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Original Research Article

Insulin resistance and metabolic syndrome in generalized anxiety disorder: a cross-sectional study

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ABSTRACT

Background: Generalized anxiety disorder (GAD) involves persistent and excessive anxiety affecting daily activities for at least six months, often accompanied by restlessness, fatigue, irritability, muscle tension, and sleep difficulties. Insulin resistance (IR) and metabolic syndrome (MetS) are linked to psychiatric disorders due to their impact on the central nervous system. This study aims to assess IR and MetS prevalence in GAD patients and explore their relationship with GAD severity.
Methods: In a six-month cross-sectional study at a tertiary care center in southern India, 66 patients aged 18-60 diagnosed with GAD per DSM-5 criteria were included. Exclusion criteria were other psychiatric disorders, significant medical conditions, and specific medication use. GAD severity was assessed using the Hamilton anxiety rating scale (HAM-A). IR was calculated using the homeostatic model assessment of insulin resistance (HOMA-IR) formula, with a value of 2.5 or higher indicating significant IR. MetS was diagnosed based on the International Diabetes Federation's criteria.
Results: Among the 66 participants (59.1% female, mean age 43.41 years), 39.4% had severe GAD. Significant IR was present in 39.4% of participants, while 34.8% met the criteria for MetS. No significant correlation was found between GAD severity and IR or MetS, although a sedentary lifestyle was notably higher in GAD patients (57.6%).
Conclusions: The study highlights a high prevalence of IR and MetS among GAD patients, without a significant correlation with GAD severity. Routine metabolic screening and integrated management strategies are recommended for GAD patients to address both mental and metabolic health concerns.

Keywords: Generalized anxiety disorder, Insulin resistance, Metabolic syndrome, HAM-A, HOMA-IR

INTRODUCTION

Generalized anxiety disorder (GAD) is characterized by persistent and excessive anxiety and worry that is difficult to control and affects daily activities for at least six months. It is often accompanied by symptoms such as motor restlessness, easy fatigability, irritability, muscle tension, and difficulty concentrating or sleeping.[1] The global prevalence of anxiety disorders ranges from 3% to 19%, with GAD being more common in females.[2] In India, the prevalence of anxiety disorders is 2.57% with a weighted prevalence of GAD being 0.57%, with higher incidence rates observed in females compared to males.[3,4]

Insulin resistance (IR), defined as the reduced ability of insulin to stimulate glucose uptake and utilization, is a central feature of metabolic syndrome (MetS). MetS is a cluster of conditions including increased blood pressure, high blood sugar levels, increased waist circumference, and abnormal lipid profiles. Both IR and MetS have been implicated in the pathophysiology of various psychiatric disorders due to their impact on the central nervous

system. Alterations in dopamine turnover due to IR can induce anxiety and depressive symptoms.[5]

This study aims to assess the insulin resistance and metabolic syndrome in relation to the severity of GAD in patients attending a tertiary care hospital over a period of six months. Specifically, the study investigates the presence and extent of IR and MetS in patients diagnosed with GAD and examines the relationship between these metabolic abnormalities and the severity of GAD. Given that no prior study has comprehensively evaluated these associations in the Indian population, this research aims to fill a significant gap in the literature. Understanding these relationships could lead to improved diagnostic and therapeutic strategies for individuals with GAD, potentially enhancing both psychiatric and metabolic outcomes.

METHODS

Study design

It was a cross-sectional, observational study.

Study place

The study was conducted at the department of psychiatry, NRI Medical College and Hospital, Mangalagiri, Guntur, Andhra Pradesh, India.

Study period

The study was conducted over a period of six months (July 2023 to December 2023).

Inclusion criteria

The inclusion criteria comprised patients aged between 18 and 60 years diagnosed with GAD according to DSM-5 criteria and who provided informed consent.

Exclusion criteria

Patients were excluded if they had other psychiatric disorders, thyroid dysfunction, type 2 diabetes mellitus, a history of myocardial infarction or stroke, were on corticosteroids, immunosuppressants, or chemotherapeutic drugs for more than three months, or had been treated for GAD for more than six months.

Sampling technique

Convenience sampling. Participants were recruited from the Department of Psychiatry outpatient department (OPD) consecutively. A total of 66 patients meeting these criteria were enrolled.

This study was conducted in accordance with the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines to ensure the reliability and transparency of our findings. The study and the pre-tested questionnaire was approved by institutional ethics committee, NRI Medical College and Hospital, Mangalagiri, Andhra Pradesh, India. The primary variables for the study were insulin resistance measured by homeostatic model assessment of insulin resistance (HOMA-IR) and the presence of metabolic syndrome diagnosed according to harmonized criteria. Secondary variables included the severity of GAD measured by Hamilton anxiety rating scale (HAM-A) scores, anthropometric measurements such as waist circumference, and lipid profile components, specifically triglycerides and HDL cholesterol levels.

Data collection involved patient evaluations, which included obtaining a detailed history, conducting general physical and systemic examinations, and taking anthropometric measurements. The severity of GAD was assessed using the HAM-A score with cut-offs as follows: 0-7 indicating no/minimal anxiety, 8-14 indicating mild anxiety, 15-23 indicating moderate anxiety, and scores of 24 or higher indicating severe anxiety.[6] Fasting blood samples were collected to measure triglycerides (TG) and high-density lipoprotein (HDL) cholesterol levels as well as serum insulin and blood glucose levels. Insulin resistance was calculated using the formula.

$$HOMA - IR = (Fasting\ insulin\ (IU/l) \times Fasting\ glucose\ (mg/dl))/405.$$

A HOMA-IR value of 2.5 or higher was considered indicative of significant insulin resistance.[7] MetS was diagnosed according to the harmonized criteria defined by the International Diabetes Federation and other major organizations in 2009.[8]

To reduce potential bias, patients with other psychiatric diagnoses and metabolic conditions were excluded from the study. Consistent measurement methods were employed across all participants to maintain data reliability. Additional efforts to minimize bias included the use of standardized diagnostic criteria and structured clinical interviews. A total of 80 patients were initially approached for participation in the study. Of these, 14 patients did not provide consent, resulting in 66 patients who were ultimately enrolled in the study. The selection process is illustrated in Figure 1. All patients appearing to the OPD and satisfying the inclusion criteria during the six-month study period were included.

Statistical analysis

It was performed using statistical package for the social sciences (SPSS) version 29.0, and the data were compiled using Microsoft excel 2017. Results were expressed in percentages for categorical variables and mean±standard deviation for continuous variables. The Chi-square test was used for categorical data with a significance level set at $p \leq 0.05$ due to the study's sample size. There were no missing data for any of the variables of interest.

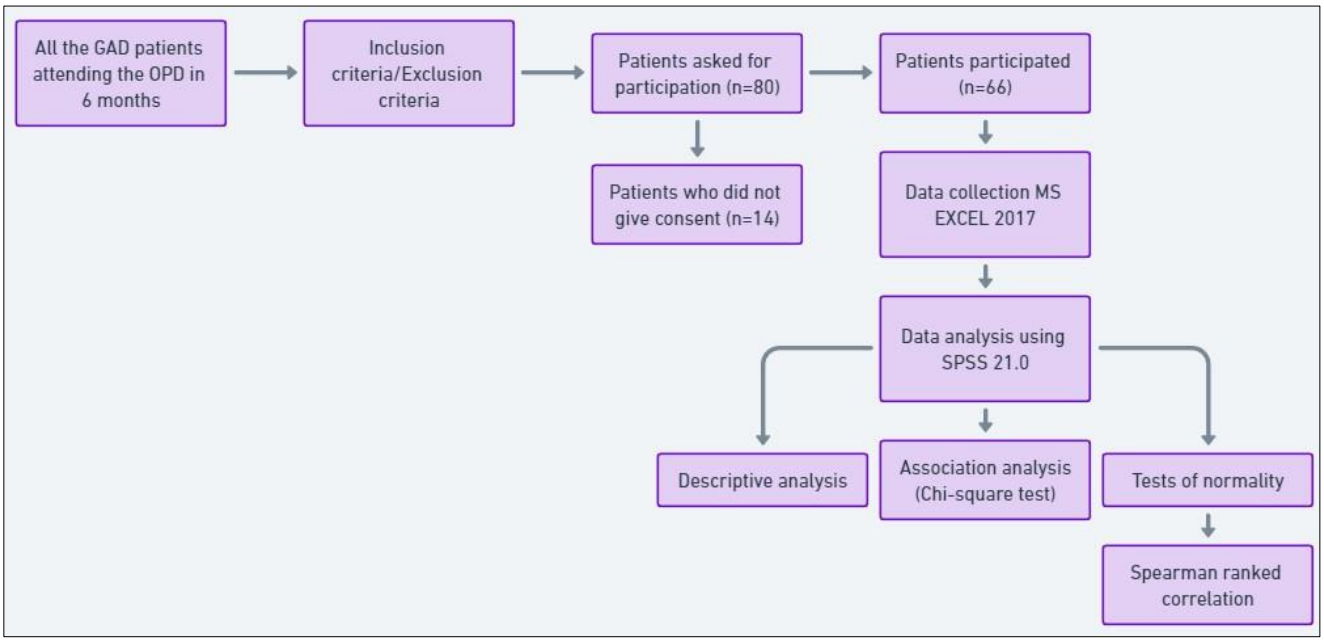

Figure 1: Study flow chart.

Tests of normality (Kolmogorov-Smirnov's and Shapiro-Wilk) were conducted to determine the distribution of the variables. For correlation analysis, Spearman's correlation was employed to evaluate the relationship between the severity of GAD, insulin resistance, and metabolic syndrome.

RESULTS

A total of 66 patients, comprising 39 females (59.1%) and 27 males (40.9%), were included in the analysis. The mean age of the participants was 43.41±7.21 years, with an age range of 31 to 60 years. The mean HAM-A score was 22.84±9.95 ranging from 9 to 43. Other descriptive results were given in Table 1.

The severity of GAD among the participants was assessed using the Hamilton Anxiety Rating Scale (HAM-A). The distribution of GAD severity was as follows - severe anxiety (HAM-A ≥24): 26 patients (39.4%), moderate anxiety (HAM-A 15-23): 26 patients (39.4%), and mild anxiety (HAM-A 8-14): 14 patients (21.2%).

The mean HOMA-IR value was 2.52±1.32, with a range from 0.97 to 5.78. A total of 26 patients (39.4%) had significant insulin resistance (HOMA-IR ≥2.5). Metabolic syndrome was diagnosed in 23 patients (34.8%). The mean TG level was 174.85±61.23 mg/dl, with a range from 93 to 458 mg/dl. The mean HDL cholesterol level was 46.52±6.70 mg/dl, with a range from 32 to 62 mg/dl.

Pearson Chi-square test has shown a significant association between HOMA-IR and MetS ($p<0.001$). No significant association was found between other variables. Severity of HAM-A score did not show significant association with presence of MetS and insulin resistance.

Table 1: Descriptive statistics of continuous variables (n=66).

Variables	Mean	Standard deviation	Range	Median
Age (years)	43.409	7.2068	29.0	43.000
Waist circumference (cm)	84.394	7.9302	32.0	84.000
HAM-A score	22.848	9.9510	34.0	20.000
TG (mg/dl)	174.848	61.2265	365.0	153.500
HDL (mg/dl)	46.515	6.6984	30.0	47.000
HbA1C (%)	5.789	0.4254	1.5	5.750
FBS (mg/dl)	95.970	14.4775	53.0	94.500
S. insulin (mIU/l)	10.2167	3.94599	14.81	8.525
HOMA-IR	2.5248	1.31643	4.81	1.930

As HAM-A score, HOMA-IR, and lipid profiles were not normally distributed, we proceeded with Spearman ranked correlations. TG has shown significant ($p<0.05$) positive correlations with HbA1C and HOMA-IR. While Waist circumference has shown negative correlation with HDL.

DISCUSSION

The present study aimed to investigate the relationship between IR, MetS, and the severity of GAD in patients attending a tertiary care hospital. Our results indicate a high prevalence of IR and MetS among GAD patients compared to the general population. However, no statistically significant correlations were found between these metabolic abnormalities and the severity of GAD.

These findings are noteworthy considering the broader literature on metabolic and psychiatric comorbidities. Studies have shown that anxiety disorders, including GAD, are associated with higher risks of metabolic abnormalities such as IR and MetS. A 2023 meta-analysis reported a pooled odd ratio (OR) of 1.07 (95% CI: 1.01-1.13) for anxiety and MetS.[9] Another study indicated that females are 1.67 times more likely to be affected by anxiety disorders compared to males, aligning with our finding that females constituted a larger proportion of the study population (59.1%).[10]

The mean HbA1c (5.79±0.43) in our study indicates that patients with anxiety were in the range of prediabetes, with 75.8% having prediabetes. The National Family Health Survey-4 has shown that only 6.63% of the South Indian population has prediabetes.[11] This suggests that a significant percentage of GAD patients are at high risk of developing diabetes in the future.

While large studies have shown a prevalence of only 16.7% of MetS in anxiety disorders, our study reported a higher prevalence of 34.8%.[12] We observed a high prevalence of insulin resistance among individuals with GAD, with a rate of 39.4%, compared to a large study conducted on the South Indian population, where the prevalence of insulin resistance was reported to be 11.2%.[13] These results underscore the substantial metabolic implications associated with GAD, suggesting a greater risk of insulin resistance in individuals with this psychiatric condition compared to the general South Indian population.

Although a higher number of patients (46.1%) with severe GAD showed higher insulin resistance, the difference between severity groups was not statistically significant. The same was true for the presence of MetS, with 57.7% of severe GAD patients having MetS.

Our study's lack of a significant correlation between GAD severity and metabolic abnormalities could be due to the multifactorial nature of GAD. Factors such as genetic predisposition, lifestyle choices, and concurrent medical conditions may independently influence both metabolic health and anxiety, thus obscuring a direct correlation. For instance, the Global Burden of Disease 2015 ranked anxiety disorders as the sixth-largest contributor to years lived with disability, emphasizing the complex interplay between mental and physical health.[14]

Moreover, the high prevalence of a sedentary lifestyle (57.6%) among GAD patients, significantly higher than the general Indian adult population's reported rate of 41.3%, suggests that GAD may contribute to decreased physical activity, which in turn exacerbates metabolic risks.[15] However, our study found no significant association between a sedentary lifestyle and MetS ($p=0.36$), or between family history of diabetes (30.3%) and psychiatric disorders (15.2%) with MetS. These findings highlight the complexity of factors influencing metabolic health in GAD patients and suggest that while these factors contribute to an overall higher risk, they do not necessarily correlate directly with MetS in this context.

Limitations

The cross-sectional design of the study precludes any inference of causality. Although we excluded patients with other psychiatric diagnoses and metabolic conditions to reduce bias, the potential for unmeasured confounding factors remains. The generalizability of our findings is limited by the study's setting in a single tertiary care hospital and the specific population studied. While the results provide valuable insights into the metabolic risks associated with GAD, they may not be applicable to all GAD patients, particularly those in different geographic or demographic settings.

CONCLUSION

In conclusion, our study highlights the elevated prevalence of insulin resistance and metabolic syndrome among patients with GAD compared to the general population. Despite this increased prevalence, we did not find statistically significant correlations between the severity of GAD and the presence of IR or MetS. This suggests that while GAD patients are at higher metabolic risk, the severity of their anxiety symptoms does not necessarily exacerbate these risks. These findings underscore the importance of routine metabolic screening and integrated management approaches for GAD patients to address both their mental and metabolic health needs. Further research, including longitudinal studies with larger sample sizes and control groups, is essential to unravel the complex interplay between GAD and metabolic health and to develop targeted interventions that can mitigate the metabolic risks associated with GAD.

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