Inducing and Aggravating Factors of Gastroesophageal Reflux Symptoms

Radhiyatam Mardhiyah*, Ari Fahrial Syam**, Siti Setiati***

*Faculty of Medicine, Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta *Division of Geriatric, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

Corresponding author:

Ari Fahrial Syam. Division of Gastroenterology, Department of Internal Medicine, Dr. Cipto Mangunkusumo General National Hospital. Jl. Diponegoro No.71 Jakarta Indonesia. Phone: +62-21-3153957; Facsimile: +62-21-3142454. E-mail: ari syam@hotmail.com

ABSTRACT

Gastroesophageal reflux disease (subsequently abbreviated as GERD) is a disease commonly found in the community. Several factors have been recognized as inducing and aggravating factors of GERD symptoms such as older age, female gender, obesity, smoking habit, alcohol consumption, certain diet and poor eating habit like eating fatty, spicy, and acid food.

Keywords: gastroesophageal reflux disease (GERD), risk factors, life style

ABSTRAK

Penyakit refluks gastroesofageal adalah penyakit yang sering ditemui di masyarakat. Beberapa hal telah diketahui dapat memicu dan memperberat keluhan penyakit refluks gastroesofageal, di antaranya adalah usia yang lebih tua, jenis kelamin perempuan, obesitas, kebiasaan merokok, konsumsi alkohol, kebiasaan makan yang kurang baik, dan konsumsi makanan tertentu seperti makanan yang berlemak, pedas, dan asam.

Keywords: penyakit refluks gastroesofageal, faktor risiko, gaya hidup

INTRODUCTION

Gastroesophageal reflux disease (subsequently abbreviated as GERD) is a gastrointestinal disorder, in which there is a recurrent reflux of gastric content into esophagus that resulting in symptoms and/or troublesome complications. ¹⁻³ It is the most commonly found disease in the community with an increasing prevalence in recent decades. ⁴ In Indonesia, no complete epidemiological data has been available; however, a study conducted at Cipto Mangunkusumo Hospital Jakarta by Syam et al has reported that there

was an increased prevalence of esophagitis from 5.7% in 1997 into 25.18% in 2002. 1,10

Gastroesophageal reflux is actually a part of normal physiological process that can be experienced by healthy individuals after meal, but when the reflux exceeding normal amount, it can cause various symptoms and intraesophageal complications such as stricture, Barrett esophagus or even malignancy.^{4,5} Factors that have been identified as inducing and aggravating factors of GERD complaints are older age, female gender, obesity, smoking habit, alcohol consumption and certain diet.

Many studies have been conducted in order to identify the correlation between age and GERD incidence; however, those studies have shown different results. Previous studies have also demonstrated that in multivariate analysis, age is not the factor that has a correlation with GERD. The result is demonstrated in some studies conducted by Sharma et al, Diaz-Rubio et al and Fujiwara et al. 6,7,8 Meanwhile, several recent studies have shown that GERD patients are generally at older age compared to the population without GERD. It can be observed in studies conducted by Bhatia et al, Fujiwara et al, Minatsuki et al and Nilsson et al. 9-12 In a study conducted by Spantideas et al, it has been found that GERD is more frequently reported by patients at the range age of 65-79 years. 13 Nevertheless, increased risk of GERD has not been always reported to be linearly correlated with increasing age. For example, in a study conducted by Minatsuki et al, they found that GERD is more frequently correlated by patient at the range age of 45-59 years compared to younger or older age group. 11

CORRELATION BETWEEN GENDER AND GERD

Studies on risk factors and prevalence of GERD have reported that GERD is more frequently found in male. However, the number of studies focusing on the correlation between gender and GERD is not as many as studies on the correlation between GERD and other risk factors. A population study in Brazil has demonstrated that GERD symptoms are more frequently reported by women.¹⁴ Some previous studies have also reported that GERD is more commonly experienced by women; while EE is more frequently experienced by men. 15-18 The most recent study of healthy subjects in Japan has found higher frequency of symptoms in female subjects such as bloating, early satiety and dismotility symptoms. 19 Similar issue has also been demonstrated by other systematic review studies. 20-21

In a study on rats with GERD, Masaka et al have reported that greater damage of esophageal tissue is experienced by male rats compared to female rats as well as by female rats that have undergone ooverctomy than female rats that still have ovarium.²² Similar issue has also been addressed by Asanuma et al who have suggested that estrogen hormon may have an effect on GERD symptoms as the estrogen modulates fat meabolism; while obesity so far has been reported as a risk factor of GERD.²³ Moreover, Asanuma et al reported that the prevalence of GERD in women is

increased drastically in post-menopausal age.²³ Another study has also reported that there is an increased incidence of EE in women with age over 50 years old.²⁴

CORRELATION BETWEEN OBESITY AND GERD

The most recent epidemiological study has demonstrated that increased prevalence of obesity and metabolic syndrome is correlated to increased prevalence of GERD in Asia.^{25,26} The underlying mechanism of GERD incidence in obesity patients including increased intra-abdominal pressure, reduced lower esophageal sphincter tone and gastric emptying dysfunction.²⁵⁻²⁷

A lot of studies have demonstrated a positive correlation between increasing body mass index (BMI) and GERD symptoms, including studies conducted by Sharma et al, Minatsuki et al, Singh et al and Kang et al.6,11,27,28 In addition, a meta-analysis performed by Hampel et al has found that obesity is correlated to GERD and its complications such as esophageal malignancy.²⁹ The meta-analysis has found that both overweight (BMI of 25-30 kg/m²) and obesity (BMI > 30 kg/m²) is correlated to GERD symptoms. Similar result has also been reported by a meta-analysis, which is conducted by Corley et al. 30 A 25-year cohort study conducted by Jacobson et al have found that subjects with overweight and obesity have two to three folds of higher risk for experiencing GERD symptoms compared to subjects with normal BMI.31 Increased risk of reflux symptoms with increasing BMI is also found in subjects with normal BMI as has been reported by Friedenberg et al.³² With further details, Stein et al have reported that each increase of five points BMI will increase GERD risk as many as 35%.³³

Other studies have also specifically showed a positive correlation between the incidence of GERD and central obesity as well as between GERD and metabolic syndrome. ^{30,34,35,36-38} A study conducted by El Serag et al has reported that in addition to increased BMI, accumulation of abdominal fat has also correlated to GERD symptoms and its complications such as Barrett esophagus. ³⁹

Considering that increasing BMI is correlated to increased GERD complaints, Singh et al have conducted a study to evaluate GERD complaints in patients who had undergone weight loss program and they found a result that subjects with weight loss also have improved GERD complaints.²⁷

Nevertheless, not all of available studies show a significant correlation between GERD and BMI. For

example, a study conducted by Smith et al shows that obesity is not an independent risk factor for the development of GERD, which is also demonstrated in the studies conducted by Bhatia et al and Watanabe et al. 9,40,41

CORRELATION BETWEEN SMOKING AND GERD

Similar to studies reporting the correlation between GERD and obesity as well as age, the results of studies reporting the correlation between smoking habit and GERD also vary. The mechanism of smoking which leads to the development of reflux symptom is correlated to reduced pressure of lower esophageal sphincter during smoking, reduced bicarbonate from the saliva and increased intra-abdominal pressure when coughing or having deep inspiration.^{6,42}

Studies conducted by Diaz-Rubio et al and Bhatia et al have reported that there is no significant correlation between smoking habit and GERD complaints.^{7,9} Meanwhile, a study conducted by Sharma et al has found that GERD complaints are more frequently found in active smokers.⁶ The result is consistent with results of other studies which also have reported increasing GERD risk in active smokers.^{7,10,11,41,43}

In addition to smoking activities, a study conducted by Nilsson et al has reported that the duration of smoking also brings effect on increasing incidence and severity of GERD complaints.¹² It is said that there is an increase of GERD risk up to 70% in active smokers who have been smoking for over 20 years.¹² Moreover, in the HUNT study, it has been reported that smoking cessation alone can reduce GERD complaints significantly. The study has reported that there is reduced GERD complaints of over more than half among subjects with smoking cessation compared to subjects who keep smoking.⁴⁴

Studies on the correlation between tobacco smoking and GERD have been conducted largely; however, a little number of studies on the association of GERD and other tobacco products has been conducted. Snus is an oral tobacco product from Sweden, which has been commonly used as a substitution for tobacco smoking or the smokeless tobacco. The HUNT 3 study has reported that a history of using snus and a subgroup analysis of snus user have demonstrated increased risk of GERD complaints; however, it has not been found in daily snus users.⁴⁵

CORRELATION BETWEEN ALCOHOL AND GERD

Alcohol consumption induces GERD complaints by reducing lower esophageal sphincter pressure,

lowering esophageal motility, increasing gastric acid secretion and delaying gastric emptying. 42,46 However, studies that have been conducted so far indicate that alcohol consumption is not always correlated to GERD symptoms.

Studies that have reported a positive correlation between alcohol consumption and GERD are those by Fujiwara et al, Minatsuki et al, and Anderson et al. 10,11,43 A study conducted by Song et al has reported that the habit of alcohol consumption is not only significantly found higher in GERD group compared to the control group, but it also increases GERD complaints significantly. The exacerbated symptoms of GERD due to alcohol consumption are acid taste and heart burn. 47

Meanwhile, studies conducted by Sharma et al, Diaz-Rubio et al, Bhatia et al and Nilsson et al have found no significant correlation between alcohol consumption and GERD complaints. 6,7,9,12 In a study conducted by Jarosz et al, GERD patients have consumed less alcohol compared to the control gorup; however, the multivariate analysis does not show a significant different between those with and without alcohol consumption on the incidence and complaints of GERD. 48

Different results of those studies are caused by the variety of alcoholic drinks consumed by the patients including different alcohol content, volume per serving and carbonation content in the available alcohol drinks.⁴⁶

CORRELATION BETWEEN FOODS, DRINKS AND GERD

It is said that some kinds of foods and drinks may serve as the inducers of reflux symptoms such as fatty, spicy, acid foods, tomato, citrus, chocolate and carbonated soft drinks. These foods and drinks induce GERD symptoms by reducing lower esophageal sphincter pressure, stimulating sensory receptors in esophagus, inducing gastric acid secretion or by inhibiting gastric emptying.^{29,42,48}

Fatty Foods

Foods with high fat content or fried foods is a group of food considered as the foods causes or aggravates GERD symptoms. The opinion is supported by studies as reported by Bhatia et al, Song et al, Jarosz et al, Mansour-Ghanaei et al and Asl et al. 9,47,48,49,50

Kubo et al have conducted a popoulation-based study to evaluate the correlation between frequency as

well as the severity of GERD complaints and patients' compliance on a predetermined dietary guideline.⁴⁶ They have found that not only there is a positive correlation between consumption of fatty foods and the frequency as well as the severity of GERD complaints, but patients with GERD complaints are more frequently consumed foods that had been previously suggested to be avoided than patients without GERD complaints.⁴⁶

Acid and Spicy Foods

Spicy foods induces GERD due to the presence of capsaicin; while acid foods due to its low pH. Both stimulate the mechanoreceptor in the esophagus. 48 The systematic review conducted by Kang et al suggests that studies on acid and spicy foods are not as many as studies on fatty foods and the results varry. 42 Some studies supported the abovementioned statement; while others suggest that there is no correlation between GERD complaints and the consumption of acid or spicy foods. 6.9,46,48-51

Coffee

Similar to studies on alcohol, varied results have also been found in studies which evaluate the correlation between coffee consumption and GERD complaints. Different results of those studies are caused by different type of coffee that had been consumed by the patients, brewing coffee technique and timing when drinking coffee, i.e. whether it is taken with an empty stomach or after meal and whether the coffee is consumed with other foods. ⁴² Bhatia et al and Song et al have reported that GERD symptoms are aggravated by coffee consumption; while Sharma et al, Nilsson et al and Asl et al have reported that there is no correlation between both of them. ^{6,9,12,47,50}

Carbonated Beverages

Carbonated beverages have been reported to increase GERD complaints by reducing lower esophageal sphincter pressure, increasing relaxation frequency of lower esophageal sphincter, increasing gastric acid secretion and enchancing gastric distention.⁵¹ Similar issue has also been reported by Hamoui et al, Shukla et al and Wu et al.^{52,53,54} A study conducted by Song et al has reported that carbonate beverage consumption increases the risk of having GERD complaints by 1.69 times and moreover, a study conducted by Seremet et al.^{47,51} has reported that the correlation is reciprocal, i.e. consumption of carbonate beverage can increase GERD complaints, but reducing the consumption can

also reduce GERD complaints.⁵¹ However, a systematic review conducted by Johnson et al has reported that carbonate beverage has not been proven to cause GERD complaints.⁵⁵

Diet Pattern

Reflux symptoms occur due to gastric distention after meal, generally between two and three hours following the meal; therefore, patients with GERD complaints are suggested to manage their meal time, bed time and their meal portion. In a systematic review conducted by Kang et al, it is reported that available studies have reported different results on the correlation between the duration of time between meal time and bedtime.⁴² Some have reported that the closer the duration between meal time and bed time, the greater increased risk of GERD and the complaints when the patient is asleep.8,10 However, Mardhiyah et al who conducted a study on subjects performing Ramadhan fasting have reported that although there is a significant improvement of GERD complaints, but there is no significant difference on the difference duration of time between the last meal and bedtime. 56 In the study, it is concluded that the difference on duration of time between the last meal and bedtime is not a factor correlated to GERD complaints.⁵⁶

Meanwhile, a study by Yamamichi et al has reported that regular diet pattern can reduce GERD risk and complaints.⁵⁷ The same study also reported that the habit of having snacks before bedtime and rapid food intake have more effect on GERD complaints compared to the habit of alcohol consumption or smoking habits.⁵⁷ Similar issue has also been reported by other studies.^{51,54}

Song et al have reported that there is an increased risk of GERD with irregular schedule daily food intake, but the risk is not increased with other habits such as large-volume meal, rapid food intake, snack eating between big meals and late evening meal or short period of time between meal time and bedtime.⁴⁷ Moreover, Bor et al have also reported that there is no significant correlation between the speed of eating and GERD complaints.⁵⁸

CONCLUSION

GERD is a disease with increasing prevalence and it has inducing and aggrevating factors that have been well known. Although the available studies have different results, GERD patients are suggested to keep an ideal body weight, to prevent inducing factors such as smoking, alcohol consumption and intake of certain kind of food such as fatty, acid and spicy food as well as carbonated soda drink and coffee and to avoid poor eating habit.

REFERENCES

- Syam AF, Abdullah M, Rani AA. Prevalence of reflux esophagitis, Barret's esophagus and esophageal cancer in Indonesian people evaluation by endoscopy. Canc Res Treat 2003;5:83.
- Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, et al. The Montreal definition and classification of gastro-esophageal reflux disease (GERD) - A global evidence-based consensus. Am J Gastroenterol 2006;101:1900-20.
- 3. Fock KM, Talley NJ, Fass R, Goh KL, Katelaris P, Hunt R, et al. Asia-Pacific consensus on the management if gastroesophageal reflux disease: update. J Gastroenterol Hepatol 2008;23:8-22.
- 4. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 2014;63:871-80.
- Makmun D. Penyakit Refluks Gastroesofageal. In: Sudoyo A, Setyohadi B, Alwi I, Simadibrata M, Setiati S, eds. Buku Ajar Ilmu Penyakit Dalam. Jakarta: Internal Publ 2006.p.317-21.
- Sharma PK, Ahuja V, Madan K, Gupta S, Raizada A, Sharma MP. Prevalence, severity, and risk factors of symptomatic gastroesophageal reflux disease among employees of a large hospital in northern India. Indian J Gastroenterol 2011;30:128-34
- Diaz-Rubio M, Moreno-elola-olaso C, Rey E, Locke III GR, Rodrigues-Artalejo F. Symptoms of gastro-esophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. Aliment Pharmacol Ther 2004;19:95-105.
- 8. Fujiwara Y, Higuchi K, Watanabe Y, Shiba M, Watanabe T, Tominaga K, et al. Prevalence of gastroesophageal reflux disease and gastroesophageal reflux disease symptoms in Japan. J Gastroenterol Hepatol 2005;20:26-9.
- Bhatia SJ, Reddy DN, Ghoshal UC, Jayanthi V, Abraham P, Choudhuri G, et al. Epidemiology and symptom profile of gastroesophageal reflux in the Indian population: report of the Indian Society of Gastroenterology Task Force. Indian J Gastroenterol 2011;30:118-27.
- Fujiwara Y, Arakawa T. Epidemiology and clinical characteristics of GERD in the Japanese population. J Gastroenterol Hepatol 2009;44:518-34.
- 11. Minatsuki C, Yamamichi N, Shimamoto T, Kakimoto H, Takahashi Y, Fujishiro M, et al. Background factors of reflux esophagitis and non-erosive reflux disease: a cross-sectional study of 10,837 subjects in Japan. PLoS One 2013;8:e69891.
- 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.
- 13. Spantideas N, Drosou E, Bougea A, Assimakopoulos D. Gastroesophageal reflux disease symptoms in the Greek general population: Prevalence and risk factors. Clin Exp Gastroenterol 2016;9:143-9.
- Latorre AMDS, Chinzon D, Eisig JN, Dias-Bastos TR. Epidemiology of upper gastrointestinal symptoms in Brazil (EpiGastro): A population-based study according to sex and age group. World J Gastroenterol 2014;20:17388-98.

- Cook MB, Wild CP, Forman D. A systematic review and meta-analysis of the sex ratio for Barrett's esophagus, erosive reflux disease, and nonerosive reflux disease. Am J Epidemiol 2005;162:1050-61.
- Ronkainen J, Aro P, Storskrubb T, Johansson SE, Lind T, Bolling-Sternevald E, et al. High prevalence of gastroesophageal reflux symptoms and esophagitis with or without symptoms in the general adult Swedish population: a Kalixanda study report. Scand J Gastroenterol 2005;40:275-85.
- Olafsdottir LB, Gudjonsson H, Jonsdottir HH, Thjodleifsson B. Natural history of functional dyspepsia: a 10-year population-based study. Digestion 2010;81:53-61.
- 18. Okumura T, Tanno S, Ohhira M, Tanno S. Prevalence of functional dyspepsia in an outpatient clinic with primary care physicians in Japan. J Gastroenterol 2010;45:187-94.
- Kawakubo H, Tanaka Y, Tsuruoka N, Hara M, Yamamoto K, Hidaka H, et al. Upper gastrointestinal symptoms are more frequent in female than male young healthy Japanese volunteers as evaluated by questionnaire. J Neurogastroenterol Motil 2016;22:248-53.
- Jung HK. Epidemiology of gastroesophageal reflux disease in Asia: a systematic review. J Neurogastroenterol Motil 2011;17:14-27.
- Kim YS, Kim N, Kim GH. Sex and gender differences in gastroesophageal reflux disease. J Neurogastroenterol Motil 2016;22:575-88.
- 22. Masaka T, Iijima K, Endo H, Asanuma K, Ara N, Ishiyama F, et al. Gender differences in oesophageal mucosal injury in a reflux oesophagitis model of rats. Gut 2013;62:6-14.
- Asanuma K, Iijima K, Shimosegawa T. Gender difference in gastroesophageal reflux diseases. World J Gastroenterol 2016;22:1800-10.
- 24. Menon S, Jayasena H, Nightingale P, Trudgill NJ. Influence of age and sex on endoscopic findings of gastrooesophageal reflux disease: an endoscopy database study. Eur J Gastroenterol Hepatol 2011;23:389-95.
- Goh KL. Gastroesophageal reflux disease in Asia: a historical perspective and present challenges. J Gastroenterol Hepatol. 2011;26:2-10.
- Chang P, Friedenberg F. Obesity & GERD. Gastroenterol Clin North Am 2015;43:161-73.
- Singh M, Lee J, Gupta N, Gaddam S, Smith BK, Wani SB, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. Obesity 2013;21:1-14.
- 28. Kang MS, Park DI, Oh SY. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. J Gastroenterol Hepatol 2007;22:1656-61.
- 29. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: Obesity and the risk for gastroesophageal reflux disease and its complications. Ann Intern Med 2005;143:199-211.
- Corley DA, Kubo A. Body mass index and gastroesophageal reflux disease: a systematic review and meta-analysis. Am J Gastroenterol 2006;101:2619-28.
- 31. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med 2006;354:2340-8.
- 32. Friedenberg FK, Xanthopoulos M, Foster GD, Richter JE. The association between gastroesophageal reflux disease and obesity. Am J Gastroenterol 2008;103:2111-22.
- 33. Stein DJ, El-Serag HB, Kuczynski J. The association of body mass index with Barrett's oesophagus. Aliment Pharmacol Ther 2005;22:1005-10.

- Edelstein ZR, Bronner MP, Rosen SN. Risk factors for Barrett's esophagus among patients with gastroesophageal reflux disease: a community clinic-based case-control study. Am J Gastroenterol 2009;104:834-42.
- 35. Nam SY, Choi IJ, Nam BH, Park KW, Kim CG. Obesity and weight gain as risk factors for erosive oesophagitis in men. Aliment Pharmacol Ther 2009;29:1042-52.
- Chua CS, Lin YM, Yu FC. Metabolic risk factors associated with erosive esophagitis. J Gastroenterol Hepatol 2009;24:1375-9.
- Chung SJ, Kim D, Park MJ, Kim YS, Kim JS. Metabolic syndrome and visceral obesity as risk factors for reflux oesophagitis: a cross-sectional casecontrol study of 7078 Koreans undergoing health check-ups. Gut 2008;57:1360-5.
- 38. Moki F, Kusano M, Mizuide M. Association between reflux oesophagitis and features of the metabolic syndrome in Japan. Aliment Pharmacol Ther 2007;26:1069-75.
- 39. El-Serag H. The association between obesity and GERD: a review of the epidemiological evidence. Dig Dis Sci 2008;53:2307-12.
- Smith KJ, O'Brien SM, Smithers BM. Interactions among smoking, obesity, and symptoms of acid reflux in Barrett's esophagus. Cancer Epidemiol Biomarkers Prev 2009;14:2481-6.
- 41. 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 2008;38:807-11.
- 42. Kang JHE, Kang JY. Lifestyle measures in the management of gastro-oesophageal reflux disease: clinical and pathophysiological considerations. Ther Adv Chronic Dis 2015;6:51-64.
- 43. Anderson LA, Cantwell MM, Watson RG, Johnston BT, Murphy SJ. The association between alcohol and reflux esophagitis, Barrett's esophagus, and esophageal adenocarcinoma. Gastroenterol 2009;136:799-805.
- 44. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Tobacco smoking cessation and improved gastroesophageal reflux: A prospective population-based cohort study: The HUNT study. Am J Gastroenterol 2014;109:171-7.
- Lie TM, Bomme M, Hveem K, Hansen JM, Ness-Jensen E. Snus and risk of gastroesophageal reflux. A population-based case-control study: the HUNT study. Scand J Gastroenterol 2016;52:1-6.
- 46. Kubo A, Block G, Charles P Quesenberry J, Buffler P, Corley DA. Dietary guideline adherence for gastroesophageal reflux disease. BMC Gastroenterol 2014;14:144.
- 47. Song JH, Chung SJ, Lee JH, Kim Y-H, Chang DK, Son HJ, et al. Relationship between gastroesophageal reflux symptoms and dietary factors in Korea. J Neurogastroenterol Motil 2011;17:54-60.
- Jarosz M, Taraszewska A. Risk factors for gastroesophageal reflux disease: the role of diet. Prz Gastroenterol 2014;9:297-301
- 49. Mansour-Ghanaei F, Joukar F, Atshani SM, Chagharvand S, Souti F. The epidemiology of gastroesophageal reflux disease: a survey on the prevalence and the associated factors in a random sample of the general population in the Northern part of Iran. Int J Mol Epidemiol Genet 2013;4:175-82.
- 50. Asl SF, Mansour-Ghanaei F, Samadi H, Joukar F. Evaluations of life style factors and the severity of Gastroesophageal reflux disease: a case-control study. Int J Mol Epidemiol Genet 2015;6:27-32.
- $51. \ \ Seremet\ N,\ Karaagaoglu\ N,\ Kaner\ G,\ Tel\ K.\ Gastroesophageal$

- reflux symptoms and nutritional preferences. Ethno Med 2015;9:305-18.
- Hamoui N, Lord RV, Hagen JA, Theisen J, Demeester TR, Crookes PF. Response of the lower esophageal sphincter to gastric distention by carbonated beverages. J Gastrointest Surg 2006;10:870-7.
- 53. Shukla A, Meshram M, Gopan A, Ganjewar V, Kumar P et al. Ingestion of a carbonated beverage decrease lower esophageal sphincter pressure and increases frequency of transient lower esophageal sphincter relaxation in normal subjects. Indian J Gastroenterol 2012;31:121-4.
- Wu KL, Rayner CK, Chuah SK, Chiu YC, Chiu KW et al. Effect of liquid meals with different volumes on gastroesophageal reflux disease. J Gastroenterol Hepatol 2014;29:469-73.
- Johnson T, Gerson L, Hershcovici T. Systematic review: the effects of carbonated beverages on gastro-oesophageal refl ux disease. Aliment Pharmacol Ther 2010;31:607-14.
- Mardhiyah R, Makmun D, Syam AF, Setiati S. The effects of Ramadan fasting on symptoms in patients with gastroesophageal reflux disease. Acta Med Indones 2016;48:169-74.
- 57. Yamamichi N, Mochizuki S, Asada-Hirayama I, Mikami-Matsuda R, Shimamoto T, Konno-Shimizu M, et al. Lifestyle factors affecting gastroesophageal reflux disease symptoms: a cross-sectional study of healthy 19864 adults using FSSG scores. BMC Med 2012;10:1-11.
- Bor S, Bayrakci B, Erdogan A, Yildirim E, Vardar R. The influence of the speed of food intake on multichannel impedance in patients with gastro-oesophageal reflux disease. United European Gastroenterol J 2013;1:346-50.