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ASSOCIATION OF OBESITY AND METABOLIC SYNDROME WITH GASTROESOPHAGEAL REFLUX DISEASE IN ADULTS PRESENTING TO TERTIARY CARE HOSPITALS IN PAKISTAN

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ABSTRACT

Objective: To determine the association of obesity and metabolic syndrome with gastroesophageal reflux disease (GERD) among adults presenting to tertiary care hospitals in Pakistan.

Material & Methods: The current descriptive cross-sectional study was performed in the Departments of Medicine and Gastroenterology in tertiary care hospitals in Pakistan after obtaining approval from the institutional ethics review board. The sample size comprised 348 adults between 18 and 65 years of age, which was achieved by employing the non-probability consecutive sampling technique. Subjects with prior surgery in the upper part of their gastrointestinal tract, malignant disease of the gastrointestinal system, chronic liver disease, chronic kidney disease, pregnancy, and severe systemic disease were excluded from the study. Information on the demographic characteristics, anthropometric measurements, and biochemical parameters like BMI, fasting glucose, triglycerides, HDL-C, and blood pressure was collected using a questionnaire form. GERD was defined on the basis of reflux symptoms and physical examination. Metabolic syndrome was determined using the modified NCEP ATP III criteria.

Results: The mean age of participants was 43.6±12.1 years, while 201 (57.8%) participants were males. Obesity was identified in 136 (39.1%) participants, and metabolic syndrome was present in 122 (35.1%) individuals. GERD was diagnosed in 151 (43.4%) participants. GERD was significantly more frequent among obese participants (74.3% vs. 23.6%, $p<0.001$) and among individuals with metabolic syndrome (73.0% vs. 27.4%, $p<0.001$). Obesity (AOR=4.1, $p<0.001$) and metabolic syndrome (AOR=3.4, $p<0.001$) were independent predictors of GERD.

Conclusion: Obesity and metabolic syndrome were significantly associated with GERD among Pakistani adults and may contribute substantially to reflux-related morbidity.

Keywords: Gastroesophageal Reflux Disease; Metabolic Syndrome; Obesity; Pakistan; Risk Factors.

INTRODUCTION

The gastroesophageal reflux disease (GERD) refers to one of the most frequent disorders of the gastrointestinal tract in terms of global prevalence and can be described as the process by which the stomach contents enter the esophagus, thus causing such problems as acid indigestion, heartburn, difficulty in swallowing, and a burning sensation in the area behind the chest. The impact of the chronic disease is enhanced due to the possible development of complications (1). It has also recently come to light that there has been a marked rise in the incidence of GERD in the global population, particularly in developing countries with high rates of urbanization and changes in lifestyle over the last 20 years. North America and Europe have reported incidences of 10% to 30% in the adult population, while the rate has seen an upward trend in Asia, estimated at 5% to 20% (2).

Obesity has appeared as a serious public health issue and is now considered one of the most important risk factors for GERD. Obesity, especially central obesity, raises intra-abdominal pressure as well as diminishes lower esophageal sphincter performance and shares with gastric contents reflux to the throat. Various international studies have shown a clear relationship between high BMI and GERD (3). In a large meta-analysis, obese patients had almost double the risk of GERD when compared to individuals with a normal BMI. Correspondingly, a study from the USA and another one from China also found that abdominal obesity and waist circumference independently predicted reflux disease (4).

GERD is also becoming increasingly associated with metabolic syndrome, which involves a combination of metabolic disorders such as high blood pressure, dyslipidemia, hyperglycemia, and abdominal obesity (5). A study conducted in Taiwan revealed a statistically significant association between metabolic syndrome and the occurrence of erosive esophagitis and symptomatic GERD (6). An estimated 42% prevalence of GERD was seen in patients suffering from metabolic syndrome in another study from Turkey.

Obesity and metabolic syndrome have become major health concerns in Pakistan because of sedentary living habits, poor nutritional intake, and decreased exercise. According to national and regional statistics, the obesity rate in Pakistan ranges from 25% to 38%, and almost one-third of the total urban population has metabolic syndrome (7). The prevalence of GERD in Pakistan, ranging from 22% to 50%, has been seen in local studies among overweight people and hospitalized patients. However, no adequate information is available in this respect regarding both obesity and metabolic syndrome together (8).

Based on the significance of obesity and metabolic syndrome among patients with GERD, this scientific analysis was carried out to determine the association between obesity, metabolic syndrome, and GERD in Pakistani adults presenting at a tertiary healthcare facility. This will aid in the early detection of patients with high risks, adopting preventive measures, and ultimately reducing the financial burden, morbidity, and mortality rates related to this condition. In addition, information derived from the study will help health professionals formulate appropriate measures to address the problem in the population of Pakistan through tackling metabolic risk factors.

METHODOLOGY

A cross-sectional descriptive study was carried out in the Departments of Medicine and Gastroenterology of tertiary care hospitals of Pakistan from 1st April 2024 to September 30th 2024, following approval by the Institutional Ethical Review Committee. The objective of the study was to assess the link between obesity, metabolic syndrome and GERD.

The required sample size was determined through the WHO sample size calculator by taking the prevalence rate of GERD among obese individuals as 26% based on regional literature (9), confidence level = 95%, and margin of error = 8%; hence, the minimum calculated sample size was 326. In order to make up for incomplete files, non-participation, and laboratory findings, a total sample size of 348 patients was included using the method of non-probability consecutive sampling technique.

Inclusion Criteria

Subjects in this study consisted of adults, aged between 18 and 65 years of either sex, visiting outpatient clinics or admitted to medical or gastroenterology wards, having symptoms indicative of GERD. Those patients suffering from heartburn, acid reflux, a burning sensation behind the sternum, sourness in the mouth, epigastric pain, or nocturnal reflux symptoms recurring twice a week for the past three months were considered eligible for inclusion. In addition, patients with obesity and/or metabolic syndrome based on operational criteria were included in this study. All subjects who were willing to take part and had informed consent forms filled out were included in the study.

Exclusion Criteria

Those patients who had undergone upper gastrointestinal surgery, esophageal cancer, gastric cancer, peptic ulcer disease, achalasia cardia, esophageal varices, severe liver cirrhosis, chronic renal insufficiency, heart failure, connective tissue disease, pregnancy, severe psychiatric disease, and acute gastrointestinal hemorrhage were excluded from this study. Those patients receiving corticosteroids, immunosuppressants, or drugs that adversely affect the lower esophageal sphincter tonicity, like nitroglycerine or calcium channel antagonists, were not recruited for the study. Subjects with inadequate clinical or laboratory data and a pre-diagnosis of Barrett's esophagus were also excluded from this study.

Data Collection

The data collection procedures included the administration of the proforma by the primary investigator and his associates after informed consent was obtained from all subjects in writing. All subjects underwent history taking, clinical examinations, anthropometric measurements, and laboratory analyses.

Sociodemographic factors involved the patient's age, sex, marital status, education, occupation, place of residence, tobacco smoking, physical exercise, diet pattern, socioeconomic status, and family history of obesity, diabetes mellitus, hypertension, and digestive system diseases. Clinical factors included duration and occurrence of GERD symptoms, use of antacid drugs, history of diabetes mellitus, hypertension, dyslipidemia, and prior gastrointestinal diseases.

GERD was diagnosed based on the presence of heartburn and/or acid regurgitation at least twice weekly in the past three months, using clinical symptoms to confirm the condition through the gastroenterologist responsible for the subject's treatment. In some cases, subjects were required to undergo upper gastrointestinal endoscopy, and the results were included in their medical files.

Anthropometric measurements were performed using standard procedures. Weight was measured in kilograms using an electronic weighing scale after participants had removed their shoes and worn only light clothes. The height of each subject was measured in meters using a wall-mounted stadiometer while the participant was standing. The BMI was calculated as BMI = weight (kg) / height $(m)^2$. Based on WHO criteria, subjects with BMI ≥ 30 kg/m² were classified as obese.

The waist circumference was measured in centimeters using a non-elastic tape measure at the halfway point between the lower border of the lowest palpable rib and the iliac crest while the participant was in a relaxed standing position. The classification of central obesity was based on modified NCEP ATP III criteria.

Blood pressure measurement was done in the seated position after 5 minutes of resting using a mercury sphygmomanometer. The two values measured after 5-minute intervals were averaged. Venous blood was drawn from subjects who fasted overnight for at least 8-12 hours for biochemical tests, including fasting plasma glucose level, serum triglyceride concentration, and HDL-cholesterol concentration. Biochemical measurements were done at the hospital laboratory using standardized enzymatic methods.

Operational Definitions

A participant was considered to have metabolic syndrome according to the revised National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Individuals who

met at least three out of the following five criteria were regarded as having metabolic syndrome: a waist circumference of more than 102cm and 88cm in men and women, respectively, blood sugar (fasting) ≥100 mg/dL, TGs ≥150 mg/dL, HDL cholesterol <40 mg/dL in men and <50 mg/dL in women, Blood pressure ≥130/85 mmHg or taking antihypertensive medication (10). Obesity was classified as BMI ≥30 kg/m² according to the WHO definition (11).

Outcome Variables

GERD was chosen as the main dependent variable in the study. The diagnosis of GERD was made based on symptom evaluation, clinical diagnosis by the attending physician, and review of relevant medical files. The other dependent variables that were measured include the prevalence of obesity and metabolic syndrome among subjects with GERD, the relationship between BMI and the intensity of the reflux symptoms, and the correlation of individual metabolic syndrome components with GERD occurrence.

Data Analysis

All gathered information was then entered into the SPSS software, version 26, and analyzed. The dataset was checked and cleaned before statistical analysis to ensure minimal errors in the process of entering data and the absence of missing values. Age, BMI, waist circumference, fasting blood glucose, triglycerides, HDL cholesterol, and systolic and diastolic blood pressure were measured in quantitative format; all those variables were reported as mean±standard deviation. Gender, obesity, metabolic syndrome, smoking, diabetes mellitus, hypertension, and GERD status were categorical variables; thus, they were reported as percentages and frequencies.

Data were stratified according to age, gender, smoking, obesity, and metabolic syndrome in order to control for potential effect modifiers. Chi-square or Fisher's exact tests were employed to determine associations between categorical variables. For continuous variables, independent-sample t-tests and one-way ANOVA were used. Multivariable logistic regression analysis was used to determine independent predictors of GERD among confounding variables. Crude and adjusted odds ratios with corresponding 95% confidence intervals were calculated. A p-value of ≤0.05 was statistically significant.

RESULTS

A total of 348 participants were included in the study. The mean age of the study population was 43.6 ± 12.1 years, with the majority of participants belonging to the age group of 41–60 years (46.3%). Of the total participants, 201 (57.8%) were males, and 147 (42.2%) were females. Obesity was identified in 136 (39.1%) participants, while metabolic syndrome was present in 122 (35.1%) individuals. Gastroesophageal reflux disease (GERD) was diagnosed in 151 (43.4%) participants presenting to tertiary care hospitals. Baseline demographic and clinical characteristics of the study participants are presented in Table 1.

Table 1: Baseline demographic and clinical characteristics of study participants (n=348)

Variable	Frequency (%)
Age Group (Years)	
18–40	124 (35.6)
41–60	161 (46.3)
>60	63 (18.1)
Gender	
Male	201 (57.8)
Female	147 (42.2)
Obesity (BMI ≥30 kg/m²)	136 (39.1)
Metabolic Syndrome	122 (35.1)
GERD Present	151 (43.4)

Smoking History	91 (26.1)
Hypertension	118 (33.9)
Diabetes Mellitus	104 (29.9)

Among obese participants, GERD was observed in 101 (74.3%) individuals compared to 50 (23.6%) non-obese participants, demonstrating a statistically significant association between obesity and GERD ($p<0.001$). Similarly, metabolic syndrome was significantly associated with GERD, as 89 (73.0%) participants with metabolic syndrome had GERD compared to 62 (27.4%) participants without metabolic syndrome ($p<0.001$). Participants with increased waist circumference, elevated fasting blood glucose, and hypertension demonstrated significantly greater prevalence of reflux symptoms. The detailed association of obesity and metabolic syndrome with GERD is presented in Table 2.

Table 2: Association of obesity and metabolic syndrome with GERD

Variable	GERD Present n (%)	GERD Absent n (%)	p-value
Obesity			
Yes (n=136)	101 (74.3)	35 (25.7)	<0.001
No (n=212)	50 (23.6)	162 (76.4)	
Metabolic Syndrome			
Yes (n=122)	89 (73.0)	33 (27.0)	<0.001
No (n=226)	62 (27.4)	164 (72.6)	

The prevalence of GERD was significantly higher among obese participants, where 74.3% individuals had GERD, compared to only 23.6% among non-obese participants. Statistical analysis revealed a highly significant association between obesity and GERD ($p<0.001$), indicating that obese individuals were considerably more likely to experience reflux symptoms than participants with normal body mass index. Figure 1.

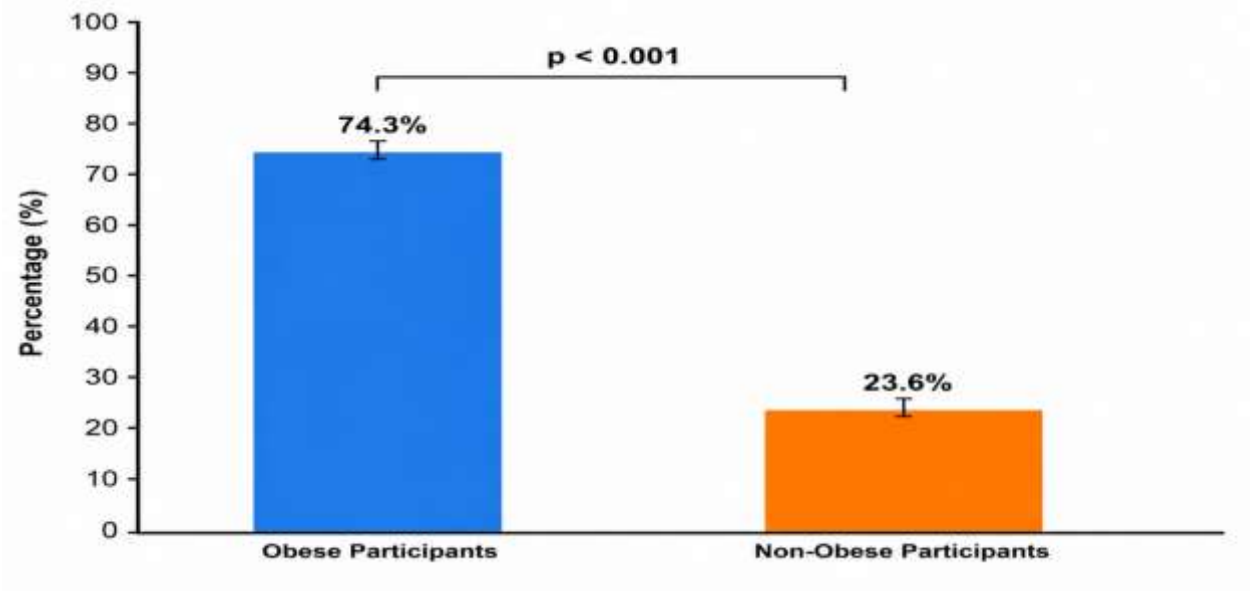


Figure 1: Frequency of GERD among obese and non-obese participants

Multivariable logistic regression analysis demonstrated that obesity and metabolic syndrome remained independent predictors of GERD after adjusting for age, gender, smoking status, diabetes mellitus, and hypertension. Obese participants had approximately 4.1 times higher odds of developing GERD (AOR: 4.1, 95% CI: 2.4–7.1, p<0.001), while metabolic syndrome increased the likelihood of GERD by nearly 3-fold (AOR: 3.4, 95% CI: 1.8–6.2, p<0.001). Smoking and hypertension also showed positive associations with GERD, although with comparatively lower statistical significance. Detailed regression analysis is shown in Table 3.

Table 3: Multivariable logistic regression analysis for predictors of GERD

Risk parameters	AOR	95% CI	p-value
Obesity	4.1	2.4–7.1	<0.001
Metabolic Syndrome	3.4	1.8–6.2	<0.001
Smoking	1.7	0.9–3.0	0.082
Diabetes Mellitus	1.5	0.8–2.8	0.117
Hypertension	1.9	1.0–3.4	0.061

AOR = Adjusted Odds Ratio; CI = Confidence Interval; GERD = Gastroesophageal Reflux Disease. p-value ≤0.05 is considered statistically significant.

DISCUSSION

The main aim of the current research was to determine the relationship between obesity, metabolic syndrome, and GERD in adults presenting to tertiary hospitals in Pakistan. Results from the study indicated a highly significant relationship between obesity, metabolic syndrome, and GERD. Individuals classified as obese were found to have significantly more cases of GERD than those not obese. On the other hand, metabolic syndrome was revealed to be a predictive factor for reflux disease. This implies that metabolic and anthropometric disorders contribute significantly to the occurrence of GERD among adults in Pakistan.

The prevalence rate of GERD in this study was found to be 43.4%, which is relatively close to the results reported by earlier regional studies. The GERD prevalence rate in Pakistan was found to be 22% to 38% in urban populations (12), while even higher percentages were observed in some hospital-based studies (13). The reason for the higher prevalence rate in this study might be the increase in obesity levels, a sedentary lifestyle, dietary changes, and the fact that the study was conducted at a tertiary-level care center, where patients with severe symptoms are usually treated. In other parts of the world, the GERD prevalence rate in the US and Europe was found to be 10% to 30%, while an increasing trend was noted among the Asian population due to the westernization of the diet and obesity (2, 14).

Obesity proved to be one of the most important factors contributing to the development of GERD in this study. Around 74.3% of the obese subjects were diagnosed with GERD, while only 23.6% were suffering from GERD among the non-obese participants. Similar results have also been observed in studies conducted in China (15), Lebanon (16), and South Korea (17), where increased BMI and abdominal obesity have been strongly correlated with the presence of reflux disease along with erosive esophagitis. A meta-analysis has also suggested that obese individuals have an almost two-fold increased incidence of having GERD than people with normal BMI (18). The reason for the above-stated correlation may be due to high intra-abdominal pressure seen in obese patients, leading to a relaxed lower esophageal sphincter, resulting in reflux.

The current study also highlighted metabolic syndrome as a strong independent risk factor for GERD. Patients with metabolic syndrome showed considerably higher rates of GERD compared to subjects who did not suffer from metabolic disturbances. Similar findings have been noted in previous studies conducted in China (19) and Tunisia (20), where metabolic syndrome and its different components independently predicted GERD and erosive esophagitis. Possible pathophysiologic pathways that link

metabolic syndrome to GERD may include factors like insulin resistance, systemic inflammation, autonomic nervous system disturbances, and increased fat accumulation in the abdomen. Furthermore, metabolic syndrome is often comorbid with obesity, hypertension, and diabetes mellitus. Diabetes, hypertension, and smoking have also shown a positive relationship with GERD in this study, although their statistical significance was relatively low after adjustment for multiple variables. Similar results have been found in several international studies and a study from Pakistan (21-23). It has been established that smoking leads to lower esophageal sphincter weakness and decreased salivary bicarbonate secretion, resulting in increased esophageal acid exposure. Diabetics can become more susceptible to developing GERD by developing autonomic neuropathy and delayed gastric emptying. The reason for the lesser correlation found in this study might be due to the relatively smaller number of patients who were smoking or had diabetes.

The prevalence of obesity and metabolic syndrome will increase in Pakistan in the coming years, thus leading to a significant increase in the burden of GERD. Prevention and treatment of obesity and metabolic syndrome may prove beneficial in avoiding GERD in patients. Proper diet and lifestyle changes, weight loss, and physical activity are key components of the prevention and treatment of reflux disease.

Although the current study provides important insights, there are some limitations associated with it. First, being a cross-sectional study, cause-and-effect relationships could not be proved. In addition, the results from this study cannot be generalized to the entire community as they were collected from tertiary hospitals only. Most of the subjects in this study were diagnosed with GERD symptomatically rather than being subjected to an endoscopy. Furthermore, dietary habits, stress, and medication compliance were not assessed, which might have affected the prevalence of reflux symptoms. Therefore, future multi-center prospective cohort studies with a large sample size and objective diagnostic techniques are required.

CONCLUSION

In conclusion, the current study revealed a strong relationship between obesity, metabolic syndrome, and gastroesophageal reflux disease in adult patients admitted to tertiary care facilities in Pakistan. The prevalence rate of GERD was much higher among obese patients and those suffering from metabolic syndrome than in non-metabolic patients. Prevention and treatment of obesity and metabolic risk factors could prove to be an effective strategy in managing GERD.

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