

# The Prevalence of Gastroesophageal Reflux Disease (GERD) in the Islamic Republic of Iran: A Systematic Review

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## ABSTRACT

### BACKGROUND

Gastroesophageal reflux disease is a common, chronic disease worldwide. The weekly prevalence of reflux in developed countries is 10% to 48%. It has previously been reported as 5% in Asian countries, but new reports show a higher level in both Asian and Arab countries. In Iran, reflux has increased over the last two decades. There are few studies concerning the prevalence of reflux in Iran. This study aims to review reports about the prevalence of reflux in Iran, as it may be different in various parts of the country. By evaluation of the existing articles, this study will reach a general conclusion about the reflux prevalence in Iran.

### METHODS

This was a qualitative, systematic review that estimated the prevalence rate of reflux in Iran. In August 2010, we reviewed all electronic database published studies that concerned the epidemiology of reflux prevalence in Iran by searching PubMed, Scientific Information Database (SID), Iran Medex, and Magiran.

### RESULTS

In our search, using specified key words and selection criteria, 15 articles fulfilled the inclusion criteria and were included in the study.

### CONCLUSION

According to the results, the data related to the estimated prevalence in Iran have a wide range. The weekly prevalence rate of 21.2% in the Tehran study is the best estimate for reflux in Iran. It seems that reflux is more common in Iran when compared to other Asian countries, and similar to reflux in Western countries. Due to the absence of comprehensive studies in Iran, we recommend that researchers conduct accurate, comprehensive, multi-dimensional studies in order to estimate reflux prevalence and its burden in Iran.

### KEYWORDS

Prevalence; Gastroesophageal reflux disease; Iran

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## INTRODUCTION

Gastroesophageal reflux disease, the regurgitation of gastroduodenal contents into the esophagus, is a common chronic disease. In addition to its symptoms, this disease causes known

complications such as dysphagia, esophageal ulcers, upper GI bleeding, stricture, and Barrett's esophagus. There are also extra-esophageal complications such as respiratory, cardiac, and oropharyngeal diseases. Because of its symptoms and complications, reflux extensively affects quality of life. The actual prevalence and incidence of reflux is unknown. This is because of the limitations in epidemiologic studies, due to the lack of both a gold standard and comprehensive, simple, practical definition for this phenomenon.<sup>1-5</sup>

One of the problems of reflux epidemiologic studies is the variety of definitions for this disease. It seems that heartburn and/or regurgitation of gastric content from the stomach to the esophagus, which happens daily, weekly, or yearly are the most commonly accepted clinical definitions in epidemiologic studies. However, in each study additional factors regarding the number of occurrences, time, and severity are added. In addition, in most epidemiologic studies the extra esophageal symptoms and complications have not been investigated, thus the present estimates may be underestimates. Some studies have reported an increasing trend in reflux. A prospective study that evaluated reports of endoscopies, which were performed from 1994 to 1999 noted a three-fold increase in the prevalence of reflux, from 20% to 70%.<sup>6-8</sup> In several epidemiologic studies, the weekly prevalence of reflux in developed countries has ranged from 10% to 48%. About 44% of Americans experience reflux symptoms at least once a month, 20% at least weekly, and 7% have daily reflux.<sup>9-11</sup>

Previously, it was reported as 5% in Asian countries, but new reports have shown a higher level in east-Asian countries.<sup>12-14</sup> Reflux is more common in Arab countries than Asian countries, and Iran has seen an increase in incidence during the past two decades. The prevalence of weekly reflux in East Asian countries is reported to be between 2.5% and 6.7%; de-

spite different rates in these countries, the trend is increasing.<sup>15,16</sup>

Based on the systematic review by Jung, the prevalence of symptom-based GERD in East Asia was found to be 2.5%-4.8% before 2005 and 5.2%-8.5% from 2005 to 2010. In South-east and Western Asia, it was 6.3%-18.3% after 2005, which was much higher than East Asia.<sup>17</sup>

There is a wide range of GERD weekly prevalence amongst Asian and Arab countries. In 2010, He et al. reported a prevalence of 5.2% in China,<sup>18</sup> Lee et al. (2009) reported a GERD prevalence 8.5% in Korea,<sup>19</sup> and Lim et al. reported a prevalence of 10.5% in Singapore.<sup>20</sup> In Turkey which is similar to Asian and middle east countries, according to Kitapçioğlu et al., the prevalence was 20%,<sup>21</sup> Whereas according to Kaji et al. (2010) it was only 7.7% in Japan<sup>22</sup> and 5% in Taiwan.<sup>23</sup> Rosaida and Goh reported a prevalence of 38.8% in Malaysia in 2004,<sup>24</sup> Jafri et al. reported a prevalence of 24% in Pakistan in 2005,<sup>25</sup> and according to Al-Humayed et al. the prevalence in Saudi Arabia was 15% in 2010.<sup>26</sup>

As can be seen, the rate of reflux is different between countries. Even within countries the reported rates in various studies range widely due to the difference in reflux definitions and lack of a standard diagnostic method.<sup>16,27</sup>

There are few studies concerning the prevalence of reflux in Iran. Conducted studies often include limited regions and populations within Iran. Therefore, there is no representative study with a sufficient population size that properly represents the country's general population. The weekly prevalence of reflux in Iran is reported to range from 6% to 33% in different studies.<sup>7,16</sup>

It is possible the prevalence of reflux may be different in various parts of the country. Therefore, this study is a review of studies that have researched the prevalence of reflux in Iran. Through evaluation of existing articles, we intend to reach a general conclusion about the

prevalence of this disease.

## MATERIALS AND METHODS

This study was a systematic review that researched all published studies on the epidemiology of reflux prevalence in Iran. Study methodologies, symptom definitions, disease diagnostic criteria, and disease risk factors were all analyzed. We used a search to select the required data in electronic databases.

In August 2010, we searched PubMed to find international resources, and Scientific Information Database (SID), Iran Medex, and Magiran to locate Farsi resources.

Initially we chose related key words to be used in the searches. Gastroesophageal reflux was chosen as the main word. MesH was the selected strategy for research. Three words were put together, and using the MesH method they were used to search PubMed: “gastroesophageal reflux” [Majr] AND “Prevalence” [MesH] AND “Iran” [MesH]. As our goal was to determine disease burden in addition to prevalence, we used other words such as “incidence, mortality, morbidity, and duration” in the searches.

The resultant articles were analyzed. If the title and abstract were related to the subjects, the full text article was read. The articles that fulfilled the following inclusion criteria were included in our study:

- estimation of reflux prevalence
- proper definition of reflux
- good methodology (proven by experts), with no obvious biases
- adult age group

Because of dissimilarities in MesH systems in the country and in Farsi database resources, two words used in Farsi articles were matched for reflux and used to search SID, Iran Medex, and Magiran. Farsi articles were selected via the following method.

First, the titles of all collected articles were reviewed and those related to the subject were

chosen. Then, abstracts of the chosen articles were read, and relevant articles were selected to have their full text read in the next step. We used the same inclusion criteria for Persian articles. If an article did not fulfill the above-mentioned conditions, it was dismissed from our study.

## RESULTS

In our search, using specified key words and the above-mentioned method, 12 articles were located in PubMed. After reviewing titles and abstracts, ten fulfilled the inclusion criteria. These ten full text articles were read by researchers, of which nine were included in this study. We rejected the other article because it did not completely fulfill validity and other criteria.

The results of searches in SID, Iran Medex, and Magiran using specified words and inclusion and exclusion criteria gave the following results. In Iran Medex, a total of 62 articles were found whose titles were analyzed, of which eight related to the subject were chosen. In Magiran, a total of 50 articles were found, of which 9 articles were chosen. Of the eight articles found in SID, one related article was chosen. A search of English titles in SID noted 32 articles, and based on the title analysis 7 were selected.

Many of the articles from these databases were the same, thus similar articles were not included. From the Iranian search engines only 13 articles were collected, of which 6 were included in this study. The study results are shown in Table 1.

After final analysis, 15 articles were chosen that fulfilled all the required conditions.<sup>5,7,28-40</sup> All articles were reviewed by two people. The summary of results and main findings of these articles are presented in Table 2.

## DISCUSSION

There are different rates for reflux prevalence in

**Table 1:** Search engine results

No.	Search engine	Number of articles found	Number of selected articles after reviewing titles	Number of selected articles after reviewing abstracts	Total number of final reviewed and selected articles
1	PubMed	12	9	9	9
2	Farsi SID	8	1	13*	6
3	English SID	32	7		
4	Iran Medex	62	8		
5	Magiran	50	9		

\*Farsi database resources had overlaps, thus search results were sometimes the same.

**Table 2:** A summary of GERD studies in Iran

	Reflux prevalence				Response rate	Definition	Data collection method and questionnaires	Sample size	Type of study and sampling criteria	Place of study	Date of study	Study author, every publication date
	At least every year	At least every month	At least every week	At least every day								
More than 85% during 6 months	18.4%	6.8%	1.9%	84.5%	Any symptom of heartburn and/or regurgitation of food from stomach to esophagus on a daily, weekly, or monthly basis during the last 6 months.	A questionnaire asking about demographics, main disease symptoms and experiences. The words "heartburn" and "regurgitation" were used to ask about symptoms.	1700	Selection of 1700 people aged 18 to 65 via phone calls in Tehran (non-pregnant residents).	Tehran	2004-2005	Nourai et al. (2007) <sup>5</sup>	
			33%	89%	Any symptom of heartburn and/or regurgitation of food from stomach to esophagus during most recent year, occurring at least once a week, with any severity and duration.	Participants were asked about reflux symptoms (heartburn, food regurgitation, pain, hoarseness and cough). There were interviews and a valid questionnaire.	748	748 people among Ghashghaee nomads. Multilevel cluster sampling, cross-sectional study.	Ghashghaee nomads, Fars Province	2006	Mostaghni et al. (2009) <sup>28</sup>	
			15.4%	54.9%	Any symptom of heartburn and/or regurgitation of food from stomach to esophagus during most recent year, occurring at least three times a week, with any severity and duration.	A questionnaire with 27 questions, completed by physicians.	1978	Population-based study among 3600 people older than 35 using cluster sampling. People were selected among those referred to a gastroenterology ward.	Shiraz	2004	Saberi Firozi et al. (2007) <sup>29</sup>	
	28.7%	18.2%		94.0%	GERD was defined as presence of at least one of two major GERD symptoms (HB or AR) during	The Mayo gastroesophageal reflux questionnaire (GORQ) and P-GORQ were used. A trained	2500	Cross-sectional, population-based study. Computer-based random cluster sampling was performed	Tehran		Nasseri-Moghaddam et al. (2008) <sup>30</sup>	

Reflux prevalence				Response rate	Definition	Data collection method and questionnaires	Sample size	Type of study and sampling criteria	Place of study	Date of study	Study author, every publication date
At least every year	At least every month	At least every week	At least every day								
					the past 12 months. Those having daily or weekly GERD were considered to have frequent GERD.	interviewer in each group distributed the P-GORQ and collected it the next day.		using the postal code of Tehran Province. 100 randomly chosen postal codes were selected as the cluster heads. These 100 clusters were divided into five groups. A trained interviewer in each group distributed the P-GORQ and collected it the next day.			
		21.2%		84.8%	Heartburn and/or regurgitation of food from stomach to esophagus weekly during last 6 months.	Interviews were direct and questionnaire was valid.	2500	Population-based cross-sectional study. Cluster sampling based on postal codes among Iranian people living in Tehran, aged 18 to 65.	Tehran	2005	Nouraei,(2007) <sup>31</sup>
39.7% record of symptoms	Any 20.9%	7.9%	10.9%		Any episode of heartburn and/or regurgitation of food from stomach to esophagus.	Direct interview using a questionnaire.	700	700 males and females with equal distribution, older than 10 years of age. Stratified sampling.	Tehran	1999	Ehsani et al., (2007) <sup>32</sup>
		9.1%		90.6%	Heartburn and/or regurgitation of food from stomach to esophagus during last three months, occurring at least once a week.	This study was done through interviews which used a questionnaire designed by Lock et al.	6325	Cross-sectional population-based interview study.	Tehran Province; Firoz-koh and Damavand districts	2006	Solhpour et al. (2008) <sup>33</sup>
	13%	6.3%		95%	Weekly heartburn and/or regurgitation of food from stomach to esophagus.	This study used a valid questionnaire.	620	Cross-sectional study in Azad University, Tabriz, using randomized sampling.	Tabriz	2005	Somi et al., (2006) <sup>34</sup>
		2.7%			Heartburn happening at least three times during the last two weeks.	Interviews asking about symptoms.	4207	Using systematic sampling, 1017 families were selected among 70 000	Tabriz	2000	Khoshbaten et al., (2003) <sup>35</sup>

Reflux prevalence				Response rate	Definition	Data collection method and questionnaires	Sample size	Type of study and sampling criteria	Place of study	Date of study	Study author, every publication date
At least every year	At least every month	At least every week	At least every day								
		29.2%			Experiencing heartburn and/or regurgitation of acid from stomach.	Interviews with participants.	782	families living in Tabriz. 4207 people were involved in the study. Cross-sectional, population-based study that excluded people with dementia and mental retardation.	<i>Firooz-koh and Damavand</i>	2006	Moghimi Dehkurdi et al., (2008) <sup>36</sup>
	34.1%	26.8%		95%	Heartburn and/or regurgitation of food from stomach to esophagus at least once a week during previous year.	Validated Mayo clinic questionnaire.	522	Cross-sectional study among staff of Imam Khomeini Hospital, Tabriz using systematic sampling.	<i>Tabriz</i>	2005	Somi et al., (2008) <sup>37</sup>
	Students in Tehran (16.3%); blood donor volunteers in Tehran (8.8%); Gonbad cohort (15.1%)				Heartburn and/or regurgitation of acid from stomach to esophagus during last year at any frequency.	Questionnaire and interviews.	3100 (New students in Tehran); 3517 (blood donor volunteers in Tehran); 1351 (cohort of persons in Gonbad).	Cross sectional study in three group using random sampling.	<i>Tehran and Gonbad</i>	2002	Pourshams (2005) <sup>7</sup>
	21.5%	12.9%	12.1%	97.9%	Heartburn and/or regurgitation of food from stomach to esophagus during last 12 months.	Face-to-face interviews.	2400	Population-based study using cluster sampling of families among people aged 20 to 70.	<i>Isfahan</i>	2004	Rogha et al., (2006) <sup>38</sup>
	25.5%			86.71%	Any experience of heartburn and/or acid production, happening once a month during previous year.	Trained interviewers asked questions from participants.	5429	Cross-sectional study in Shahrekurd using cluster sampling among people older than 20.	<i>Shahrekurd</i>		Hosine asl, et al., (2004) <sup>39</sup>
		12.3%		98.4%	Experiencing heartburn or	Direct interviews.	1016	Systematic random clus-	<i>Gonbadka-</i>	2005	Aletaha et al., (2007) <sup>40</sup>

Reflux prevalence				Response rate	Definition	Data collection method and questionnaires	Sample size	Type of study and sampling criteria	Place of study	Date of study	Study author, every publication date
At least every year	At least every month	At least every week	At least every day		regurgitation of acid from stomach to esophagus at least weekly during			ter sampling of families among people aged 18 to 40.	voos and Kalaleh		

Iran. In our study there were only 15 articles for review, which had some limitations for determining outcomes.<sup>5, 7, 28-40</sup> In order to obtain enough data for assessing reflux prevalence, the researchers considered more inclusion indicators.

Although the definitions used include dyspepsia regurgitation, they are different regarding symptom intervals and periods, questionnaire validity, type of data collection, as well as trained and experienced interviewers, among others. These differences may cause bias in estimations, and we have only considered those studies with the least amount of bias.

In none of the studies did the population size involve the entire country, but only involved a proportion of a city or district. Thus, none was representative of the entire country. From all studies,<sup>11</sup> were conducted in the three provinces of Tehran, Shiraz, and Tabriz.<sup>5,7,28-37</sup> One study was done in Isfahan,<sup>38</sup> one in Shahrekurd,<sup>39</sup> a part of a study in Gonbad and Kalaleh,<sup>40</sup> and a part of another study in Gonbadka-voos.<sup>7</sup> Iran has 31 provinces with different cultural, ethnical, and geographical variations, therefore the geographical range of these studies did not represent all parts of the country. Only one case involved a rural population, whereas in the other studies the subjects were chosen from people who lived in cities. This was a limitation for these studies.

Most did not use valid questionnaires, a standard population, or a proper definition for reflux. Therefore, the first item that needs attention is research regarding reflux prevalence and burden, which should include a proper population size, methodology, and valid questionnaires such that the results could be generalized to the entire country. The population size should estimate the reflux prevalence in all subgroups.

Reflux diagnosis is closely related to the quantity and severity of reflux symptoms. In these studies, reflux prevalence has been estimated on either a daily, weekly, monthly, or yearly basis. Daily reflux prevalence was estimated in three studies. However, it was difficult to make an estimation based on the results of these studies because they used dissimilar and inaccurate methodologies and definitions. Nonetheless, it seemed that the prevalence rate of 1.9% in the Noraei et al.<sup>5</sup> study was methodologically more reliable. Based on an evaluation of the results, the researchers have suggested that the daily reflux prevalence was less than 5%, and 1.9% was an acceptable prevalence rate. Most studies<sup>14</sup> estimated reflux prevalence on a weekly basis, with a wide range from 6.8% to 33%.

As previously mentioned, estimations of weekly reflux prevalence varied greatly between studies. These differences were the results of different definitions and methodologies, populations chosen with various characteristics, and invalid questionnaires. Based on the evaluation and standardization of methodologies and questionnaire validity, there were three studies that fulfilled the criteria for an acceptable rate. The three studies estimated prevalence at 21.2% in Tehran,<sup>31</sup> 18.2% in Tehran,<sup>30</sup> and 12.3% in Kalaleh.<sup>40</sup> Based on better methodology and age group selection, we have suggested the weekly prevalence rate of 21.2% found in the Tehran study to be the most representative.<sup>31</sup>

By these studies, the monthly prevalence rate is greater than 20% in people older than 20. The estimations of 21.5% in one study,<sup>38</sup> and 25.5% in a study in Shahrekurd,<sup>39</sup> represent more accurate estimations when compared to other studies. The yearly prevalence rate has been estimated as greater than 85% in one of the studies.<sup>5</sup> According to re-

search by Ehsani, et al.<sup>32</sup> the prevalence has been reported as 39.7%, which could be accepted for the yearly rate.

When considering the above-mentioned studies, it seems that reflux is more prevalent in Iran than other Asian and African countries.<sup>9,16</sup>

In a systematic review of the prevalence of GERD in Asia, GERD is defined as having at least weekly episodes of heartburn or acid regurgitation.

The prevalence in Asian and Arab countries have been reported as follows: China 4.1%-7.3%, Japan 7.7%, Korea 3.5%-8.5%, Taiwan 12.4%, Singapore 10.5%, Iran 6.3%-18.2%. Ethnic and geographical differences are important factors in studying disease frequencies. The prevalence of endoscopic reflux esophagitis in East Asia has increased from 3.4%-5.0% before 2000 to 4.3%-15.7% after 2005. The prevalence of symptom-based GERD in East Asia was 5.2%-8.5% from 2005 to 2010. Most studies in west and central Asia have been conducted in Iran. The prevalence of GERD in Iran was 6.3%-18.3%.<sup>17</sup> Based on this study the prevalence in Iran was higher than other countries.

According to new studies, the prevalence of symptom-defined GERD is 3.1% in China,<sup>18</sup> 7.7% among Japanese workers,<sup>41</sup> 8.5% in Korean subjects,<sup>19</sup> and 6.2% in Shanghai, China.<sup>42</sup>

These findings show that reflux in Iran is similar to Western countries, where the weekly reflux prevalence is reported to be about 10% to 20%.<sup>12</sup> More than 44% of American people experience reflux monthly, 20% weekly, and 7% daily.<sup>9-11</sup> The Iranian weekly rates are similar to American studies.

There is no study in Iran that has estimated reflux for the entire country. A study in China has reported a weekly prevalence rate of 1.9% for the entire population.<sup>43</sup> The estimate of reflux prevalence among the entire Iranian population would be higher than seen in China.

Iran and other Asian countries have shown an increase in reflux prevalence due to the increased imitation of a Western lifestyle.<sup>44</sup> As noticed in other studies, this increase in reflux is parallel to an increase in Western models of living in Asian countries

as well.<sup>35, 45-47</sup>

In one study, people who have been assessed in 1994 were again assessed after several years to determine reflux prevalence; both heartburn and reflux prevalence were four times higher.<sup>12, 20, 47</sup>

Iranian people are increasing in weight and more are settling in cities. Meanwhile, the economical and social status of people has changed rapidly. Therefore, some studies have reported that the above-mentioned items are risk factors.<sup>24</sup>

Studies are needed to determine the main causes of reflux prevalence in Iran. These studies should include those factors that increase reflux prevalence in addition to discussing the increased prevalence of reflux in Iran when compared with other Asian countries.

Based on the results, the data related to estimations of prevalence have a wide range. These extensive differences may be the result of limitations of population-based studies in which accurate diagnostic methods such as PH metric assay cannot be applied. People's perception of symptoms may also be different. Some of these differences come from the lack of a comprehensive standard for classifying symptoms and complications of reflux, which makes the comparison between studies difficult.

Some differences in reported reflux prevalence rates may originate from cultural and ethnical differences in comprehending, expressing, and understanding reflux symptoms. For example, in some regions and among some ethnicities there is a difference in describing symptoms and diseases, whereas other groups do not pay attention to disease symptoms. It has been pointed out that different groups and cultures have various perceptions of the word "heartburn". In a study in Boston among different ethnicities, only 13% of Chinese and Korean people had a correct understanding of the word "heartburn".<sup>48</sup> Although in the assessed studies this word is translated in Farsi as "sozeshe sare del", it is necessary for further studies to choose another word or definition which would be more acceptable to the different dialects of countryside people. In future studies, validation of the questionnaires should be considered.

Considering the results of this study, the following important points about reflux need more attention:

- 1- Increase people's knowledge about this disease and give required recommendations for punctual treatment in order to control the high prevalence of reflux in Iran.
- 2- Improving the knowledge of physicians and health workers in primary health care in order to train, treat, control, and timely refer patients.
- 3- Providing a comprehensive and standard reflux definition for quick diagnosis.
- 4- Determining and defining disease prevalence in all geographical, ethnical, and cultural subgroups.
- 5- Defining disease risk factors in order to control the increasing trend of reflux prevalence in Iran.
- 6- Compiling a national guideline for GERD.

Importantly, it is suggested that accurate, comprehensive, multi-dimension studies should be undertaken in order to estimate reflux prevalence and its burden, to define scales for disease origination, morbidity prevalence, and its complications and costs to Iran.

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#### CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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