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Laryngopharyngeal reflux in war-torn Syria and its association with smoking and other risks: an online cross-sectional population study

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ABSTRACT

Objectives To demonstrate the burden of laryngopharyngeal reflux (LPR) in Syria and its associated variables.

Design This is a cross-sectional study that used online questionnaires that included demographics, smoking, war-related questions and reflux symptom index (RSI).

Setting This research was conducted online across Syria and included the general population.

Participants Participants who lived in Syria, agreed to participate, and responded to all the RSI questions were included. This research comprised 734 participants, with 94.6% response rate, 75.5% being females, and a mean age of 24 years.

Results Overall, 31.9% of subjects had symptoms suggestive of LPR. Participants who were 30 years and younger had fewer symptoms suggestive of LPR compared with the older group p=0.012 (OR 0.534; 95% CI 0.325 to 0.877). While having an epigastric burning sensation, chest pain and indigestion were the most common symptoms, having a sore throat was the least common. Being distressed from war noises was associated with more symptoms p=0.009 (OR 1.562; 95% CI 1.117 to 2.183). However, losing someone or changing place of living due to war were not significantly associated with these symptoms p>0.05. RSI scores were associated with cigarette and/or shisha smoking p<0.05. Finally, asthma, allergic disorders and having a job were associated with having LPR symptoms p<0.05. No significant findings were observed in consanguinity, marital status, educational level and socioeconomic status.

Conclusions War, smoking, asthma, allergies, respiratory conditions and having a job were associated with LPR symptoms. However, they may be associated with these symptoms independently from LPR; for instance, similar symptoms can be caused by the mental disorders from war, the unique environment and irritant substances of the laryngeal mucosa.

Strengths and limitations of this study

- This study was about the general population across Syria during the war.
- It used a validated tool in the language of participants and simple and straightforward questions.
- It measured laryngopharyngeal reflux symptoms using the self-reported reflux symptom index questionnaire without a medical diagnosis.
- As it was an anonymous online study, people who were severely affected might have not been porperly targeted.
- No clinical examinations, or tests were conducted; it included a young population with a relatively high socioeconomic status.

INTRODUCTION

Laryngopharyngeal reflux (LPR) is considered one of the most common extra-oesophageal complications of gastro-oesophageal reflux (GORD). It occurs when the retrograde flow of the stomach reaches the laryngopharynx and interacts with the upper aerodigestive tract.[1] Data have shown that 60% of patients with GORD have LPR symptoms.[2] Furthermore, it is debatable whether to consider LPR as an atypical presentation of GORD or an independent medical condition.[3] The severity of symptoms cannot be determined by the severity of posterior laryngitis and pharyngeal reflux, or by using dual sensor pH probe.[4] Nevertheless, visits to otolaryngologists were increased by 500% due to LPR in recent years,[5] which caused a huge burden on the medical sector. Many laryngeal medical conditions are speculated to be associated with LPR, such as laryngitis, laryngeal carcinoma, subglottic stenosis, granulomas, contact ulcers and vocal cord nodules. Dysphonia can also be found in around half of patients with LPR.

Although LPR is quite common, the diagnosis is widely debated, as most studies are controversial. Otolaryngologists suggest that LPR is diagnosed when the laryngeal symptoms get resolved by proton pump inhibitors (PPIs).[6] Scoring systems can also be used to evaluate the possibility of LPR,[6] such as reflux

symptom index (RSI).[7 8] Having a score higher than 13 is indicative for an empirical therapeutic trial such as diet, lifestyle change, and implementing high doses of PPI.[6]

Syria has entered its eighth year of war at the time of the survey, and over 80% have been living under poverty line in a deteriorating economic status. This imposed a challenge to the healthcare sector from the lack of adequate staff and equipment. The Syrian population is chronically exposed to unusual substances from smoking habits, mate drinking, the unique environment and war aspects.[9 10] In Syria, it was found that around half of the population suffered from allergic rhinitis,[11] and >90% of the population were exposed to war aspects.[12] LPR has a wide variety of symptoms from the laryngeal irritation such as coughing, having a sore throat, hoarseness, dysphonia and globus pharyngeus.[13] When LPR diagnosis is not promptly made, patients can suffer for a long time of symptoms that severely affect their quality of life. Most LPR symptoms and signs are unspecific and overlap with other aetiologies, such as voice abuse and irritations from smoking and alcohol drinking. Despite being quite common, LPR is not well-studied in the low- and middle-income countries. We aim to estimate the burden of symptoms associated with LPR and its different factors.

METHODS AND MATERIALS

Sampling

This is a cross-sectional study that collected online data from Social Media groups covering the period between 26 March 2019 and 26 April 2019, while covering various cities in Syria. Every responder who lived in Syria and aged 16 years and more was enrolled provided that they replied to every RSI question. Any responder with missing data in the RSI or basic demographic questions was excluded.

Consent and approval for study

Electronic informed consent was taken for participating in the research, and for using and publishing of the data.

Questionnaires

Socioeconomic status

Socioeconomic status (SES) was assessed by using three questions that included the education of the person or the working family member, their profession and the monthly family income. As a result, SES was divided into five categories: lower, upper-lower, lower-middle, upper-middle, and upper. This method was proved to be adequate in the Syrian society.[12]

Reflux symptom index

RSI is a self-administered questionnaire which was validated in Arabic.[14] RSI relies on a scoring system based on LPR symptoms to evaluate the possibility of having LPR.[7 8] These symptoms are hoarseness, throat clearing, mucus in the throat, difficulty swallowing, coughing after lying down or eating, difficulties of breathing, coughing, globus pharyngeus and heartburn. The scale ranges from 0 when answering 'no problem' to 5 when answering 'severe problem' for each item. The total score ranges from 0 to 45. The cut-off point is set to 13 or more to suggest the possibility of LPR.[8]

Other questions

Demographic questions included gender, age, educational level, governorate of current living and having consanguineous parents. War exposure, both directly and indirectly, including change of place of living due to war, losing someone close and being distressed from war noises were also included in the questionnaires.

We asked the participants to declare having any medical condition. We also asked two simple questions about smoking which were "do you smoke cigarettes daily" and "do you regularly smoke shisha".

Definitions

Respiratory diseases in this study were defined as chronic bronchitis and chronic obstructive pulmonary medical condition. Education in the medical field included medicine, dentistry and pharmacy. Social science category included faculties of law, education, economy, literature and arts. We defined a low educational level as having a high school degree or lower. Allergic reactions are defined as having food or skin-related allergies. Being a specialist is defined as having a degree and working such as an engineer. Being a technician is being a worker with an institute degree. Labourer is a worker without a degree such as a builder and porter.

Data process

Data were processed using IBM SPSS software V.26 for Windows (SPSS, Illinois, USA). One-way analysis of variance (ANOVA), χ^2 and Pearson's correlation tests were used. We calculated ORs and the 95% CIs by using the same software. Values <0.05 for the two-tailed p values were considered statistically significant. Forward linear regression was also used to model the relationship between RSI scale and other variables.

Patient and public involvement

The research question did not interfere with patients' priorities as participants only had to do the survey in their free time with no follow-ups. Patients were involved by responding to the questionnaires estimating the symptoms they had. Their experience with war and symptoms had a major influence on their responses. However, results could be disseminated as the study had random participants from Syria with no particular risk factors. However, data should be cautiously generalised as it included higher SES and younger age groups than the normal population, and it is a self-reported online study.

RESULTS

Characteristics of the subjects are demonstrated in table 1. In our study, 820 received the questionnaire with a 94.6% response rate. Although 776 accepted to be enrolled, the

Table 1 Characteristics of the subjects

Characteristic	Frequency (n=734)	Percentage (%)
Gender		
Male	180	24.5
Female	554	75.5
Place of living		
Damascus, Rif-Dimashq and Aleppo	474	70
Homs and Hama	102	15.1
Al-Jazira region	3	0.4
Southern Syria	18	2.7
Syrian coast	76	11.2
Idlib	4	0.5
Educational level		
Primary school	1	0.1
High school	42	5.7
College or higher institute certificate	575	78.6
Masters or PhD	114	15.6
Smoking cigarettes		
No	622	84.7
Yes regularly	112	15.3
Smoking shisha		
No	517	70.4
Yes regularly	217	29.6
SES level		
Lower	14	1.9
Upper-lower	151	20.6
Lower-middle	177	24.1
Upper-middle	372	50.7
Upper	20	2.7
Employment		
Unemployed	474	648
Employed	258	35.2
Social status		
Single	598	82
In a relationship	5	0.7
Engaged	35	4.8
Married	86	11.8
Divorced	3	0.4
Widowed	2	0.3

Table 2 Other characteristics of war, current medical conditions and medications and reflux symptoms index results for the subjects

Characteristic	Frequency	Percentage (%)
Changing area of living		
No	362	49.9
Yes, but not due to the war	140	19.3
Yes	223	30.8
A relative being endangered by the war		
No	228	31.2
Yes	502	68.8
Losing someone due to the war		
No	417	57.2
Yes	312	42.8
Being distressed from the war noises		
No	263	36
Yes	468	64
Medical conditions		
No	435	72.4
Pulmonary	6	1
Cardiac	12	2
Endocrine	53	8.8
Urinary	7	1.2
Neurological	20	3.3
Skeletal	20	3.3
Asthma	12	2
Allergic reaction	36	6
Drugs		
No	394	59.3
Yes, some supplements	37	5.6
Yes, over-the-counter drugs	70	10.5
Yes, prescribed drugs	163	24.5
Possibility for LPR		
No	500	68.1
Yes	234	31.9

sample consisted of 734 subjects as some replies were invalid or had some RSI questions unanswered. The sample comprised 180 (24.5%) males and 554 (75.5%) females. The mean age was 23.97±6.59 years, and the age group of 18–30 years constituted 88.3% of the sample. Other characteristics of war exposure, current medical conditions and reflux symptoms index of the subjects are demonstrated in table 2. Symptoms associated with LPR were found in 31.9% (95% CI 28.2 to 35.4) of the sample. Subjects who worked in the medical field had less symptoms p=0.033.

Comparisons between subjects with negative and positive LPR symptoms are demonstrated in table 3. The age group younger than 30 years had lower rates of symptoms p=0.012 (OR 0.534; 95% CI 0.325 to 0.877) than the older group. Having any medical condition was associated with more symptoms compared with not having any medical condition p=0.003 (OR 1.843; 95% CI 1.223 to 2.780). This was also evident when associating the symptoms with having a chronic medical condition such as asthma p>0.0001 (OR 13.750; 95% CI 2.969 to 63.690), allergic reactions p=0.001 (OR 3.074; 95% CI 1.545 to 6.115) and pulmonary medical conditions p=0.029 (OR 5.500;

Table 3 Comparisons between subjects with negative and positive reflux symptoms index

Characteristics	Positive reflux symptoms	Percentage (%)	Negative reflux symptoms	Percentage (%)	P value	OR
Gender					0.084	1.390 (0.956 to 2.021)
Male	48	20.5	132	26.4		
Female	186	79.5	368	73.6		
Consanguinity					NS	–
Negative	176	81.5	374	82.2		
Positive	40	18.5	81	17.8		
Marital status					NS	–
Single	184	79	414	83.5		
Non-single	49	21	82	16.5		
Educational level					NS	–
Low	19	8.2	24	4.8		
High	214	91.8	475	95.2		
Cigarette smoking					0.002	1.920 (1.273 to 2.894)
No	184	78.6	438	87.6		
Yes daily	50	21.4	62	12.4		
Shisha smoking					0.126	1.299 (0.929 to 1.815)
No	156	66.7	361	72.2		
Yes regularly	78	33.3	139	27.8		
Smoking both shisha and cigarettes						2.323 (1.395 to 3.869)
No	201	85.9	467	93.4	0.001	
Yes regularly	33	14.1	33	6.6		
SES						–
Low	57	24.6	104	20.9		
Medium	172	74.1	377	75.7	0.286	
High	3	1.3	17	3.4	0.12	
Age group (years)					0.005*	–
0–17	9	3.8	6	1.2		
18–30	193	82.5	455	91		
31–45	25	10.7	32	6.4		
46+	7	3	7	1.4		
Working					0.032	1.419 (1.029 to 1.957)
Unemployed	138	59.2	336	67.3		
Employed	95	40.8	163	32.7		
Type of work					NS	–
Labourer	8	6.1	11	9.7		
Clerk or in a restaurant	10	7.6	11	9.7		
Technician	31	23.7	51	45.1		
Specialist	76	58	35	31		
Employee	6	4.6	5	4.4		
Medical conditions except gastro						–
Negative	115	61.8	319	77.2		
Respiratory	4	2.2	2	0.5	<0.0001†	
Cardiac	4	2.2	8	1.9		
Endocrine	11	5.9	42	10.2		
Urinary	3	0.3	4	1		
Neurological	10	5.4	10	2.4		
Skeletal	10	5.4	10	2.4		
Asthma	10	5.4	2	0.5		
Allergic reaction	19	10.2	16	3.9		

Continued

Table 3 Continued

Characteristics	Positive reflux symptoms	Percentage (%)	Negative reflux symptoms	Percentage (%)	P value	OR
Losing someone close due to war					NS	–
No	68	40.5	149	44		
Yes a loved one or a close friend	2	1.2	3	0.9		
Yes a relative	98	58.3	187	55.2		
Distressed from war noises					0.009	1.562 (1.117 to 2.183)
Negative	68	29.2	195	39.2		
Positive	165	70.8	303	60.8		
Changing place of living due to war					NS	–
Negative	116	50.2	246	49.8		
Positive	115	49.8	248	50.2		

*This p value is among all age groups. However, p=0.012 when comparing age groups (0–30) years with older than 30 years and p=0.008 when comparing age group 18–30 years with older than 30 years.
†P value when comparing having any disease or not was p=0.003.
NS, not significant; SES, socioeconomic status.

95% CI 0.994 to 30.428) compared with not having any chronic medical condition.

Furthermore, when using RSI scores instead of cut-off points, higher scores were found with cigarette smoking p<0.0001, shisha smoking p=0.035 and smoking them both p<0.0001. No correlation was found when comparing RSI score with age or number of times changing place of living due to war p>0.05. When using one-way ANOVA test, SES classification was not associated with RSI scores p>0.05.

The mean score of RSI in all subjects was 10.50±9.02 (95% CI 8.47 to 9.58). The mean score of each question of the index in subjects and number of people who had moderate or more severe symptoms in table 4. The mean RSI score in each governorate and gender is shown in figure 1. When using forward linear regression on RSI score with the significant variables from table 3, it was significant for medical condition category, smoking both shisha and cigarettes, being distressed from war noise, having a work. Regression results are demonstrated in table 5.

Table 4 Mean scores and symptoms of each reflux symptom index question in the participants

Characteristic	Mean score±SD	Moderate or more severe symptoms prevalence (%)
Sore throat	0.86±1.207	69 (9.4%)
Sputum production	1.31±1.422	146 (19.9%)
Excessive secretions	1.25±1.476	137 (18.7%)
Dysphagia	0.87±1.309	92 (12.5%)
Coughing after eating, sleeping or laying down	1.22±1.519	133 (18.1%)
Breathing difficulties	1.07±1.409	113 (15.4%)
Extreme coughing episodes	1.16±1.541	131 (17.9%)
A sense of a foreign body in throat	1.17±1.457	112 (15.3%)
Epigastric burning sense, chest pain, indigestion, GORD	1.69±1.643	199 (27.1%)
Total	10.50±9.022	–

GORD, gastro-oesophageal reflux.

DISCUSSION

Many studies proved that females had more reflux symptoms such as heartburn,[15] which is not similar to our findings. Meanwhile, there are conflicting data about the effect of smoking on reflux disease.[16] Although smoking might not be a dominant risk factor, it was suggested that smoking cessation with the appropriate pharmacological therapy might be beneficial in relieving severe GORD symptoms,[17] and smoking cessation should be recommended for patients with GORD.[18] In our study, cigarette smoking was associated with more LPR symptoms. The high prevalence of smoking might be one of the factors for the high prevalence of LPR symptoms in Syria,[9] mainly that there are no regulations to prevent smoking in public places and transportations, causing a high exposure to all people as non-smokers are highly exposed to second-hand smoking.[9] Smoking can also irritate the laryngeal mucosa causing coughing, hoarseness and other symptoms similar to LPR.

GORD was associated with respiratory diseases and asthma,[19] and LPR was associated with allergic rhinitis.[20] This is similar to our findings as LPR symptoms were correlated with the aforementioned risk factors. However, these medical conditions can cause symptoms that can be misinterpreted by RSI as LPR symptoms, particularly that allergic rhinitis was found in half of a studied population in Syria,[11] which could explain the high prevalence of LPR symptoms.

A large number of patients with LPR struggled from higher rates of depression and had a lower health-related quality of life.[21] In addition, the psychological factors

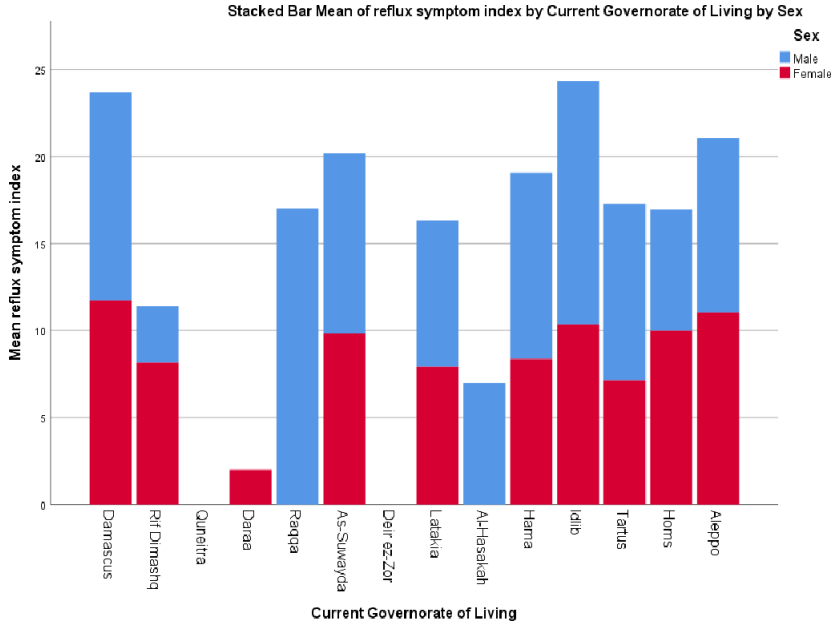

Figure 1 Mean reflux symptom index score in each governorate with gender prevalence.

caused a deterioration of the symptoms of GORD,[22] which was also associated with a decline in quality of life.[23] This decline was dependent on the severity of LPR regardless of marital status and household income.[24] We speculate that the high psychological stress and mental disorders in Syria[12] could contribute to our findings as they might cause or amplify these symptoms. Similarly, we found an association between LPR symptoms and being distressed from war noises but not with marital status or other war-related factors. LPR symptoms were also more frequent among subjects with a job, but we found no association with type of work.

GORD symptoms were more common among participants of lower income and educational level.[23 25] Furthermore, being from low or middle SES doubled the risk for severe symptoms of GORD despite adjusting for body mass index and smoking.[26] These observations can be explained by the fact that people from a lower SES tend to have a lifestyle that encourages GORD. This is similar to Syrians in the lower educational levels who tend to have unique lifestyles that may encourage this as well.[10] More symptoms that were associated with LPR were observed in our study in lower SES and educational level but with no statistical significance.

Untreated LPR may scar the true vocal folds, especially when it is corresponded with chronic vocal abuse. LPR is also associated with untreated GORD and Barret oesophagitis which is cancerous.[27] Furthermore, GORD symptoms may precede the diagnosis of cancer in about 60% of patients with oesophageal adenocarcinoma. In the same study, the OR for oesophageal adenocarcinoma was 43.5 in individuals with long-standing and severe symptoms of reflux.[28] As there is a dramatic increase in the incidence of carcinoma of the distal oesophagus, there is an urgent need for early recognition and treatment of GORD and the medical conditions associated with it.

We found a significant decrease in RSI scores in subjects who worked in the medical field, suggesting that these symptoms tend to be less frequent in this group, possibly due to prior awareness of such symptoms. The rest of the educational fields were not significantly associated with symptoms of LPR. The group of subjects aged 30 years and more had higher RSI scores than the younger subjects, but there was no correlation when directly comparing age and RSI scores. One study found that elderly people might have a higher baseline RSI.[29] In contrast, another study found that patients in the older groups had significantly lower RSI.[30]

Table 5 Forward linear regression on RSI scores with its relevant statistically significant variables

					Change statistics		
	Model	R^2	Adjusted R^2	SE of the estimate	R^2 change	F change	Sig. F change
LPR score	Medical condition category	0.034	0.033	8.961	0.034	22.946	<0.001
	Smoking both shisha and cigarettes	0.070	0.067	8.800	0.036	24.972	<0.001
	Being distressed from war noise	0.091	0.087	8.705	0.021	15.264	<0.001
	Having a work	0.098	0.092	8.681	0.006	4.510	0.034

LPR, laryngopharyngeal reflux; RSI, reflux symptom index.

Limitations

We identify that this study has many biases and confounders. Despite LPR being commonly diagnosed based on symptoms, most measures lack some of the criteria to diagnose LPR.[31] We used RSI which estimates having a probable LPR based on symptoms, and we did not use a medical diagnostic test. However, these symptoms are unspecific, and it is hard to distinguish from other aetiologies that can have similar symptoms such as asthma, smoking, alcohol consumption and chronic rhinosinusitis. Dysphonia is another symptom that is evaluated by RSI and was found to improve with treatment regardless of the aetiology.[32] Furthermore, RSI has only met 13 out of 18 of the developmental criteria for LPR and lacks some of the common symptoms, but it was the only measurement tool that met at least one criterion in each domain.[31 33] RSI is also effective in showing responsiveness to treatment.

We could not include the severity of allergic reactions and asthma in this study. The change of RSI scores with empirical therapy was also beyond the study scope. The sampling was made online which made it hard to determine the population. However, this method was the most convenient due to the financial hurdles, and it ensures accessibility and anonymity for participants which is an important issue in Syria, mainly when asking questions regarding war.[12]

Another confounder was from the majority of the sample were young who lived in major cities and had a relatively higher SES level which may impose a hurdle in the generalisation of the findings. However, this study found no statistical significance when comparing LPR symptoms and the SES and educational level. Furthermore, lower RSI scores were found in participants who worked in the medical sector as they consisted 27.8% of the sample which may indicate that the prevalence could be even higher in the normal population as these participants had lower LPR symptoms compared with other works. Finally, self-reported measures tend to the overestimation of symptoms which could explain our findings.

In conclusion, diagnosing LPR is difficult and is commonly overlooked. It has a wide range of unspecific symptoms, and a proper diagnostic approach is needed to ameliorate patient care and prevent LPR complications, especially in high-risk populations. These symptoms were found in more than one-third of the population living in Syria. While epigastric burning sensation, chest pain and indigestion were the most common symptoms, a sore throat was the least common. War exposure, mainly distress from war noise, may increase the symptoms of LPR by a variety of ways which need more studies to be identified. Cigarette smoking, asthma, allergic disorders and having a job were also associated with symptoms of LPR. However, gender, marital status, educational level and shisha smoking were not associated with LPR.

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Patient consent for publication Not required.

Ethics approval This study was approved by Damascus University, Faculty of Medicine and approved according to the principles embodied in the Declaration of Helsinki.

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