RESEARCH **ORIGINAL ARTICLE**

Gastro-esophageal Reflux Disease (GERD) Among Medical Students During COVID-19 Pandemic

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ABSTRACT

INTRODUCTION- Gastro-esophageal reflux is a physiological process defined as the involuntary backflow of the gastric content back to the esophagus primarily due to the relaxation of the lower esophageal sphincter. It becomes a disease (GERD) once there are complications and/or symptoms. Lifestyle factors like tobacco use, alcohol consumption, and stress have been known culprits that cause gastro-esophageal reflux disease, especially in stressful lifestyles such as that of medical students, as their lives were subjected to significant changes during the COVID-19 pandemic. In this study, we aimed to estimate the prevalence of GERD among medical students in Jordan. We also assessed the prevalence of common risk factors among medical students and their association with GERD during the pandemic.

METHODS - A cross-sectional study based on the GERDQ questionnaire; a questionnaire of 6 questions of the duration of seven days prepared on google forms and electronically. Data was collected in the period between 31st January 2021 and 18th April 2021. Various risk factors were evaluated, and GERD-related COVID-19 infection was assessed. Statistical methods included descriptive analysis, Cramer's V statistics, and the Chi-square test as measures of effect sizes.

RESULTS - Out of 1009 subjects, 438 (43.4%) were males, and 571 (56.6%) were females. The most common reported symptoms were heartburn (n=421, 41.7%) and regurgitation (n=325, 32.2%). A total of 199 (19.7%) students were infected by COVID-19, but it was not statistically significant to attribute the infection to GERD (P >0.05). However, alteration in GERD symptoms in those who were infected with COVID-19 was found to be statistically significant (P < 0.05). Conclusion: Our findings suggest that the most frequent symptoms of GERD reported by medical students are heartburn and regurgitation. Furthermore, some of the students who were COVID-19 infected were in the high-risk group, but it was not significant enough to attribute that COVID-19 infection is associated with GERD. However, the alteration in the feeling of GERD symptoms was found to be statistically significant.

KEYWORDS - GERD, Regurgitation, COVID-19, Pandemic.

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INTRODUCTION

Gastro-esophageal reflux is a physiological process defined as the involuntary backflow of the gastric content to the esophagus primarily due to the relaxation of the lower esophageal sphincter. It becomes a disease (GERD) once there are complications and/or symptoms [1]. GERD is a common disease, with a prevalence of 8.7%–33.1% in the Middle East [2], 24.0% in Pakistan [3], and 18.4% in Iran [4]. The prevalence of GERD among Indonesian physicians was 27.4% [5]. The most common reported symptom is heartburn, in addition to many symptoms such as chest pain, dysphagia, and regurgitation. Lifestyle factors such as tobacco, alcohol, stress, chocolate, coffee, high-fat food intake, and high body mass index (BMI) have been known to cause GERD. Persistent symptoms increase the risk of complications such as esophageal ulcers, strictures, Barrett's esophagus, and adenocarcinoma [6,7].

GERD is diagnosed either by history and symptoms and their response to the acid suppression test or with an objective investigation such as upper endoscopy and esophageal PH monitoring [8]. The GERDQ questionnaire could be used to diagnose GERD in primary care. It could also be used to measure the impact of the disease on patients' lives, treatment methodology, and their response to the treatment [9]. The GERDQ questionnaire was authenticated and evaluated in a diamond study, and it was found that implementing GERDQ might reduce the need for invasive investigations such as upper endoscopy [10,11].

Medical personnel life is usually stressful [12]. What's more, many changes occurred in people's lives during the pandemic, including medical students, as their study life was significantly altered, forcing them to change their plans and go through new methods to take their classes, which increased their stress, particularly during the quarantine period. A study on the prevalence of GERD in Saudi Arabia during the pandemic showed an increase in the prevalence of GERD during the pandemic to 34.2% from 24.8% before the pandemic. It also stated that their symptoms were more evident during the pandemic than before. Also, 41.2% of the population needed to take painkillers more frequently compared to 26.0% before the pandemic [13]. Another study was conducted on the prevalence of GERD symptoms among medical students at King Abdul-Aziz University, Saudi Arabia, which was found to be 25.9% [14]. In this questionnaire-based cross-sectional study, we aim to estimate the prevalence of GERD among medical students in Jordan and assess the common risk factors among medical students and their association with GERD during the pandemic.

METHODS

STUDY DESIGN - A cross-sectional study was conducted through an online google form of 1009 medical students. The data was collected from the 31st of January 2021 to the 16th of April 2021. A disclaimer was made clear that the data will be strictly confidential and will only be shared with study conductors. No personal information will be required, and the survey questions were approved by the corresponding professors.

The study relied on the diagnosis of GERD based on the GERDQ questionnaire, a questionnaire based on the type and frequency of self-assessment of the primary symptoms reported by medical students. Also, we included demographic questions like age, gender, university, and year of study. This questionnaire has been developed from three well-established diagnostic criteria for GERD to be an easy and effective method for identifying GERD among patients.

Questionnaire respondents with a score of eight or above are considered high risk (8-11 have a 79% chance, and 11-18 have an 89% chance). Respondents with a score below eight are considered low risk (3-7 have a 50% chance, while those who score 0-2 have a 0% chance). The GERD questionnaire has a sensitivity of 65% and a specificity of 71% for diagnosing GERD [11].

It consists of 6 questions for a duration of seven days regarding heartburn, regurgitation, epigastric pain, nausea, difficulty sleeping due to the symptoms of heartburn and regurgitation, and a history of medication. The first and last two questions are considered positive predictors of GERD, which means that the more frequent the symptoms, the higher the chance of having GERD. Meanwhile, the third and fourth questions about epigastric pain and nausea are negative predictors of GERD, which means that the lower the symptoms, the higher the score. The last two questions, five and six, assess the effect of symptoms on daily life. Two additional questions were added in this study before the medication history, asking whether the students take anti-GERD medications or not and how often in a month.

The study also included questions related to all the symptoms that GERD patients could complain of, such as heartburn, chest pain, difficulty swallowing, regurgitation, feeling of a mass, dyspepsia, acid taste, frequent throat clearing, water brash, postprandial nausea and vomiting, early satiety, cough, sore throat,

dental erosion, and voice hoarseness. Moreover, a question about various risk factors of GERD such as endoscopy, hernia, esophageal motility, meals before sleeping, smoking, alcohol, chocolate, caffeine, high-fat diet, high BMI, stress, and a question regarding medications that could cause or exacerbate GERD symptoms such as non-steroidal anti-inflammatory drugs (NSAIDs), calcium channel blockers (CCBs), nitrates, antidepressants, aspirin, bisphosphate, and anticholinergic drugs were included [15,16]. It also included questions about risk factors such as the number of cigarettes, shisha, e-cigarettes, alcohol, and carbonated drinks consumed per month, as well as whether they had stress and the degree of stress prior to the pandemic, as well as factors related to this stress. In addition to questions about stress during the pandemic, factors related to stress, whether they were infected with COVID-19, and the effect of infection on GERD symptoms were included.

STATISTICAL ANALYSIS - Data were analyzed using IBM SPSS version 26 [17]. Descriptive measures for categorical data included counts and proportions, which were presented as mean, standard of deviation (SD), and percentages (%). 95% of CIs of Cramer's V statistics were calculated using the bootstrapping method. A two-sided p-value of ≤0.05 was considered statistically significant. Chi-square was used to assess the significance of variables to GERD. This study was done in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [18].

RESULTS

GENERAL DEMOGRAPHICS - A total of 1009 subjects responded to the survey, of which 438 (43.4%) were males, and 571 (56.6%) were females. A total of 428 students (42.42%) were from universities in the center of Jordan, including the University of Jordan, Hashemite University, and Balqa Applied University. A total of 476 students (47.18%) were from universities located in the north of Jordan, including Yarmouk University and Jordan University of Science and Technology and 105 students (10.41%) were from Mutah University, southern Jordan.

GERDQ RESULTS - Students who scored eight or more were considered high risk/probability, and those who scored below eight were considered low risk/probability. Based on these scores, 333 (33%) of medical students in Jordan were found to have a high risk/probability of developing or having GERD, and 676 (67%) were found to have a low risk/probability of developing or having GERD (Table 1).

GERD SYMPTOMS - Many symptoms were assessed during the survey. The most common reported symptoms were heartburn (n=421, 41.7%) and regurgitation (n= 325, 32.2%). Several other symptoms were evaluated in terms of frequency and significance in high-risk patients (Table 2). Cough and sore throat were statistically significant ($P < 0.05$).

RISK FACTORS - This study analyzed several potential risk factors for GERD, as shown in Table 3. Previous studies have reported several factors that indicate an increased risk of GERD. In this study, the most frequent risk factors were stress (n=595,59%), caffeine intake (n=314, 31.1%), smoking (n=223 ,22.1%), and eating before sleeping (n=308, 30.5%). A history of hernia, endoscopy, and decreased motility in the esophagus were statistically significant, along with eating before sleeping, smoking, eating much chocolate, caffeine intake, high BMI, and stress ($P < 0.05$). However, the type of smoking (shisha, e-cigarettes) and alcohol consumption were not found to be statistically significant.

Certain families of drugs known to increase the risk of GERD were also assessed in this study. The most common drugs used were NSAIDs (n=131, 13%). Students who take NSAIDs, CCBs, and anticholinergics showed statistical significance ($P < 0.05$).

STRESS AND GERD - The main factors attributed to the medical students' stress before the pandemic were evaluated in our study. 457 (45.3%) students answered that they experienced stress before the pandemic outbreak, while 317 (31.4%) students reported that they suffered from minimal or no stress. Before the pandemic, medical students' most common attributing factor of stress was studying (n=827,82%). We found 283 (34%) students that were stressed due to studying were stratified as part of the high-risk patients.

Stress was also assessed during the pandemic, as shown in Table 4. A sum of 926 students(91.8%) reported that they had some level of anxiety for several reasons. The most worrisome factors during the pandemic were found to be changes in personal life (n=629, 62.3%) which was also a pre-pandemic concern for (n=611, 60.6%) of students, online education (n=562, 55.7), and changes in their future plans (n=533,52.8%).

COVID-19 INFECTION AND SYMPTOMS - The impact of COVID-19 infection was evaluated in our study, as shown in Table 5. 199 (19.7%) medical students were infected with COVID-19, but it was not significant enough to suggest an association of COVID-19 infection as a cause

Table 1. GERDQ Questionnaire results

Questionnaires questions and percentage	All Patients (N=1009)	By Answer Frequency	
		N	%
Percentage of having GERD(%)	Score by (%)		
Gerd score	0% GERD chance	6	0.6
	50%	670	66.4
	79%	268	26.6
	89%	65	6.4
How often did you have a burning feeling behind your breastbone per week?	GERDQ score		
	0	433	42.9
	1	272	27
	2	204	20.2
	3	100	9.9
How often did you have stomach contents (liquids or food) moving upwards to your throat or mouth (regurgitation) per week?	0	454	45
	1	311	30.8
	2	180	17.8
	3	64	6.3
How often did you have pain in the center of the upper stomach per week?	0	75	7.4
	1	155	15.4
	2	270	26.8
	3	509	50.4
How often did you have nausea per week?	0	69	6.8
	1	177	17.5
	2	245	24.3
	3	518	51.3
How often did you have difficulty getting a good night's sleep because of your heartburn and/ or regurgitation per week?	0	627	62.1
	1	217	21.5
	2	113	11.2
	3	52	5.2
How often did you take additional medication for your heartburn and/ or regurgitation, other than what the physician told you to take? (Such as Tums, Rolaids, Maalox) per week?	0	923	91.5
	1	50	5
	2	24	2.4
	3	12	1.2

Table 2. Symptoms in high risk and low risk patients

Symptoms	All Patients (N=1009)	By risk classification			
		Low Risk (N=676)	High Risk (N=333)	Total	P Value
		N (%)	N (%)	N	
Heartburn	No	399(68)	189(32)	588	0.492
	Yes	277(66)	144(34)	421	
Chest pain	No	575(67)	280(33)	855	0.685
	Yes	101(66)	53(34)	154	
Difficulty Swallowing (dysphagia)	No	612(67)	297(33)	909	0.502
	Yes	64(64)	36(36)	100	
Regurgitation	No	467(68)	217(32)	684	0.210
	Yes	209(64)	116(36)	325	
Lump Sensation	No	587(68)	278(32)	865	0.152
	Yes	89(62)	55(38)	144	
Dyspepsia	No	554(67)	273(33)	827	0.991
	Yes	122(67)	60(33)	182	
Acid Taste	No	536(67)	264(33)	800	0.997
	Yes	140(67)	69(33)	209	
Frequent Throat cleaning	No	639(67)	308(33)	947	0.206
	Yes	37(60)	25(40)	62	
Water Brash	No	583(68)	272(32)	855	0.058
	Yes	93(60)	61(40)	154	
Postprandial Nausea and Vomiting	No	577(67)	278(33)	855	0.437
	Yes	99(64)	55(36)	154	
Satiety	No	584(68)	277(32)	861	0.176
	Yes	92(62)	56(38)	148	
Coughing	No	622(68)	292(32)	914	0.027
	Yes	54(57)	41(43)	95	
Sore Throat	No	612(69)	280(31)	892	0.003
	Yes	64(55)	53(45)	117	
Dental Enamels	No	637(67)	310(33)	947	0.479
	Yes	39(63)	23(37)	62	
Hoarseness of voice	No	628(68)	302(32)	930	0.219
	Yes	48(61)	31(39)	79	

Table 3. Risk factors for GERD

Risk factor	All Patients (N=1009)	By risk classification			
		Low Risk (N=676)	High Risk (N=333)	Total	P Value
		N (%)	N (%)	N	
Endoscopy	No	643(68)	297(32)	940	0.000
	Yes	33(48)	36(52)	69	
Hernia(hiatal)	No	669(68)	320(32)	989	0.002
	Yes	7(35)	13(65)	20	
Esophageal Motility	No	673(67)	325(33)	998	0.005
	Yes	3(27)	8(73)	11	
Sleeping after Meals	No	493(70)	208(30)	701	0.001
	Yes	183(59)	125(41)	308	
Smoking	No	539(69)	247(31)	786	0.045
	Yes	137(61)	86(39)	223	
Alcohol	No	655(67)	321(33)	976	0.676
	Yes	21(64)	12(36)	33	
Chocolate	No	574(69)	258(31)	832	0.004
	Yes	102(58)	75(42)	177	
Caffeine	No	487(70)	208(30)	695	0.002
	Yes	189(60)	125(40)	314	
High-fat Diet	No	558(68)	268(32)	826	0.424
	Yes	118(64)	65(36)	183	
High Body Mass Index	No	610(69)	279(31)	889	0.003
	Yes	66(55)	54(45)	120	
Stress	No	299(72)	115(28)	414	0.003
	Yes	377(63)	218(37)	595	

Table 4. Stressors during the pandemic

Cause of Stress	All Patients (N=1009)	By risk classification			
		Low Risk (N=676)	High Risk (N=333)	Total	P Value
		N (%)	N (%)	N	
Personal Life Changes	No	267(70)	113(30)	380	0.086
	Yes	409(65)	220(35)	629	
Peer Pressure	No	552(67)	275(33)	827	0.719
	Yes	124(68)	58(32)	182	
Online Education	No	297(66)	150(34)	447	0.739
	Yes	379(67)	183(33)	562	
Fear of Infection	No	397(67)	197(33)	594	0.896
	Yes	279(67)	136(33)	415	
Loss of Family Members	No	515(67)	255(33)	770	0.890
	Yes	161(67)	78(33)	239	
Expectations of being knowledgeable	No	567(67)	284(33)	851	0.562
	Yes	109(69)	49(31)	158	
Future getting disrupted	No	326(68)	150(32)	476	0.341
	Yes	350(66)	183(34)	533	
Economic Status	No	494(67)	246(33)	740	0.788
	Yes	182(68)	87(32)	269	
Lockdown	No	426(68)	200(32)	626	0.363
	Yes	250(65)	133(35)	383	
Exacerbation of Stress	No	157(64)	90(36)	247	0.000
	Yes	295(76)	93(24)	388	
	Maybe	224(60)	150(40)	374	

Table 5. COVID 19 infection and symptoms exacerbation

COVID19 infection and symptoms effect	All Patients (N=1009)	By risk classification			
		Low Risk (N=676)	High Risk (N=333)	Total	P Value
		N (%)	N (%)	N	
Infected or Not	No	549(68)	261(32)	810	0.287
	Yes	127(64)	72(36)	199	
COVID-19 effect on GERD Symptoms	Infected with no exacerbation	107(60)	72(40)	179	0.000
	Infected with exacerbation	18(35)	34(65)	52	
	Symptoms decreased	8(62)	5(38)	13	
	Did not get infected	543(71)	222(29)	765	

of GERD (P > 0.05). However, the alteration in the feeling of GERD symptoms was found to be statistically significant (P < 0.05).

DISCUSSION

This study presents a comprehensive insight into the burden of the ongoing COVID-19 pandemic on medical students from all Jordanian medical universities. The results of this survey point to the critical restrictions imposed by the pandemic on medical students in Jordan. In this regard, quarantine and closures changed their study methods and their future, such as those who wanted to conduct their elective training in hospitals outside Jordan, such as the United States, Germany, Qatar, and others where the pandemic affected this aspect so they could no longer conduct their training outside which added to their stress.

The prevalence of GERD among medical students in Jordan, according to the GERDQ questionnaire results in our cohort study is (n=333, 33.0%), which is higher in comparison to other studies such as the study conducted by Sharma et al. on 600 students on the prevalence and risk factors of GERD among medical students that reported that the prevalence of GERD symptoms among medical students was 25% (14.65% had mild, 9.65% had moderate, and 0.68% had severe reflux symptoms) [19].

The most common symptoms of GERD are heartburn and regurgitation. It can also present with other symptoms such as chest pain, water brash, cough, hoarseness, and dysphagia [20]. Among the high-risk group in our study, 144 students (34%) reported heartburn, 116 (36%) reported regurgitations, 69 (33%) reported an acid taste in their mouth, and 61 (40%) reported water brash and those were the most commonly reported symptoms.

A study on the prevalence and risk factors of GERD among Shaqra University students in Saudi Arabia was conducted on 400 students, (n=227,56%) were males and (n=173,43%) were females, revealed that the patient's gender, smoking, family history of GERD, high BMI (>25 kg/m2), fast food consumption, carbonated beverages, and tea consumption, eating the meals quickly, and sleeping within 1 hour of dinner are associated with symptomatic GERD (P < 0.05) [21]. In our study, 13 students (65%) who had a history of hernias were in the high-risk group. Also, 125 students (41%) who sleep within an hour after consuming a meal were part of the high-risk group in our study.

Medical students usually have a stressful life and consume a lot of caffeinated drinks and nicotine during their day. A study conducted in Ethiopia revealed that the prevalence of stress among medical students was 52.4%. Stress had a negative impact on their academic performance. Substance usage, student income, and academic year were linked to stress [22]. In our study, 218 students (37%) suffered from stress, 125 (40%) consumed high amounts of caffeine, and 86 (39%) of smokers were classified as part of the high-risk population. Smoking has a significant effect on GERD; a study on medical students in Saudi Arabia showed an increased prevalence of smoking during the pandemic [13]. Various methods of smoking were included in our study. (n=35,43%) who smoked cigarettes only, (n=27,30%) who smoked water pipe only, (n=16, 32%) who smoked e-cigarettes only, and (n=34, 41%) of poly-smokers were classified among the high-risk population.

A study was conducted using esophageal manometry, the gold standard to diagnose esophageal motility. High-resolution manometry was used to overview the pathogenesis of GERD. The results were esophageal motility abnormalities most importantly transient lower esophageal sphincter relaxations (TLESRs), hypotensive lower esophageal sphincter (HLES), and ineffective esophageal motility (IEM) were strongly attributed to the development of GERD [23]. Our cohort study found a significant correlation between students with a history of esophageal motility abnormalities and GERD (P<0.05).

A study conducted by Zschau et al. reported that most GERD patients received proton pump inhibitors (PPI) before referring them for endoscopy, even though their symptoms do not respond to PPI therapy [24]. In our study (n=112, 67.47%), patients taking anti-GERD medications such as PPIs, H2 blockers, and antacids were part of the high-risk populations.

A study that was conducted by Mungan et al. noted that certain drugs, such as CCBs, nitrates, antidepressant medications, benzodiazepine, anticholinergic drugs, theophylline, and NSAIDS, were correlated to cause GERD [15]. Moreover, in our study we found a significant correlation between patients who reported taking NSAIDS, CCBs, and anticholinergic and the exacerbation of GERD symptoms (P<0.05).

A previous cross-sectional study conducted by Choi et al. showed a statistical significance in that anxiety and depression were higher in GERD patients compared to controls in that study [25]. Our study examined the relationship between

stress and exacerbation of GERD symptoms before and during the COVID-19 pandemic. Before the pandemic (n=169,37%) of patients who reported stress were high-risk patients, (n=283, 34%) who reported stress due to study load as medical students were high-risk patients. During the pandemic, (n=150, 40%) of patients who reported having more stress were in the high-risk group. (n= 133,35%) were stressed due to lockdown situations, (n=183, 34%) due to future plans changes, and (n=220, 35%) due to personal life changes.

We also studied the relationship of stress with the exacerbation of GERD symptoms in case of infection with COVID-19. (n=72, 40%) of patients who were infected with the COVID-19 virus and had no symptoms exacerbations were high-risk patients, (n=34,65%) who were infected and experienced an exacerbation of GERD symptoms were part of the high-risk population. On the other hand, (n=222,29%) of high-risk patients were not infected by COVID-19.

Numerous studies have shown a disordered gut-brain axis in the pandemic. Therefore, we have thought that it is possible that the symptoms may not have been acid-driven in a significant proportion of those in this study [26].

Lastly, given these alarmingly high rates of stress and anxiety among students, we recommend that increased institutional efforts be invested in dealing with this burden to avoid further exacerbation of this problem. The proposed measures to manage this problem include providing advisory sessions to help them in developing their future, providing free psychiatric and psychotherapeutic sessions, and holding seminars on effective mechanisms to deal with stress.

LIMITATIONS

The main limitation of our study is the small sample size and limited generalization of results, so multicenter national studies with larger samples are still needed to confirm these findings on a large scale. In addition, the study design based on data collection through an online survey questionnaire may contribute to response bias that cannot be managed and controlled. Moreover, the reflux symptom questionnaires do not differentiate between functional heartburn and esophageal hypersensitivity, non-erosive reflux disease (NERD), and GERD.

Also, lack of contextual information with previous data on GERD for populations in the pre-pandemic period and lack of diagnostic workup with endoscopy/pH studies are considered major limitations.

CONCLUSIONS

Our findings suggest that the most frequent symptoms of GERD reported by medical students are heartburn and regurgitation. Furthermore, some of the students who were COVID-19 infected were in the high-risk group, but it was not significant enough to attribute that COVID-19 infection is associated with GERD. However, the alteration in the feeling of GERD symptoms was found to be statistically significant.

AUTHORS CONTRIBUTIONS

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