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Gasroesophageal Reflux Disease and its Association with Overweigh and Obesity –A Case-Control Clinical Study

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Original Article

ABSTRACT

Background: Gasroesophageal Reflux Disease (GERD) is a prevalent disease in worldwide. Previous studies investigated the relationship between GERD and BMI, however, few studies with large sample are available in Iraq

Objective: *To study the effect of weight on intensity of symptoms*

Patients & Methods*: A prospective Case-Control study conducted during a period of 2 years (2017-2018), in the Department of Medicine, Almajar Alkabir Hospital, Maysan, Republic of Iraq. Including 100 GERD patients and 100 healthy individual as control group. Both groups compared with regard to their body mass index and obesity*

Results*: Both groups almost matched for demographic variables including age and gender. Mean BMI of GERD group was significantly higher than that of controls, (P. value < 0.05), Obese/overweight individuals were about 2.7-fold more likely to have GERD than normal BMI group, (OR = 2.67, P. value < 0.05), a strong direct correlation was found between GERD score and BMI of the patients*

Conclusions: *Overweight / Obesity was significant risk factor for GERD. Overweight and obese patients were more likely to have more frequent and more severe heartburn, acid regurgitation and other symptoms. GERD score was significantly increase with increasing BMI in direct dependent correlation*

Keywords: *Gasroesophageal Reflux Disease, GERD, Body mass Index, overweight, obesity*

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1. INTRODUCTION

Gastroesophageal reflux disease (GERD) is a chronic disease caused by primary esophageal dysfunction, weakening of the antireflux barrier of the lower esophageal sphincter, slowing of gastric emptying and irritation and inflammation of the esophagus due to the return of gastric contents. According to the Montreal definition, GERD defined as "a condition of troublesome symptoms and complications that result from the reflux of stomach contents into the esophagus". (1,2).

The prevalence of GERD is poorly understood, due to the variability of clinical manifestations. In different countries, no sex variation in prevalence of GERD as in USA, while in Argentina , GERD observed in 7.5-11.5% of men and 9.6-16.4% in women (4). Over the past 40 years, the incidence of GERD has increased significantly and has become one of the main clinical problems in gastroenterology. In North America it is noted in 18.1-27.8%, in Europe - in 2.5-7.8%, in the Middle East - in 8.7-33.2% of cases (5,6).

Etiology and pathogenesis. The following factors are important in the development of the disease (7,8):

*Disorders of protective factors***:** (9)

Anti-reflux function of the lower esophageal sphincter;

Esophageal cleansing (clearance);

Resistance of the mucous membrane of the esophagus due to impaired endothelial regeneration;

Timely removal of gastric contents

Functional reasons:

Gastric motility disorders

Decrease in pressure and length of the lower esophageal sphincter

Slowing of saliva secretion;

Duodeno-gastroesophageal reflux of bile

Reduction of the anti-reflux barrier (10,11)

Smoking, and some dietary factors overeating, beverages containing caffeine (coffee, tea, cocoa, cola), juices, oranges, lemons, grapefruits, milk, onions, horseradish, peppers, garlic, alcohol, etc. increase the acid-forming function of the stomach and reduce the tone of the

lower esophageal sphincter (12–16).

Taking medications like that have an irritative effect on lining of esophagus causing heartburn pain, such as antibiotics like tetracycline and clindamycin, NSAIDs, potassium supplements and ferrous sulfate, or increase the severity of GERD or those which have an indirect effect that increase the acid reflux and worsen GERD such as anticholinergics, Tricyclic antidepressants , Calcium channel blockers, statins, angiotensin-converting enzyme (ACE) inhibitors, Progesterone, Narcotics , Sedatives and Theophylline (17).

Clinical classification of GERD (3,18,19)

1. Erosive GERD (endoscopic positive variant, GERD with esophagitis). The degree of esophagitis is determined by the Los Angeles classification:
2. Non-erosive GERD (non-erosive reflux disease). Barrett's esophagus (intestinal metaplasia of incomplete type, in the distal part of the esophagus).

Diagnosis:

To diagnose and evaluate the effectiveness of treatment of patients with GERD, as well as to predict the dynamics of the disease developed a questionnaire scale GERD-Q, consisting of 6 questions and self-filled by the patient. The GERD scale allows to compare the dynamics of the patient's condition and assess the impact of the disease on the quality of life of the patient, as well as the effectiveness of therapy. The questionnaire is completed at the initial stage of care without endoscopic intervention (20–24)

Treatment

General measures for the treatment of the disease; frequent meals (up to 5-6 times a day) in small portions with high protein content and the last meal no later than 3 hours before bedtime; lifestyle changes; take food while standing, slow walking after eating for 30 minutes; avoid excessive food intake; avoid lifting weights over 8-10 kg, exclude from the diet foods that aggravate gastroesophageal reflux, exclusion of drugs that reduce the tone of the lower esophageal sphincter, Smoking cessation and stop alcohol consumption; Normalization of body weight; contraindicated tight clothing. In the presence of erosive esophagitis prescribe antianginal, antireflux drugs . When the disease is complicated certain medication prescribed . In some cases surgery is an option (20–22,25–28)

Relationship between obesity and GERD:

The prevalence of obesity has increased dramatically in the past 20 years. The same happened with cases of gastroesophageal reflux. This relationship is not accidental and there is a clear link between these two health changes. In Iraq , a national survey found 33.3% of Iraqi population were obese (29)

Many literatures and previous studies found a significant association between overweight/obesity and frequency of GERD symptoms. Studies indicate that obese patients are up to three times more likely to develop the disease and its complications than a person with ideal weight, in addition to being more subject to complications. The higher the body mass index, the greater the probability of the disease occurring. It is known today that people with reflux and who are overweight or obese have an index of exposure to gastric acid five times higher than those with reflux, but with normal weight. This increase refers to both the intensity of reflux and the number of episodes during the day. These data are confirmed through specific studies for the control and diagnosis of gastroesophageal reflux, such as Esophageal 24-hour pH/impedance reflux monitoring. This alone shows how the pattern of acid aggression to the esophagus is higher in those with weight gain, which is more evident when the body mass index (BMI) is greater than 30 . (25,27,30–36)

It is also important to note that some complications of gastroesophageal reflux such as erosive esophagitis, Barrett's esophagus and esophageal cancer are clearly associated with an increase in body mass index (BMI) and obesity. In addition, obese people usually have a non-acid reflux pattern, which does not respond well to conventional treatment with drugs that decrease gastric acidity, which makes weight control even more relevant. Many studies suggested that A structured weight loss program can completely eliminate the symptoms of GERD in most of these people(36,37).

Hence in this article we aimed to assess the effect of weight reduction on the frequency and intensity of GERD symptoms among group of Iraqi patients.

2. PATIENTS and METHODS

This was a prospective Case-Control study conducted during a period of 2 years (2017-2018), in the Department of Medicine, Almajar Alkabir Hospital, Maysan, Republic of Iraq.

Patients (cases) : The study included 100 adult individuals aged 20 -50 years who had

recurrent symptoms of GERD ; heartburn, acid regurgitation or both at least once per month during the last 12 months and those were suspected to have GERD and proved diagnosed by history and clinically by gastroenterologist. When GERD confirmed, patients considered as GERD cases (Cases group).

Control group:

A total of 100 apparently healthy individual and did not have any GERD symptoms during the last 12 months were enrolled as control group, and they almost matched with cases with regard to age and gender

Inclusion criteria:

For cases, adult patients aged 20 – 50 years of both genders who agreed to participate in the study with proved diagnosed GERD by history and clinically.

For Control: Apparently health individual with no symptoms of GERD during the last 12 months, almost matched to cases and agreed to participate in the study.

Exclusion criteria:

Participant (case or control) was excluded if he/she had one or more of the following:

1. Gastric surgery for any reason
2. Malignancy
3. Pregnancy (for women)
4. Chronic user of calcium-channel blockers and nitrates.
5. Current user of Proton pump inhibitors , H2 receptor antagonist
6. Using contraceptive medications (for women)
7. On hormonal replacement therapy
8. Refused to participate in the study

Case Definition:

Assessment of Heartburn (as pathognomonic feature) and acid regurgitation used because these two symptoms are the more specific and reliable. GERD diagnosis was considered depending the GERD symptoms check-list and the GERD questionnaire (Table 1) (38,39)

Table 1. GERD questionnaire

SYMPTOM	***how many days does this occur per week?***			
	0 days	***1 day***	***2-3 days***	***4 -7 days***
Burning feeling behind the breastbone (heartburn)	0	1	2	3
Stomach contents moving up to the throat or mouth (regurgitation)	0	1	2	3
Pain in the middle of the upper stomach area	3	2	1	0
Nausea	3	2	1	0
Trouble getting a good night's sleep because of heartburn or regurgitation	0	1	2	3
Need for over-the-counter medicine for heartburn or regurgitation in addition to the medicine your doctor prescribed	0	1	2	3
Total score of 0 to 2 points = 0 percent likelihood of GERD; *3 to 7 points = 50 percent likelihood;* *8 to 10 points = 79 percent likelihood;* *11 to 18 points = 89 percent likelihood.*				

Data collection:

Data collected using a pre-constructed data collection sheet by direct interview with the study participants. Full history taken and clinical examination performed. Data including demographic characteristics of participant,; age, sex, level of education, occupation, smoking, menopausal status (for women). Anthropometric measurements ; weight , height and body mass index (BMI), weight and height were measured using standard calibrated scales in standing position. Study participants (both groups) then categorized according to their BMI to be underweight ,normal, overweight or obese , according to the World Health Organization BMI Classification for adults where BMI of < 18.6 kg/m^2 considered underweight , 18.6-24.9 kg/m^2 normal, 25-29.9 kg/m^2 overweight and 30 kg/m^2 considered obese.

Data management and Analysis:

Data were managed , analyzed and processed using the statistical package for social sciences (SPSS) version 25, Variables presented as mean, standard deviation, frequencies, and simple percentage according to the variable type. Chi-square test used to compare categorical

(nominal, ordinal) variables. Fisher's exact test used as an alternative when chi square was inapplicable. Student's t test used to compare mean of a variable across the two groups(cases and control). Level of significance (P. value) set at or less than 0.05 considered to be statistically significant. Finally, Regression analysis was performed and odds ratio was calculated for each possible risk factor to assess its association with GERD.

3. RESULTS

A total of 100 GERD patients were enrolled in this study with a mean age 34.6 ± 4.8 (range: 20-50) years. In addition, 100 individual with no GERD were enrolled as controls and their mean age was 34.1± 5.2 (range; 20 – 50) years. Males represented 40% of cases and 40% of controls, both groups were matched for age and gender, (P > 0.05), similarly, no significant difference in education level , occupation, or residence, (P>0.05) (**Table 2**).

The mean body mass index in GERD cases was significantly higher than that in controls, (**Figure** 1). Furthermore, cross-tabulation between BMI categories against groups revealed a significant association between being overweight/Obese and GERD. Odds ratio indicated that Obese/overweight individuals were about 2.7-fold more likely to have GERD than normal BMI group, (OR = 2.67, P. value < 0.05), (**Table 3**).

Additionally, overweight and obese cases were more likely to have heartburn; 95.4% of obese/overweight group reported heartburn for at least once per week compared to 77.1% among normal BMI group, with an OR of 6.12 indicated that overweight and obese were about 6 folds more likely to have heartburn than those with normal BMI, (P. value < 0.05). similarly, a significant association was found between overweight/obesity and regurgitation (OR = 4.02, P. value < 0.05), Pain in the middle of the upper stomach area (OR = 2.88) and nausea (OR = 3.75, P. value < 0.05). From other point of view, Trouble getting a good night's sleep was more frequent in overweight/obese cases compared to those with normal BMI, (OR = 1.85, P. value < 0.05). BMI was not significantly associated with the need for medicine to treat heartburn or regurgitation , (P. value >0.05), (**Table 4**)..

When GERD score calculated for each participant of the 100 cases and curve regression estimation performed, a strong direct correlation was found between GERD score and BMI of the patients , (R = 0.812, P. value < 0.001), (**Figure 2**),

Table 2. Socio-demographic characteristics of the studied groups

		Group				P. value*
		GERD group		Controls		
		No.	%	No.	%	
Age (year)	20 - 29	18	18.0	20	20.0	0.820
	30 - 39	37	37.0	33	33.0	
	40 - 50	45	45.0	47	47.0	
Gender	Male	40	40.0	39	39.0	0.885
	Female	60	60.0	61	61.0	
Residence	Rural	36	36.0	33	33.0	0.655
	Urban	64	64.0	67	67.0	
Marital state	Married	83	83.0	77	77.0	0.539
	Unmarried	15	15.0	20	20.0	
	Divorced/Widow	2	2.0	3	3.0	
Occupation	Employed	26	26.0	23	23.0	0.622
	Unemployed	74	74.0	77	77.0	
Education	Primary lower	27	27.0	31	31.0	0.822
	Secondary	31	31.0	29	29.0	
	College & Higher	42	42.0	40	40.0	
Smoking	Yes	21	21.0	23	23.0	0.733
	No	79	79.0	77	77.0	
*No significant difference in all variables between both groups						

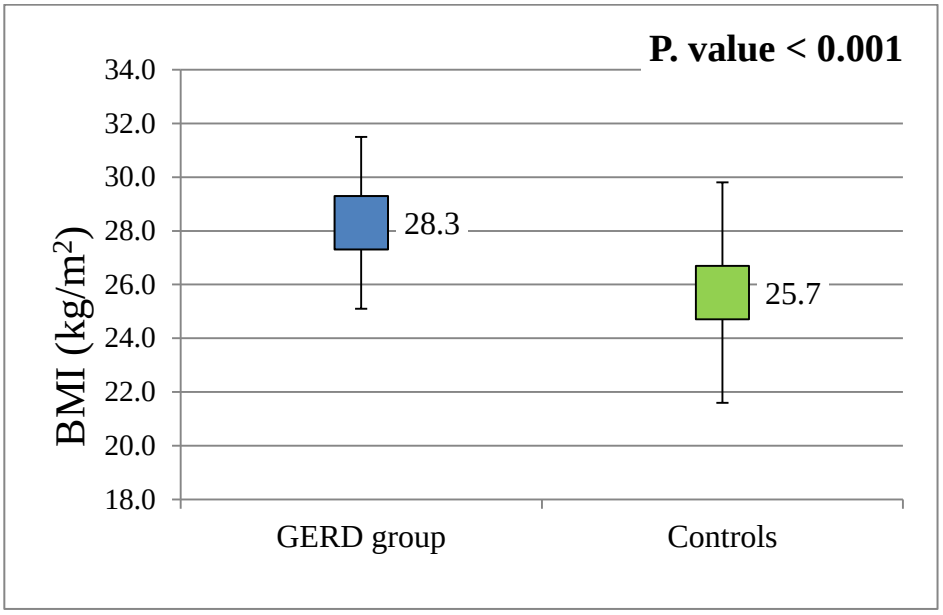

Figure 1. Comparison of mean BMI between GERD and control groups

Table 3. Relationship between overweight / obesity and GERD

	Group			
BMI category*	GERD group		Controls	
	No.	%	No.	%
Overweight/Obese	65	65.0	41	41.0
Normal	35	35.0	59	59.0
Total	100	100.0	100	100.0
Odds ratio = 2.67 (1.51 – 4.74) **P. value = 0.003 significant**				

*Normal: BMI = 18.6 - 24.9 kg/m^2 , Overweight: BMI = 25 - 29.9 kg/m^2
Obese: BMI ≥30 kg/m^2

Table 4. Relationship between GERD symptoms experienced by GERD patient for at least one day per week

Symptom	Overweight/Obese (N = 65)		Normal (N = 35)		OR*	P. value
	No.	%	No.	%		
Heartburn	62	95.4	27	77.1	**6.12**	**0.005***
Regurgitation	44	67.7	12	34.3	**4.02**	**0.001***
Pain in the middle of the upper stomach area	37	56.9	11	31.4	**2.88**	**0.015***
Nausea	43	66.2	12	34.3	**3.75**	**0.002***
Trouble getting a good night's sleep	23	35.4	8	22.9	1.85	**0.0196***
Need medicine for heartburn or regurgitation	38	58.5	23	65.7	0.73	0.478**
*Significant difference , **Not significant difference						

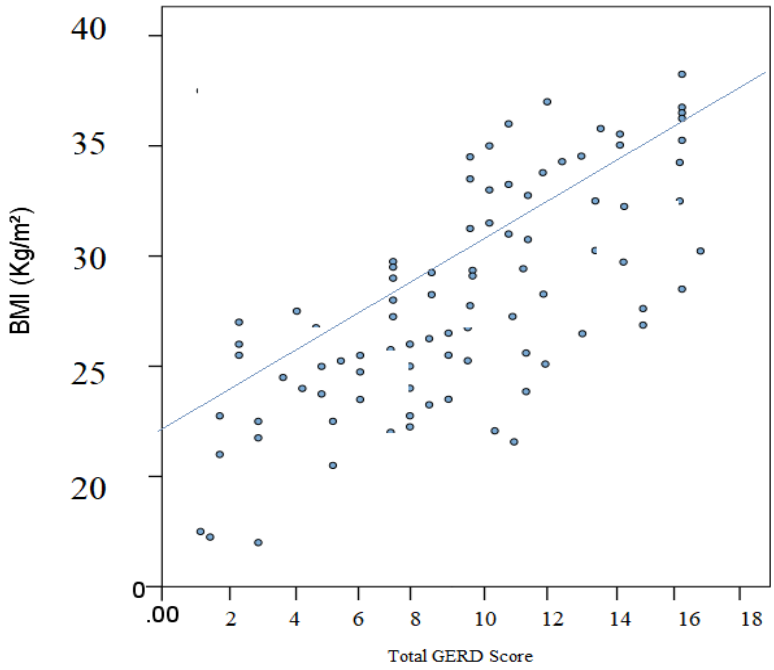

Figure 2. Relationship between total GERD score and BMI among GERD patients (R = 0.812, P. value < 0.001)

4. DISCUSSION

Gastroesophageal Reflux Disease (GERD) is a prevalent disease in worldwide, with variation between developed and developing countries. There is evidence indicates that excessive food intake, translated into repeated, frequent and prolonged gastric distention can damage the mechanisms of the anti-reflux barrier at the cardial level . Therefore, there are at least two facts that are linked to GERD in adults: excessive food intake and its logical consequence, being overweight or obese.

Many previous studies investigated the relationship between GERD and BMI, however, few studies with large sample enough are available in Iraq in addition majority of these studies are cross-sectional , descriptive, or correlate their findings with endoscopic examination, therefore, in this case-control study we aimed to assess the association between large BMI (overweight/obesity) with incidence, frequency and intensity of GERD symptoms. We included prospectively a total of 100 GERD patients and 100 apparently health individual who did not experienced at least one GERD symptom in the last three months as control group, both groups were almost matched for their demographic characteristics. In our study, we compared the mean BMI between GERD group and control, we found that the mean BMI was significantly higher in GERD than control group 28.3 kg/m2 and 25.7 kg/m2, respectively. Further assessment was performed to assess the prevalence of overweight/obesity among GERD and control groups, our findings showed that prevalence of overweight and obesity was significantly higher in GERD group than controls, 65% vs. 41%, respectively, and the overweight/obese patients were about 1.51 to 4.74-fold more likely to have GERD than normal population. Furthermore, GERD symptoms frequency and severity increased significantly with increase in BMI, therefore, our findings suggest that patients with severe and morbid obesity have GERD more than those with lower BMI.

We found that heartburn and acid regurgitation were the most frequent symptoms among GERD patients, this was not unexpected as the heartburn is a pathognomonic specific feature of GERD followed by acid regurgitation, however, other symptoms; nausea, pain in the middle of the upper stomach area was also frequent, and trouble in sleeping were also frequent but less than heartburn. We found a direct strong correlation between total GERD score and BMI , Our study clearly demonstrates that patients with severe and morbid obesity have reflux, and there is a direct correlation between greater weight and more GERD symptoms. Similar findings were also

reported in previous studies; Vaishnav et al. found that frequency and severity of heartburn and regurgitation increased significantly with larger BMI (40) . Chowdhury et al. (33) from India found that BMI > 25 is significant risk factor of GERD. Kristo et al. (41) documented impaired esophageal function in morbidely obese patients which result in GERD.

Furthermore, AbdelKader et al. (30) found a significant association between obesity and severity of GERD. Adekanle et al. (31) found Central obesity is a long-term erosive GERD risk factor among Nigerian women, but not men. Other studies found no direct association between BMI and GERD; which demonstrated that acute increases in intra-abdominal pressure decrease the resistance of the gastroesophageal junction in gradients similar to normal and obese patients. Therefore, they concluded that obesity appears not to predispose to GERD, but creates an intra-abdominal condition that may predispose to GERD if the sphincter barrier is weak or incompetent.

In an earlier study, Fraser-Moode (36) assess 111 obese patients of different magnitude, and showed that only 32% of them had heartburn and that there was no correlation between BMI and a more hypotensive gastroesophageal sphincter. There are several studies which show that weight loss with medical treatment did not achieve a significant decrease in the presence of GERD symptoms . Lundell et al. (42) in 50 morbidly obese patients with a BMI of 42 kg/m2, did not show endoscopic esophagitis in any patient and morbid obesity was not associated with any severe GERD. Fisher et al. (35) conducting a study similar to ours in 30 morbidly obese and hyper-obese patients, evaluated with manometry and 24-hour pH, they concluded that in these patients there is significantly greater pathological acid reflux, with a correlation between BMI and the presence of gastroesophageal reflux, despite having a value of the lower esophageal sphincter in the lower limits of normal. However, in our study, even when this correlation was positive in severely obese and morbid patients, it was not clearly observed in hyper-obese patients, because we did not perform manometry and 24-hour pH . We were struck by the fact that hyper obese patients, with a BMI < 40 kg/m2, have a lower prevalence of GERD than those who are severely obese or morbid ≥ 40 kg/m2. This suggests that obesity per seit is not a primary factor in producing GERD but can generate conditions to increase or aggravate a previously present GERD. From other point of view, studies that investigated the effect of bariatric surgery , found that symptoms of GERD have completely disappeared in all cases, as it is an excellent anti-reflux technique (25,27,28,32) . However, the association between obesity and GERD still

under debate and different mechanisms were suggested, Del Grande et al. (43) attributed the pathophysiology of GERD to the high Transdiaphragmatic pressure gradient associated with high abdominal pressure in obese patients Świdnicka-Siergiejko et al . (44) concluded no association between weight loss and improvement in GERD symtoms in addition the hormonal effect could not explain the high prevalence of GERD in obese.

Jamal et al. (45) found that GERD symptoms occurred independently of BMI and the association could be true in western than Asian population. However, barriers that prevent GERD are insufficient in overweight/obese patients. or obese and the association between BMI and GERD still need further investigation for more precise evaluation and conclusion,

5. CONCLUSIONS

Overweight / Obesity was significant risk factor for GERD. Overweight and obese patients were more likely to have more frequent and more severe heartburn, acid regurgitation and other symptoms. GERD score was significantly increase with increasing BMI in direct dependent correlation

Ethical Clearance

Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, verbal informed consent obtained from all participants. Data and privacy of participants were kept confidentially. .

Conflict of interest: Authors declared none

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