Original Article

Gastroesophageal Reflux Disease Burden in Iran

Alireza Delavari MD[1], Ghobad Moradi MD MPH PhD•[2], Elham Elahi MSc PhD Student[3], Maziar Moradi-Lakeh MD MPH[4]

Abstract

Background: Gastroesophageal reflux disease is one of the most common disorders of the gastrointestinal tract. The prevalence of this disease ranges from 5% to 20% in Asia, Europe, and North America. The aim of this study was to estimate the burden of gastroesophageal reflux disease in Iran.

Methods: Burden of gastroesophageal reflux disease in Iran was estimated for one year from 21 March 2006 to 20 March 2007. The definition was adjusted with ICD-code of K21. Incident-based disability-adjusted life year (DALY) was used as the unit of analysis to quantify disease burden. A simplified disease model and DisMod II software were used for modeling.

Results: The annual incidence for total population of males and females in Iran was estimated 17.72 and 28.06 per 1000, respectively. The average duration of gastroesophageal reflux disease as a chronic condition was estimated around 10 years in both sexes. Total DALYs for an average of 59 symptomatic days per year was estimated 153,554.3 (60,330.8 for males and 93,223.5 for females).

Conclusion: The results of this study showed that reflux imposes high burden and high financial costs on the Iranian population. The burden of this disease in Iran is more similar to that of European countries rather than Asian countries. It is recommended to consider the disease as a public health problem and make decisions and public health plans to reduce the burden and financial costs of the disease in Iran.

Keywords: Gastroesophageal reflux, incidence, Iran, prevalence

Introduction

Gastroesophageal reflux disease (GERD), defined as an abnormal reflux of the stomach contents into the esophagus, is one of the most common gastrointestinal tract disorders which is a threat to the quality of life. The impaired function of the Lower Esophageal Sphincter and acid clearance of the distal esophagus causes the disease. Patients affected by GERD can be usually treated via lifestyle changes, antacid/alginates, H2A, PPI or a combination of these methods.[1-3]

The prevalence of GERD is about 5% in Asia while it reaches 10% to 20% in Europe and North America, respectively.[4]

Heartburn and acid regurgitation are the most common symptoms of GERD which make it easy to diagnose the disease so that in most cases the disease is easily identifiable on the basis of symptoms alone. However, it is difficult to diagnose the disease in patients with a decreased frequency of heartburn, and in such cases the best method to diagnose GERD is endoscopy. The West and Asia differ significantly in terms of the frequency of endoscopic tests. GERD can appear along with ear, nose, and throat symptoms and side effects, including laryngitis and it can cause known complications such as dysphagia, esophageal ulcers, upper gastrointestinal bleeding, stricture, and Barrett's esophagus. Other problems caused by the disease include respiratory, cardiac, and oropharyngeal diseases. The symptoms and complications can largely affect the quality of life. It is worth mentioning that many GERD patients are unaware of the gastroesophageal etiology of their symptoms.[5,6]

Compared with other Asian countries, it seems that GERD is more common in Iran and its prevalence is similar to that of Western countries. The weekly prevalence of 21.2% in Tehran study is the best estimate for reflux in Iran.[7]

Based on the abovementioned studies, it seems that the disease imposes high burden and cost on the society. This study aimed to determine the burden of GERD in the society. The results can help national health policy makers to adopt effective strategies and policies to reduce the burden of this disease.

Materials and Methods

The burden of GERD in Iran was estimated just for one year from March 21, 2006 to March 20, 2007. The definition of GERD was adjusted with ICD-code of K21. Incident-based disability-adjusted life year (DALY) was used as the unit of analysis to quantify the disease burden. To estimate DALY, we need the incidence and duration of GERD induced disability. Since there was not any report of GERD-induced mortality in the national death registry, case-fatality of GERD was considered zero in all age groups. As a result, the years of live lost (YLL) was equal to zero and DALY was equal to the years lived with disability (YLD).

Authors' affiliations: [1]Associated Professor of Internal Medicine, Digestive Disease Research center, Shariati Hospital, Tehran university Of Medical Sciences, Tehran, Iran. [2]Assistant Professor of Epidemiology, Kurdistan Research Center for Social Determinants of Health (KRCSDH), Kurdistan University of Medical Sciences, Sanandaj, Iran. [3]Department of Observatory on Health and Health System, National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran. [4]Associated Professor, Gastrointestinal and Liver Disease Research Center (GILDRC), Department of Community Medicine, Iran University of Medical Sciences, Tehran, Iran.

•**Corresponding author and reprints:** Ghobad Moradi MD MPH PhD, Assistant Professor of Epidemiology, Kurdistan Research Center for Social Determinants of Health (KRCSDH), Kurdistan University of Medical Sciences, Sanandaj, Iran. **Address:** Department of Epidemiology and Biostatistics, School of Medicine, Kurdistan University of Medical Sciences (MUK), Sanandaj, Iran. P.O. Bax: 66177-13446, Sanandaj, Iran, Tel: +988733131366, E-mail: moradi_gh@yahoo.com.

Accepted for publication: 31 December 2014

Since we did not find any estimate for incidence of GERD, we used the prevalence and remission rate data in combination with zero mortality for modeling. A simplified disease model and Dis-Mod II software were used for modeling.[8] DisMod II provides a set of internally consistent output epidemiologic estimates which includes prevalence, incidence rate, remission rate, duration, mortality rate, case fatality rate and relative-risk of mortality. A group of experts assessed and approved the plausibility of the output of our final GERD model.

Input prevalence data were extracted from a systematic review on studies of GERD prevalence in Iran.[7] Considering different definitions used in the available studies, we used Nouraie's article as the source of prevalence data.[9] The prevalence of the disease among age groups older than 65 years was assumed equal to that of the age group of 56-65 years and for people younger than 18 years, it was assumed zero.

Following the recommendations of an expert panel in the Gastro-intestinal and Liver Disease Research Centre (GILDRC), GERD was considered as a chronic condition. GERD had not been included in the list of global burden of disease (GBD) as an independent disease; it was classified as one of the "other digestive system diseases" in the cluster of non-communicable diseases.

We used data from a cohort study by Naseri-Moghaddam, et al., on GERD to estimate the remission rate.[10] The cases who did not need to take medicine to alleviate their symptoms for at least 2 weeks were considered as remitted. In their study, 260 cases of GERD did not need to continue symptomatic therapy during 2912 person-year of follow-up; the remission rate was estimated 8.9 per 100 person-year. Table 1 presents a summary of input data used for modeling.

GBD list for Disability Weights (DW) does not contain any item for GERD.[11] We assumed a DW for each symptomatic day

of GERD equal to patients with peptic ulcer disease (0.0660 out of 1). Based on Nouraie's study,[12] an average 59 for symptomatic days per year and a DW of 0.0107 for GERD (as a chronic condition) were considered for base analysis. Then, DALYs were estimated based on different assumptions of annual number of symptomatic days (31, 62, 183 and all days).

An annual discount rate of three percent and full age weighting were used for estimating DALYs. We used an Excel template designed by the World Health Organization for estimating DALYs.[13]

Baseline data of population and general mortality were respectively extracted from the national population census (2006) and death registration system of the Ministry of Health (2006). The death registry covers all provinces of Iran except Tehran and its population coverage is estimated around 90 percent.

Results

The output of disease model for men and women is shown in table 2. The annual incidence for total population of males and females in Iran were estimated 17.72 and 28.06 per 1000, respectively. The average duration of GERD as a chronic condition was estimated around 10 years in both sexes (Table 2).

Based on the zero case-fatality rate, the YLL of GERD was estimated zero for all age groups. Total DALYs for an average 59 symptomatic days per year was estimated 153,554.3 (60,330.8 for males and 93,223.5 for females). Figure 1 shows the distribution of these DALYs among different age-sex groups.

DALYs estimates for different assumptions of annual symptomatic days are shown in table 3. Total DALYs varied from 80,681.1 based on assumption of average 31 symptomatic days per year to 949,954.9 (presence of symptoms on all days for all cases).

Table 1. Input data for modeling of GERD in Iran. *: Assumption

Age group	Prevalence (%)		Case Fatality Rate	Remission Rate
	Males	Females		
0–17	0*	0*		
18–25	14	15		
26–35	14	25		
36–45	20	29	0.0 (per 1000 PY)	8.9 (per 1000 PY)
46–55	24	30		
56–65	22	34		
66+	22*	34*		

Table 2. Incidence, age-at-onset and duration of GERD based on modeling on prevalence, remission and case-fatality data.

Age group	Incidence (per 1000)		Age at onset		Duration (Years)	
	Males	Females	Males	Females	Males	Females
0–4	0.00	0.00	2.4	2.4	0.0	0.0
5–14	0.54	0.58	14.3	14.3	10.9	11.1
15–29	21.24	32.37	21.8	23.0	10.8	11.0
30–44	24.20	38.49	37.8	37.0	10.4	10.7
45–59	26.85	41.56	51.1	51.9	9.6	9.8
60–69	24.26	44.15	64.7	64.5	8.0	8.2
70–79	24.28	43.89	74.5	74.5	6.5	6.1
80+	24.36	43.84	95.3	90.4	5.3	2.9
Total	**17.72**	**28.06**	**36.3**	**36.5**	**10.1**	**10.2**
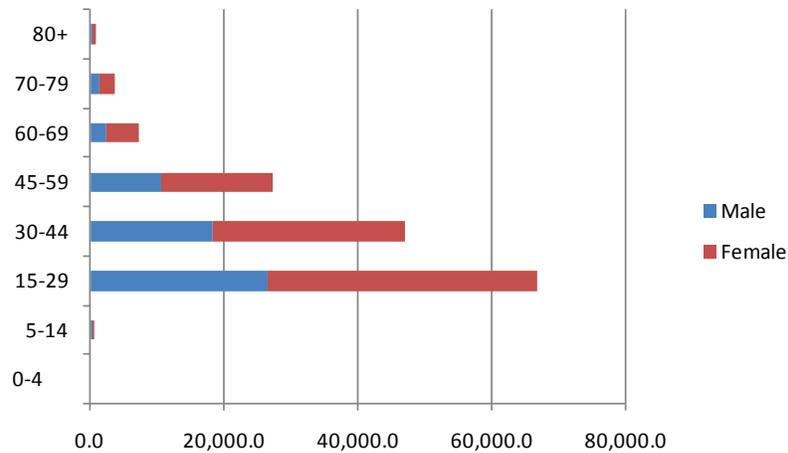
Figure 1. DALYs attributed to incident cases of GERD among different age-sex groups in Iran (2006).

Table 3. Disability adjusted life years (DALYs) attributed to GERD in Iran (2006) based on different assumptions for symptomatic days.

Symptomatic days (per year)	31 d/yr		62 d/yr		183 d/yr		365 d/yr	
DW for chronic condition	DW1 = 0.0056		DW2 = 0.0112		DW3 = 0.0330		DW4 = 0.066	
Sex	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
0–4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5–14	162.8	168.9	325.7	337.9	961.2	997.2	1,917.2	1,989.0
15–29	13,956.8	21,132.8	27,913.6	42,265.6	82,390.1	124,751.8	164,330.0	248,821.9
30–44	9,654.3	15,084.1	19,308.6	30,168.2	56,991.6	89,044.9	113,671.7	177,603.3
45–59	5,621.6	8,729.4	11,243.3	17,458.9	33,185.8	51,531.8	66,190.3	102,782.1
60–69	1,313.3	2,474.6	2,626.7	4,949.3	7,753.0	14,608.3	15,463.6	29,136.8
70–79	764.4	1,179.4	1,528.8	2,358.7	4,512.4	6,962.1	9,000.2	13,886.1
80+	225.9	212.5	451.8	425.0	1,333.6	1,254.5	2,660.0	2,502.2
Subtotal	31,699.2	48,981.8	63,398.5	97,963.6	187,127.8	289,150.8	373,233.0	576,721.5
Total	**80,681.1**		**161,362.1**		**476,278.5**		**949,954.5**	

Discussion

According to the results, the annual incidence of disease for all males and females in Iran was estimated 17.72 and 28.06 per 1000, respectively. Considering GERD as a chronic disease, it was estimated that the average duration of the disease was around 10 years in both males and females. In view of the zero case-fatality rate, the YLL of GERD was estimated zero for all age groups. For cases with an average 59 symptomatic days per year, total DALYs were estimated 153,554.3. It should be noted that total DALYs differed from 80,681.1 based on assumption of average 31 symptomatic days per year to 949,954.9 (presence of symptoms on all days for all cases).

Some studies did not estimate the disease burden; however, they analyzed the costs associated with the disease. The economic costs of GERD are also high for people with the disease. The high economic cost of this disease is consistent with what we have found in our study about the disease burden in Iran. In other parts of the world, the disease has high burden and therefore high costs. According to a study by Francis, et al., the mean direct costs imposed on patients for EER in the first year was $5,438 per patient. Additionally, the medical and non-medical factors re-

quired an expenditure of $5,154 and $283. They concluded that to improve a patient's condition during five years, a total of $13,700 was needed. The results of their study are in line with our results about the burden of the disease and shows that the disease needs special care.[14]

There are some other studies which have shown the high costs of this disease. In a study by Wagner, et al., two case and control groups were compared and it was found that the burden of disease was substantially higher in case groups affected by GERD and the direct costs and costs due to lost productivity were estimated US$3143 and US$1435, respectively. Based on the results, those who experience GERD both day and night have lower quality of life and experience higher costs than those with diurnal-only or nocturnal-only symptoms.[15]

A study by Shin, et al., study showed that a case group of GERD patients had a productivity loss of 11.7hr/week compared with the control group. They assumed that the average hourly wage was $14.12; therefore, the average wage lost was $165.07 per person. This study also shows the high burden of the disease and is consistent with our results.[16]

In a population based study in Iran, 18180 people older than 18 years were enrolled among whom 41.9% of males were af-

fected by GERD. The direct and indirect costs of disease were PPP$97.70 and PPP$13.7, respectively.[17]

Based on a study by Darbà J, et al., the number of people with poorly treated GERD with Barrett's esophagus in Spain, Germany, and Italy was estimated at 29678, 19327, and 10079, respectively. However, for people with Barrett's esophagus were estimated to be €18, 12 and 7 million, respectively, for each country. Additionally, the total costs caused by absenteeism among employees with poorly treated GERD with Barrett's esophagus were €10 million for Germany, €1 million for Italy and none for Spain.[18]

According to the results of a study by Agréus, et al., in Sweden in 1997, GERD together with dyspepsia, and PUD had a total cost of $US63 per adult. The total cost was $US424 million which included $US258 million (61%) direct costs and $US166 million (39%) indirect costs. Drugs and sick leave accounted for 37% and 34% of costs, respectively which formed the highest proportions of costs. Since 1985, drug costs had increased substantially while the cost of sick leave had decreased.[19]

In a systematic review by Vakil, et al., a small number of studies which have been conducted to assess the effectiveness of treatment, the main focus has been on patients. The models which utilized quality-adjusted life years, instead of patients, used an expert panel to estimate the value of different treatment methods. In fact, the results obtained from expert panels were more precise than those form people. Willingness to pay studies indicate that patients place a high value on complete symptom relief which has been shown to restore quality of life to normal. Economic models on trials of therapy have assumed that the subsequent costs of endoscopy can be avoided.[20]

Most of studies verify the high burden of this disease. It causes high financial costs in the country. It is difficult for patients and national health system to compensate the costs. It is very important to consider the disease as a public health problem. It is recommended to take the disease as a public health problem and to make national and public health plans to reduce and eliminate the burden of the disease. Considering rapid changes in lifestyles and disease patterns, an increase in the prevalence of some diseases like GERD is likely.

Lack of multiple data sources from different parts of the country, generalizable to the total population of Iran, is a limitation of this study. Therefore, it is recommended to conduct updated studies of burden of diseases and to eliminate the limitations of our study using new models to estimate the burden of diseases.

Conflict of interest

There is no conflict of interest

Acknowledgments

References

1. Bredenoord AJ, Pandolfino JE, Smout AJ. Gastro-oesophageal reflux disease. *Lancet*. 2013; **381(9881):** 1933 – 1942.
2. Banks M. The modern investigation and management of gastro-oesophageal reflux disease (GORD). *Clin Med*. 2009; **9(6):** 600 – 604.
3. Al Talalwah N, Woodward S. Gastro-oesophageal reflux. Part 1: smoking and alcohol reduction. *Br J Nurs*. 2013; **22(3):** 140 – 142, 4 – 6.
4. Olmos JA. Systematic review: Epidemiology of gastroesophageal reflux disease in Latin America. *Acta Gastroenterol Latinoam*. 2011; **41(1):** 7 – 8.
5. Kusano M. Review article: diagnosis and investigation of gastro-oesophageal reflux disease in Japanese patients. *Aliment Pharmacol Ther*. 2004; (**Suppl 8):** 14 – 18.
6. Yuksel ES, Vaezi MF. Therapeutic strategies for laryngeal manifestations of gastroesophageal reflux disease. *J Clin Gastroenterol*. 2013; **47(3):** 195 – 204.
7. Delavari A, Moradi G, Birjandi F, Elahi E, Saberfirozi M. The Prevalence of Gastroesophageal Reflux Disease (GERD) in the Islamic Republic of Iran: a Systematic Review. *Middle East J Dig Dis*. 2012; **5:** 5 – 15.
8. Barendregt JJ, Van Oortmarssen GJ, Vos T, Murray CJ. A generic model for the assessment of disease epidemiology: the computational basis of DisMod II. *Popul Health Metr*. 2003; **14; 1(1):** 4.
9. Nouraie M, Radmard AR, Zaer-Rezaii H, Razjouyan H, Nasseri-Moghaddam S, Malekzadeh R. Hygiene could affect GERD prevalence independently: a population-based study in Tehran. *Am J Gastroenterol*. 2007; **102(7):** 1353 – 1360.
10. Nasseri-Moghaddam S RH, Alimohamadi SM, Mamarabadi M, Ghotbi MH, Mostajabi P, et al. Prospective Acid Reflux Study of Iran (PARSI): methodology and study design. *BMC Gastroenterol*. 2007: **20(7):** 42. doi:10.1186/1471-230X-7-42
11. WHO. Disability weights, 2001. Available from: URL: http://www.who.int/healthinfo/global_burden_disease/tools_national/en/ (Accessed by 11.17.2013).
12. Nouraie M, Razjouyan H, Assady M, Malekzadeh R, Nasseri-Moghaddam S. Epidemiology of gastroesophageal reflux symptoms in Tehran, Iran: a population-based telephone survey. *Arch Iran Med*. 2007; **10(3):** 289 – 294.
13. WHO. National burden of disease studies: a practical guide: DALY calculation tool. 2001. Available from: URL: http://www.who.int/healthinfo/global_burden_disease/tools_national/en/ (Accessed by 11.17.2013).
14. Francis DO, Rymer JA, Slaughter JC, Choksi Y, Jiramongkolchai P, Ogbeide E, et al. High economic burden of caring for patients with suspected extraesophageal reflux. *Am J Gastroenterol*. 2013; **108(6):** 905 – 911.
15. Wagner JS, DiBonaventura MD, Balu S, Buchner D. The burden of diurnal and nocturnal gastroesophageal reflux disease symptoms. *Expert Rev Pharmacoecon Outcomes Res*. 2011; **11(6):** 739 – 749.
16. Shin WG, Kim HU, Kim SG, Kim GH, Shim KN, Kim JW, et al. Work productivity and activity impairment in gastroesophageal reflux disease in Korean full-time employees: a multicentre study. *Dig Liver Dis*. 2012; **44(4):** 286 – 291.
17. Moghimi-Dehkordi B, Vahedi M, Khoshkrood Mansoori B, Kasaeian A, Safaee A, Habibi M, et al. Economic burden of gastro-oesophageal reflux disease and dyspepsia: a community-based study. *Arab J Gastroenterol*. 2011; **12(2):** 86 – 89.
18. Darba J, Kaskens L, Plans P, Elizalde JI, Coma M, Cuomo R, et al. Epidemiology and societal costs of gastroesophageal reflux disease and Barrett's syndrome in Germany, Italy and Spain. *Expert Rev Pharmacoecon Outcomes Re*s. 2011; **11(2):** 225 – 232.
19. Agreus L, Borgquist L. The cost of gastro-oesophageal reflux disease, dyspepsia and peptic ulcer disease in Sweden. *Pharmacoeconomics*. 2002; **20(5):** 347 – 355.
20. Vakil N, Ryden-Bergsten T, Bergenheim K. Patient-centred endpoints in economic evaluations of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther*. 2002; **16(8):** 1469 – 1480.