

ORIGINAL ARTICLE

# The Prevalence of Symptoms Suggestive of Common Esophageal Disorders Among Taif City Population, Taif University, College of Medicine Taif, Saudi Arabia

Mohammad Eid Mahmoud Mahfouz<sup>1</sup>, Shahad Khalid Alsherbi<sup>2\*</sup>, Dhuha Abdulrahman Alhumaidi<sup>3</sup>, Fatima Moeesh Altalhi<sup>3</sup>, Rabeah Ahmed Alsofyani<sup>4</sup>

## ABSTRACT

**Background:** Symptoms suggestive of esophageal disorder are prevalent among all populations. There have been no studies to estimate the prevalence of the symptoms in Saudi Arabia. This study aims to assess the prevalence of these symptoms, the risk factors, and severity among Taif city population, Saudi Arabia.

**Methodology:** A cross-sectional study was conducted using a questionnaire in Arabic language from February to May 2019 among Taif city population, Saudi Arabia. The weblink of the questionnaire was distributed using social media to collect the data needed for the research. The data were analyzed by the Statistical Package for the Social Sciences version 23.

**Results:** Among the total of 503 participants, 71.8% were females and 28.2% were males. The mean age was found to be  $25.9 \pm 8.2$  years with a mean weight of  $64.80 \pm 19$  kg. Among the total, 21.9% of the participants had some systemic disease, whereas 39.2% of them had some form of allergy. The prevalence of regurgitation was 33.6%, heartburn was 46.3%, and chest pain 29.4%. Furthermore, 13.7% of participants reported pain while swallowing, and 15.9% of them reported it while vomiting. The prevalence of sensations of something sticking in the throat was found to be present in 21.7%, and 15.5% had reported difficulty in swallowing solid food. No association was observed between the age and the prevalence of esophageal symptoms.

**Conclusion:** The prevalence of the symptoms in the study population was very high. Many factors such as obesity were found to be associated with the symptoms. People with these symptoms had reported severe breathing difficulty. Hence, this study recommends the need of awareness about the symptoms, risk factors, and disorders among the study population.

**Keywords:** Symptoms, suggestive, esophageal disorders, prevalence.

## Introduction

The esophagus is a luminal organ formed mainly of muscles, which connects the mouth to the stomach to deliver food and drinks during swallowing [1]. The lower esophageal sphincter (LES) is the point, where the esophagus meets the stomach. It opens to allow the food and drinks to pass into the stomach and then closes to keep the stomach content inside [2]. When the LES is damaged and does not close, the stomach content returns properly back to the esophagus and irritates it causing uncomfortable sensation "heartburn," which is called "gastroesophageal reflux disease (GERD)" [3,4]. The prevalence of GERD in Saudi Arabia is 28.7% [3,4]. The estimated range of the prevalence of symptoms suggestive of GERD was found

to be 25% [5]. Histologically, the stratified squamous non-keratinized epithelium is the lining of the esophagus. When the lining of the esophagus becomes more like the intestinal lining (simple columnar) due to the frequent

**Correspondence to:** Shahad Khalid Rafee Alsherbi

\*Medical student, college of medicine, Taif university, Taif, Saudi Arabia.

**Email:** Shahad0alsherbi@gmail.com

*Full list of author information is available at the end of the article.*

**Received:** 24 June 2020 | **Accepted:** 10 July 2020

reflux of stomach acid to the lower end of the esophagus that is called "Barrett's esophagus (BE)," it is associated with GERD, and it results in uncomfortable sensation "heartburn" and dysphagia [6]. The prevalence of BE in Saudi Arabia was 0.31% based on the recent retrospective study. Furthermore, this study reported that the symptoms of BE are dyspepsia (4 cases), hematemesis (2 cases), and dysphagia (2 cases) [7]. The international prevalence of esophageal rings and webs is unknown [8]. However, in the US, the prevalence of lower esophageal rings (6%-14%) and esophageal webs (5%-15%) have been reported [8]. There is no previous specific study that has assessed the prevalence of symptoms suggestive of common esophageal disorders in all regions of Saudi Arabia. In this study, we aim to estimate the incidence of the common esophageal disease among the general population in Saudi Arabia

**Methodology**

A cross-sectional study was conducted from February to May 2019 among the general population in the city of Taif, Saudi Arabia. A pre-tested and validated questionnaire in the Arabic language was used to collect the data. A translated English version was also prepared for the need for data translation after the responses were received. Both versions were tested for its validity and reliability on a sample of 30 random subjects in a pilot study. The weblink of the questionnaire was distributed through some of the commonly used social media applications, and the responses were recorded accordingly. A minimum sample size of 415

was calculated for this study. Initially, the questionnaire was sent to 968 people randomly and finally received a total of 503 completed responses, which we used for the analysis, thus giving a response rate of 51.96% for this study.

The Research and Ethics Committee of the College of Medicine, Taif University, approved the study. Consents were obtained from participating students, and confidentiality was ensured for the information they provided. The questionnaire consisted of two parts; part I included sociodemographic details of the participants such as age, gender, nationality, location, marital status, education level, and occupation. The next part recorded the symptoms suggestive of GER and esophageal disorders such as regurgitation, heartburn, chest pain, and pain while swallowing and vomiting. The questionnaire also recorded experiences of participants related to food consumption and a medication used. Information was also recorded regarding smoking, tobacco consumption, weight, and height and concurrent diseases.

The data were collected and tabulated using software Microsoft Excel by an expert in data management. The statistical analysis was carried out using the Statistical Package for the Social Sciences version 23. The descriptive statistics using frequencies and percentages were performed for continuous data. The Pearson's Chi-square test was used for finding any statistical relationship between categorical variables. All statistical analyses were two-sided and had significant value ( $\alpha$ ), and  $p < 0.05$  was considered to be statistically significant, and the power of the test ( $\beta$ ) was set at 80%.

**Results**

This cross-sectional study was conducted in the Taif city, which included 503 participants who represented the region. The analysis showed that 71.8% were females and 28.2% were males. The other sociodemographic details are shown in Table 1. The mean age of this study population was found to be  $25.9 \pm 8.2$  years, and the mean weight was found to be  $64.80 \pm 19.5$  kg. When the medical history of the participants was enquired, it was found that 21.9% had some for systemic diseases and 39.2% had one or other some forms of allergy. More than half of the participants (53.7%) reported that they did not do any physical activity or exercise (Table 2).

**Table 1.** Sociodemographic details.

		<i>n</i>	%
Gender	Female	361	71.8
	Male	142	28.2
	Total	503	100.0
Marital status	Divorced	11	2.2
	Married	117	23.3
	Single	375	74.6
Education	Primary	2	0.4
	Intermediate	4	0.8
	Secondary	98	19.5
	Tertiary	399	79.3

**Table 2.** Medical history of patients.

		<i>n</i>	%
Prevalence of medical History	Medical history in one or any forms	110	21.9
	No medical history	393	78.1
Physical activity (Exercise)	1-3 times/week	175	34.8
	More than 3 times/week	58	11.5
	None	270	53.7
History of Allergy	Allergy history	197	39.2
	No allergy	306	60.8

## The prevalence of symptoms suggestive of common esophageal disorders

In this study, when the prevalence of different esophageal disorders was recorded, it was found that the incidence of regurgitation was found to be 33.6%, heartburn was 46.3%, and chest pain was 29.4%. About 13.7% reported pain while swallowing, and vomiting was present in 15.9% of the participants. The prevalence of sensations of something sticking in the throat was found to be present in 21.7%, and 15.5% had reported difficulty in swallowing solid food (Table 3). There was no association observed between the age of the participants and the prevalence of esophageal symptoms (Table 4).

The prevalence of weight loss was found to be 14%. It was found that 21.3% of the people who had regurgitation had also reported unexplained weight loss, and this was statistically significant,  $p < 0.001$  (Table 5). There was also a significant positive association between chest pain

and weight loss ( $p < 0.001$ ) and even between vomiting and weight loss ( $p < 0.001$ ) (Table 5). It was also observed that the prevalence of heartburn, chest pain, and pain during swallowing was comparatively more in obese people and overweight people,  $p < 0.05$  (Table 5). The relationship of body mass index (BMI) with esophageal symptoms showed a statistically significant association, where obese and overweight people had more prevalence of heartburn and chest pain compared to other BMI grades (Table 5). The analysis showed that 13.5% ( $n = 68$ ) experienced unexplained weight loss, and the assessment showed that this type of weight loss had a significant relationship with all the symptoms such as regurgitation ( $p < 0.001$ ), chest pain ( $p < 0.001$ ), heartburn ( $p < 0.05$ ), pain on swallowing ( $p < 0.05$ ), and vomiting ( $p < 0.001$ ) (Table 5).

**Table 3.** Prevalence of esophageal disorders.

		N	%
Sensations of something sticking in the throat	No	394	78.3
	Yes	109	21.7
Difficulty swallowing of liquids	No	443	88.1
	Yes	60	11.9
Difficulty swallowing of solid food	No	425	84.5
	Yes	78	15.5
Difficulty swallowing of soft foods	No	461	91.7
	Yes	42	9.3
Regurgitation	No	334	66.4
	Yes	169	33.6
Heartburn	No	270	53.7
	Yes	233	46.3
Chest pain	No	355	70.6
	Yes	148	29.4
Pain while swallowing	No	434	86.3
	Yes	69	13.7
Vomiting	No	423	84.1
	Yes	80	15.9

**Table 4.** Relationship of symptoms and age.

		Age groups (years)						Total	p-value
		<20	20-30	30-40	40-50	50-60	>60		
Regurgitation	Absent	65	196	39	25	6	3	334	>0.05
	Present	34	107	16	9	3	0	169	
Heartburn	Absent	55	163	30	17	4	1	270	>0.05
	Present	44	140	25	17	5	2	233	
Chest pain	Absent	65	214	39	26	3	8	355	>0.05
	Present	34	89	16	8	0	1	148	
Pain swallow	Absent	77	266	51	30	8	2	434	>0.05
	Present	22	37	4	4	1	1	69	
Vomiting	Absent	77	253	51	31	8	3	423	>0.05
	Present	22	50	4	3	1	0	80	

## The prevalence of symptoms suggestive of common esophageal disorders

It was found that 33% and 15% of the participants had reported a burning feeling from the stomach and feeling of sickness or nausea, respectively (Figure 1). When the timing of these discomforts was asked, it was found that 23% reported to have it within 2 hours after taking food, whereas, for 16% of people, it was at a particular time of the day or night with no relationship to food intake (Figure 2). When the relationship of these discomforts with the type of food was assessed, it was found that there was a statistically significant relationship observed. About 8.9% of the people had improvement with natural foods, and 35.4% and 32.2% experienced worsening of these discomforts ( $p < 0.001$ ) (Table 6). The prevalence of smoking and alcohol consumption among the participants was found to be 8.2% and 1.2%, respectively. There was no statistically significant association observed between esophageal symptoms and these habits,  $p > 0.05$  (Table 7).

In this study population, there was an improvement reported in regurgitation and heartburn when they took

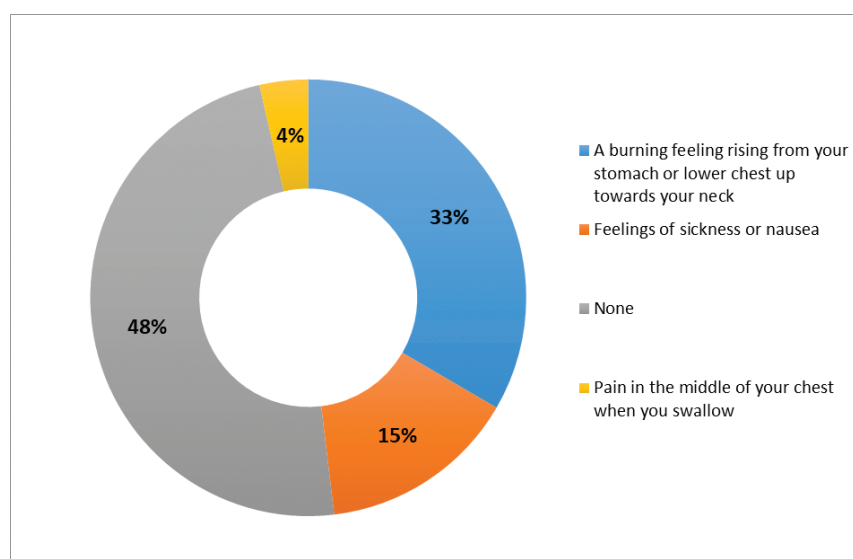
proton pump inhibitors (PPIs), and this was statistically significant,  $p < 0.001$  (Table 8). Sleep disturbances were reported in 31.8% of participants, and 2.6% mentioned that they had the difficulty of swallowing food for more than 10 years (Table 9). When the association of symptoms with breathing difficulties was assessed, it was observed that breathing difficulties were either severe or very severe in all the symptoms reported, and this was statistically significant,  $p < 0.001$  (Table 10).

### Discussion

To date, there were no studies conducted in Saudi Arabia to assess the prevalence of the different types of esophageal disorders, their symptoms, and associated factors. The research was conducted in the city of Taif city, which included 503 participants' responses. The prevalence of regurgitation in this study was reported 33.6%, and 46.3% reported heartburn. A recent study done in Saudi Arabia regarding GERD had published a

**Table 5.** Relationship of esophageal symptoms with weight loss and BMI.

		Unexplained weight loss in the past year		p-value	BMI				p-value
		No	Yes		Underweight	Normal	Overweight	Obese	
Regurgitation	Absent	302	32	<0.001	42	164	72	56	>0.05
	Present	133	36		25	73	41	30	
Heartburn	Absent	242	28	<0.05	40	140	53	37	<0.05
	Present	193	40		27	97	60	49	
Chest pain	Absent	323	32	<0.001	38	174	74	69	<0.01
	Present	112	36		29	63	39	17	
Pain during swallow	Absent	382	52	<0.05	53	215	88	78	<0.01
	Present	53	16		14	22	25	8	
Vomiting	Absent	376	47	<0.001	50	198	95	80	<0.05
	Present	59	21		17	39	18	6	



**Figure 1.** Reported discomfort by the participants.

The prevalence of symptoms suggestive of common esophageal disorders

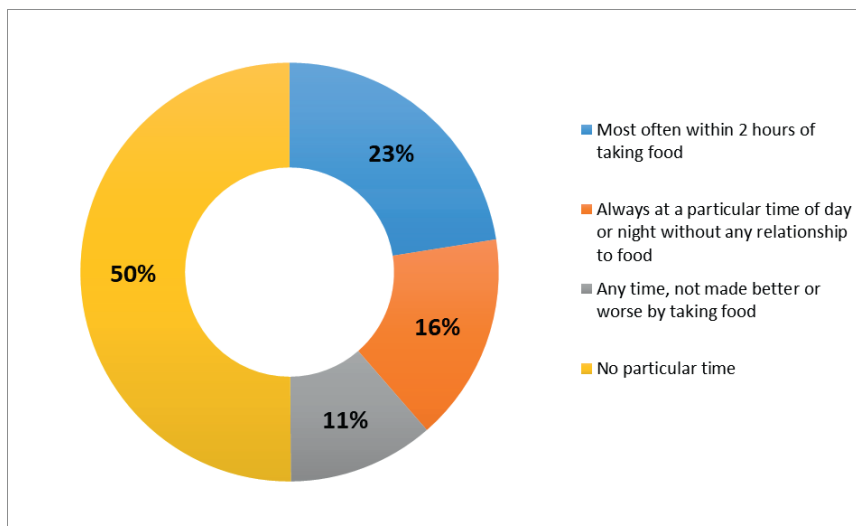


Figure 2. Timing of the discomfort.

Table 6. Relationship of type of foods and discomfort.

Type of foods	Type of discomfort				Total	p-value
	Improve	No effect	Unsure	Worsen		
Usual meals	45 (8.9%)	337 (67%)	83 (16.5%)	38 (7.6%)	503	<0.001
Food rich in fat	32 (6.4%)	236 (47%)	57 (11.3%)	178 (35.4%)	503	
Strongly flavored or spicy food	34 (6.8%)	246 (48.9%)	61 (12.1%)	162 (32.2%)	503	

Table 7. Relationship of esophageal symptoms with deleterious habits.

		Do you smoke?			Total	p-value	Alcohol consumption			p-value
		No	Quit smoking	Yes			Yes	No	Total	
Regurgitation	Absent	291	17	26	334	>0.05	3	331	334	>0.05
	Present	149	5	15	169		3	166	169	
Heartburn	Absent	234	13	23	270	>0.05	1	269	270	>0.05
	Present	206	9	18	233		5	228	233	
Chest pain	Absent	309	17	29	355	>0.05	3	352	355	>0.05
	Present	131	5	12	148		3	145	148	
Pain during swallow	Absent	377	20	37	434	>0.05	4	430	434	>0.05
	Present	63	2	4	69		2	67	69	
Vomiting	Absent	372	20	31	423	>0.05	3	420	423	>0.05
	Present	68	2	10	80		3	77	80	

prevalence of 28.7% [3]. A study done by Ruth et al. [5] had reported that 25% of the participants had symptoms suggestive of esophageal disorders. Another study done in English speaking western population that included a sample from countries such as the USA, UK, and Canada reported that 17% of them suffered from at least one form of an esophageal symptom [9]. These symptoms can significantly reduce the quality of life which has led to high healthcare utilization [10,11].

In these findings, there was no relationship observed for the prevalence of these symptoms with age. This finding supports the pieces of evidence that suggest that there

is only a mild or minimal effect seen in esophageal physiology as age increases [12]. It also reported that systemic diseases such as scleroderma, systemic lupus erythematosus, diabetes mellitus, polymyositis, dermatomyositis, "overlap" collagen syndromes, amyloidosis, alcoholism, and rheumatoid arthritis may affect esophageal motor dysfunction which could produce some esophageal discomfort or disorder symptoms [13,14]. Patients who are diagnosed with systemic sclerosis can experience "absent contractility" and could predispose to GERD [15]. In this study, we found that 21.9% had at least one or more forms of systemic

The prevalence of symptoms suggestive of common esophageal disorders

**Table 8.** Relationship of PPI intake and type of discomfort.

		Discomfort Improvement with PPIs				Pearson's Chi-Square	p-value
		Yes	No	Do not know	Not used		
Regurgitation	Absent	43	15	51	225	21.771	<0.001
	Present	48	12	24	85		
Heartburn	Absent	27	14	40	189	27.759	<0.001
	Present	64	13	35	121		
Chest pain	Absent	64	18	48	225	2.363	0.501
	Present	27	9	27	85		
Pain during swallow	Absent	77	20	64	273	4.503	0.212
	Present	14	7	11	37		
Vomiting	Absent	71	25	61	266	5.0735	0.166
	Present	20	2	14	44		

**Table 9.** Experiences related to esophageal discomfort.

		Frequency	Percentage
Sleep disturbances due to discomfort	No	343	68.2
	Yes	160	31.8
Time since the difficulty of swallowing started	Past 6 months	26	5.2
	1-2 years	13	2.6
	3-5 years	26	5.2
	5-10 years	22	4.4
	7-12 months	12	2.4
	More than 10 years	13	2.6
	None	391	77.7

**Table 10.** Relationship between symptoms and breathing difficulties.

		Breathing difficulties or choking episodes within last month						p-value
		No problem	Very mild	Mild	Moderate	Severe	Very severe	
Regurgitation	Absent	264	36	16	9	2	7	<0.001
	Present	76	34	20	13	11	15	
Heartburn	Absent	206	30	23	6	2	3	<0.001
	Present	134	40	13	16	11	19	
Chest pain	Absent	268	47	19	13	4	4	<0.001
	Present	72	23	17	9	9	18	
Pain swallow	Absent	313	57	30	16	9	9	<0.001
	Present	27	13	6	6	4	13	
Vomiting	Absent	307	56	26	13	7	14	<0.001
	Present	33	14	10	9	6	8	

diseases, and hypertension and diabetes mellitus were commonly seen as diseases. Laique et al. [14] reported that there is a correlation of hypertension with GERD, and it was demonstrated that antacid therapy with PPIs reduced this discomfort by maintaining normal BP. The findings also supported the above report, which showed a statistically significant improvement in regurgitation and heartburn with the intake of PPIs. In this study, we observed that obese and overweight people had increased

the prevalence of esophageal symptoms such as heartburn, chest pain, and pain during swallowing. The studies show that obesity is a risk factor for esophageal disorders even though this relationship is controversial [16–18]. This could be due to the increase in abdominal pressure leading to increased acid reflux or could also be due to the presence of hiatal hernia [19,20]. We also observed that weight loss was seen in people who had

vomiting, which, when correlated with underweight people, was statistically significant.

The findings of this study showed that the type of food consumed had some relationship with esophageal discomfort. Participants who took fatty and spicy foods had shown a worsening effect on the symptoms. This is in contrast to the other studies which reported that fatty foods, alcohol, and coffee showed no significant association with GERD [21–23]. On the contrary, it is said that consuming capsaicin could help to alleviate the esophageal motor disorders [24]. Even though some research works show that an increased ingestion of fatty foods, coffee, and chocolate has found to induce gastroesophageal reflux, the exact correlation is not proved yet [25]. We noticed that there was a significant association of esophageal discomforts with breathing in this study population. The severity of breathing difficulties increased as the participants experienced these symptoms. Evidence suggests that GERD could act as a trigger for extraesophageal manifestations such as asthma, chronic cough, chronic obstructive pulmonary disease, cystic fibrosis, and non-cystic fibrosis bronchiectasis [26,27]. In asthmatic patients, due to pulmonary hyperinflation, there could be diaphragmatic dysfunction leading to bronchoconstriction, thus affecting change in pressure between the thorax and stomach, which stimulates GERD symptoms [27,28].

The descriptive epidemiological studies always carry some limitations. Hence, it should be noted that the assessment of esophageal disorders is still dependent on the use of questionnaires. Similar to most of the questionnaire studies, the current study may also overestimate the prevalence of the variables being studied since people free of symptoms have got a less chance to respond. The response rate of the questionnaire may support this shortfall. Another drawback for this study could be a low level of accuracy as many patients who have common visceral neural pathways may experience unspecific symptoms. Furthermore, it was difficult to analyze the temporal relationships between many risk factors and diseases. There were many other typical and atypical symptoms, which we did not include in the questionnaire that could have led to the underestimation of esophageal disorders prevalence in the region. The strength of this study is that we used a pre-tested and validated Arabic version of the questionnaire which may unlikely affect the language and educational differences of the respondents as the translation of these symptoms is more descriptive and exact than English. Furthermore, we used semiquantitative scales for the variables instead of the dichotomous variables, which allowed us to explore a more comprehensive relationship between the categorical variables. There is a need to do a broader study to examine the role of other physical and environmental factors that could influence the onset of these symptoms.

## Conclusion

The prevalence of esophageal discomforts was very high in the study population. Among the many factors suspected

of precipitating these symptoms, obesity was found to be one. People who experienced esophageal disorders had encountered severe breathing difficulties. It was observed that these disorders are associated with many modifiable risk factors, and therefore, actions should be taken to raise awareness about these disorders and its risk factors.

## List of Abbreviations

BE	Barrett's esophagus
BMI	Body mass index
GERD	Gastroesophageal reflux disease

## Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

## Funding

None.

## Consent for publication

Informed consent was obtained from all the participants.

## Ethical approval

Ethics approval was granted by Ethics Committee of Taif University, Letter/reference number: 40-36-0154, dated 07-April-2019.

## Author details

Mohammad Eid Mahmoud Mahfouz<sup>1</sup>, Shahad Khalid Alsherbi<sup>2</sup>, Dhuha Abdulrahman Alhumaidi<sup>3</sup>, Fatima Moeesh Altalhi<sup>3</sup>, Rabeah Ahmed Alsofyani<sup>4</sup>

1. Associate Professor of surgery and consultant surgeon; College of Medicine, surgical department, Taif University, Taif, Saudi Arabia
2. Medical student, college of medicine, Taif university, Taif, Saudi Arabia
3. Medical Intern, College of Medicine, surgical department, Taif University, Taif, Saudi Arabia
4. Pediatric resident, Taif children hospital, Taif, Saudi Arabia

## REFERENCES

1. Chaudhry SR, Bordoni B. Anatomy, thorax, esophagus. StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing [cited 2019 Apr 8]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482513/>
2. Zaninotto G, DeMeester TR, Schwizer W, Johansson KE, Cheng SC. The lower esophageal sphincter in health and disease. *Am J Surg.* 1988;155(1):104–11. [https://doi.org/10.1016/S0002-9610\(88\)80266-6](https://doi.org/10.1016/S0002-9610(88)80266-6)
3. Alsuwat OB, Alzahrani AA, Alzhrani MA, Alkathami AM, Mahfouz MEM. Prevalence of gastroesophageal reflux disease in Saudi Arabia. *J Clin Med Res.* 2018;10(3):221–5. <https://doi.org/10.14740/jocmr3292w>
4. Alkathami AM, Alzahrani AA, Alzhrani MA, Alsuwat OB, Mahfouz ME. Risk factors for gastroesophageal reflux disease in Saudi Arabia. *Gastroenterol Res.* 2017;10(5):294–300. <https://doi.org/10.14740/gr906w>
5. Ruth M, Månsson I, Sandberg N. The prevalence of symptoms suggestive of esophageal disorders. *Scand J Gastroenterol.* 1991;26(1):73–81 <https://doi.org/10.3109/00365529108996486>

## The prevalence of symptoms suggestive of common esophageal disorders

6. Runge TM, Abrams JA, Shaheen NJ. Epidemiology of Barrett's esophagus and esophageal adenocarcinoma. *Gastroenterol Clin.* 2015;44(2):203–31. <https://doi.org/10.1016/j.gtc.2015.02.001>
7. Gadour MO, Ayoola EA. Barrett's oesophagus and oesophageal cancer in Saudi Arabia. *Trop Gastroenterol.* 1999;20(3):111–5.
8. Wong PW, Shaffer R, Kadakia SC. Esophageal manometry, 24-hour pH monitoring and clinical characteristics in 12 adults with multiple esophageal. *Gastroenterology.* 2000;118(4 Pt 1):A491. [https://doi.org/10.1016/S0016-5085\(00\)84083-4](https://doi.org/10.1016/S0016-5085(00)84083-4)
9. Josefsson A, Palsson O, Simrén M, Sperber AD, Törnblom H, Whitehead W. Oesophageal symptoms are common and associated with other functional gastrointestinal disorders (FGIDs) in an English-speaking Western population. *United European Gastroenterol J.* 2018;6(10):1461–9. <https://doi.org/10.1177/2050640618798894>
10. Wiklund I, Carlsson J, Vakil N. Gastroesophageal reflux symptoms and well-being in a random sample of the general population of a Swedish community. *Am J Gastroenterol.* 2006;101:18–28. <https://doi.org/10.1111/j.1572-0241.2005.00343.x>
11. Ronkainen J, Aro P, Storskrubb T, Lind T, Bolling-Sternevald E, Junghard O, et al. Gastro-oesophageal reflux symptoms and health-related quality of life in the adult general population—the Kalixanda study. *Aliment Pharmacol Ther.* 2006;23:1725–33. <https://doi.org/10.1111/j.1365-2036.2006.02952.x>
12. Tack J, Vantrappen G. The aging oesophagus. *Gut.* 1997;41:422–4. <https://doi.org/10.1136/gut.41.4.422>
13. Mukhopadhyay AK, Graham DY. Esophageal motor dysfunction: in systemic diseases. *Arch Intern Med.* 1976;136(5):583–8. <https://doi.org/10.1001/archinte.1976.03630050063011>
14. Laique S, Singh T, Dornblaser D, Gadre A, Rangan V, Fass R, et al. Clinical characteristics and associated systemic diseases in patients with esophageal "absent contractility"—a clinical algorithm. *J Clin Gastroenterol.* 2019;53(3):184–90. <https://doi.org/10.1097/MCG.0000000000000989>
15. Van Hoeij FB, Bredenoord AJ. Clinical application of esophageal high-resolution manometry in the diagnosis of esophageal motility disorders. *J Neurogastroenterol Motil.* 2016;22(1):6–13. <https://doi.org/10.5056/jnm15177>
16. Murray L, Johnston B, Lane A, Harvey I, Donovan J, Nair P, et al. Relationship between body mass and gastro-oesophageal reflux symptoms: the Bristol helicobacter project. *Int J Epidemiol.* 2003;32(4):645–50. <https://doi.org/10.1093/ije/dyg108>
17. 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(3):199–211. <https://doi.org/10.7326/0003-4819-143-3-200508020-00006>
18. Lagergren J, Bergstrom R, Nyren O. No relation between body mass and gastro-oesophageal reflux symptoms in a Swedish population based study. *Gut.* 2000;47(1):26–9. <https://doi.org/10.1136/gut.47.1.26>
19. Barak N, Ehrenpreis ED, Harrison JR, Sitrin MD. Gastro-oesophageal reflux disease in obesity: pathophysiological and therapeutic considerations. *Obes Rev.* 2002;3(1):9–15. <https://doi.org/10.1046/j.1467-789X.2002.00049.x>
20. Wilson LJ, Ma W, Hirschowitz B. Association of obesity with hiatal hernia and esophagitis. *Am J Gastroenterol.* 1999;94(10):2840–4. <https://doi.org/10.1111/j.1572-0241.1999.01426.x>
21. Ruhl C, Everhart JE. Overweight, but not high dietary fat intake, increases risk of gastroesophageal reflux disease hospitalization: the NHANES I epidemiologic followup study. *Am Epidemiol.* 1999;9(7):424–35. [https://doi.org/10.1016/S1047-2797\(99\)00020-4](https://doi.org/10.1016/S1047-2797(99)00020-4)
22. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Lifestyle related risk factors in the aetiology of gastroesophageal reflux. *Gut.* 2004;53:1730–5. <https://doi.org/10.1136/gut.2004.043265>
23. Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd. Risk factors associated with symptoms of gastroesophageal reflux. *Am J Med.* 1999;106(6):642–9. [https://doi.org/10.1016/S0002-9343\(99\)00121-7](https://doi.org/10.1016/S0002-9343(99)00121-7)
24. Grossi L, Cappello G, Marzio L. Effect of an acute intraluminal administration of capsaicin on oesophageal motor pattern in GORD patients with ineffective oesophageal motility. *Neurogastroenterol Motil.* 2006;18(2):632–6. <https://doi.org/10.1111/j.1365-2982.2006.00793.x>
25. Surdea-Blaga T, Negrutiu DE, Palage M, Dumitrascu DL. Food and gastroesophageal reflux disease. *Curr Med Chem.* 2019;26(19):3497–511. <https://doi.org/10.2174/0929867324666170515123807>
26. Morice AH. Airway reflux as a cause of respiratory disease. *Breathe.* 2013;9(4):256–66. <https://doi.org/10.1183/20734735.000513>
27. Gaude GS. Pulmonary manifestations of gastroesophageal reflux disease. *Ann Thorac Med.* 2009;4(3):115–23. <https://doi.org/10.4103/1817-1737.53347>
28. Richter JE. Gastroesophageal reflux disease and asthma: The two are directly related. *Am J Med.* 2000;108:153S–8S. [https://doi.org/10.1016/S0002-9343\(99\)00356-3](https://doi.org/10.1016/S0002-9343(99)00356-3)