterol* 2005; 100: 2633-6.
16. van Herwaarden MA, Katzka DA, Smout AJ, Samsom M, Gideon M, Castell DO. Effect of different recumbent positions on postprandial gastroesophageal reflux in normal subjects. *Am J Gastroenterol* 2000; 95: 2731-6.
17. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Lifestyle related risk factors in the aetiology of gastro-oesophageal reflux. *Gut* 2004; 53: 1730-5.
18. Nocon M, Labenz J, Willich SN. Lifestyle factors and symptoms of gastro-oesophageal reflux -- a population-based study. *Aliment Pharmacol Ther* 2006; 23: 169-74.
19. Dean BB, Crawley JA, Schmitt CM, Wong J, Ofman JJ. The burden of illness of gastro-oesophageal reflux disease: impact on work productivity. *Aliment Pharmacol Ther* 2003; 17: 1309-17.
20. Piesman M, Hwang I, Maydonovitch C, Wong RK. Nocturnal reflux episodes following the administration of a standardized meal. Does timing matter? *Am J Gastroenterol* 2007; 102: 2128-34.
21. Watanabe Y, Fujiwara Y, Shiba M, Watanabe T, Tominaga K, Oshitani N, et al. Cigarette smoking and alcohol consumption associated with gastro-oesophageal reflux disease in Japanese men. *Scand J Gastroenterol* 2003; 38: 807-11.
22. Stermer E. Alcohol consumption and the gastrointestinal tract. *Isr Med Assoc J* 2002; 4: 200-2.
23. Galmiche JP. Endoscopy-negative reflux disease: part of the spectrum of gastro-oesophageal reflux disease [corrected] or a separate disorder? Implications for treatment. *Aliment Pharmacol Ther* 2005; 21 (Suppl 1): 9-10, 21-4.
24. Zagari RM, Fuccio L, Wallander MA, Johansson S, Fiocca R, Casanova S, et al. Gastro-oesophageal reflux symptoms, oesophagitis and Barrett's oesophagus in the general population: the Loiano-Monghidoro study. *Gut* 2008; 57: 1354-9.
25. El-Serag HB, Petersen NJ, Carter J, Graham DY, Richardson P, Genta RM, et al. Gastroesophageal reflux among different racial groups in the United States. *Gastroenterology* 2004; 126: 1692-9.