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PREVALENCE OF METABOLIC SYNDROME IN PATIENTS ON ANTIPSYCHOTIC DRUG THERAPY

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ABSTRACT

Introduction: Psychiatric disorders are often chronic disorders requiring antipsychotic drug therapy along with psychotherapy. These antipsychotic drugs have been said to produce various side effects particularly the extrapyramidal side effect with the typical and the metabolic side effect with the atypical antipsychotic drugs. Limited data on the prevalence of metabolic side effects with the antipsychotic drug in Indians exist. **Material and method:** A cross sectional study conducted in a Tertiary Care Hospital, Pune. A total of 140 patients (18 - 65 years) who had taken a single antipsychotic drug for at least 4 months were enrolled after informed written consent. Patients were labeled to have metabolic syndrome if he/she fulfills 03 or more of the following parameters: (a) Waist Circumference > 102 cm in men and 88 cm in women, (b) Serum triglyceride level ≥ 150 mg/dL, (c) High density lipoprotein (HDL) < 40 mg/dL in men and < 50 mg/dL in women, (d) Blood pressure ≥ 130/85 mm Hg, (e) Fasting serum Glucose level ≥ 110 mg/dL as per the criteria set by the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP ATP III). **Results:** Overall the prevalence of metabolic syndrome was 22.1%, significantly higher in the female population, patients of age > 40 years, olanzapine treated patients and longer duration treated patients. **Conclusions:** The prevalence was not observed to be higher than in the general population probably due to inclusion of younger patients, shorter exposure of therapy, differences in genetic profile, level of urbanization, lifestyle and socioeconomic status.

KEY-WORDS: Typical Antipsychotic drugs, Atypical antipsychotic drug, Metabolic syndrome, NCEP ATP III

INTRODUCTION

The metabolic syndrome is a well described cluster of interrelate risk factors for development of cardiovascular disease and type 2 diabetes. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension.[1]

The criteria for the definition of metabolic syndrome have evolved since the original definition by the World Health Organization in 1998, reflecting growing clinical evidence and analysis by a variety of consensus conferences and professional organizations. Since then many international organizations and expert groups, such as the European Group for the study of Insulin Resistance (EGIR), the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), The American Association of Clinical Endocrinology (AACE), International Diabetes Federation (IDF) have attempted to incorporate all the different parameters to define metabolic syndrome.[2] The most widely used criteria are those of NCEP ATP III and IDF.

An individual is said to have metabolic syndrome if he/ she fulfills three or more of the following parameter as per the NCEP ATP III criteria: (a) waist circumference more than 102 cm in men and 88 cm in women, (b) serum triglyceride level equal or more than 150 mg/dL, (c) High density lipoprotein (HDL) less than 40 mg/dL in men and less than 50 mg/dL in women, (d) Blood pressure equal or more than 130/85 mm Hg, (e) Fasting blood glucose level equal or more than 110 mg/dL.[3] Individuals with metabolic syndrome have 3 fold increased risk for cerebrovascular stroke and coronary artery diseases, 6 fold increased risk for cardiovascular mortality and 5 fold higher risk of diabetes. [4, 5]

Prevalence of metabolic syndrome as defined by NCEP ATP III and other criteria ranges from11 - 41% in different regions of India. [6 - 9] Data available shows that the prevalence of the metabolic syndrome in Asian Indians varies according to region, extent of urbanization, lifestyle patterns, socioeconomic/cultural factors and co- morbidities like psychiatric illness.

Patients of schizophrenia have been reported to have 2 – 4 times higher prevalence of this syndrome [10,11] where as patients of bipolar disorders have 30% higher prevalence compared to the general population. [12] Higher prevalence of metabolic syndrome has been contributed in these disorders by unhealthy lifestyles exacerbated by the psychiatric symptoms, poor accessibility & quality of physical health care and adverse effects of drug treatment. [13, 14] Increased body weight associated with antipsychotic drug treatment is usually a causative factor for insulin resistance (major cause of metabolic syndrome) and for changes in plasma glucose and lipid levels. [15]

Highest risk of metabolic syndrome has been reported with clozapine and olanzapine, intermediate risk with iloperidone, quetiapine, risperidone, paliperidone, sertindole & zotepine and the least risk has been reported with amisulpride, aripiprazole, asenapine, lurasidone and ziprasidone. However, no antipsychotic drug is believed to be free of metabolic side effects; even those usually without such effects may cause them in specific situations. Since long-term side effects tend to come to light usually after a drug has been in the market for some time, and most data on the side effects of antipsychotics have been retrieved from trials on patients with many years of prior drug exposure, the possibility of underestimation of side effects cannot be ruled out.[15] Moreover, the information available in existing literature is limited and the prevalence of this syndrome in Indian population may be different from their counterparts in other regions of the world. Hence, the present study was carried out to assess the prevalence of metabolic syndrome in patients on antipsychotic drug therapy.

MATERIALS AND METHODS

The aim of the study was to find out the prevalence of metabolic syndrome in patients who were taking antipsychotic drug therapy.

Study design

A cross sectional study was conducted in patients receiving antipsychotic drugs for at least four months at a Psychiatric Centre, Pune. Both indoor patients and outdoor patients were included in the study.

A total of 140 patients in the age group of 18 – 65 years of any sex and taking antipsychotic drug treatment for at least 4 months without any break were included in the study from psychiatry outpatient department and ward. Patients who were non - compliant with the antipsychotic drug treatment, pregnant, lactating and/or active substance abusers were excluded.

Each patient included in the study was subjected to measurements of blood pressure, fasting blood glucose, triglycerides, high-density lipoprotein (HDL) and waist circumference and were screened for the metabolic syndrome as per the criteria set by the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP ATP III).

Statistical analysis: The prevalence was calculated as the proportion of patients with metabolic syndrome within total patients on antipsychotic drug therapy included in the study. The association of metabolic syndrome with different age, gender, antipsychotic drugs and duration was evaluated by chi – square test using Graph pad statistical software. The level of significance was set at $P < 0.05$.

RESULTS

The study was conducted during October 2013 to October 2015. A total of 140 patients as per the inclusion and exclusion criteria were involved in the study.

The demographic profile of patients, pattern of antipsychotic therapy, prevalence of metabolic syndrome & its association with gender, age and drug therapy observed are as under:

Demographic profile

78 (55.7%) were males and 62 (44.3%) were females. The mean age of study population was 34 ± 7.9 years with mean age 32.8 ± 7.5 years in male and 35.6 ± 8.1 years in female. Among the total recruited patients, 28 patients (20%) were in the age group 21 – 30 years, 75 patients (53.6%) in the age group 31 – 40 years, 28 patients (20%) in the age group 41 – 50 years and 9 patients (6.4%) in the age > 50 years.

Pattern of antipsychotic therapy

The most commonly prescribed antipsychotic drug in the study population was olanzapine 25.7% (36 patients), risperidone 22.1% (31 patients), quetiapine 19.4% (27 patients), aripiprazole 11.4% (16 patients) and amisulpiride & haloperidol each 10.7% (15 patients each).

Among the patients enrolled in the study, 52.9% (74 patients) were taking the antipsychotic drug therapy for a period of four to five months, 26.4% (37 patients) were taking for a period of 6 to 7 months and 20.7% (29 patients) were taking it for eight to nine months.

Prevalence of metabolic syndrome

Out of total 140 patients who were screened for the metabolic syndrome as per the NCEP ATP III criteria, 31 were found to have metabolic syndrome with an overall prevalence of 22.1%. Among the 31 patients who had metabolic syndrome, 16.4% (23 patients) fulfilled 3 criteria, 4.3% (6 patients) fulfilled 4 criteria and 1.4% (2 patients) fulfilled all 5 criteria while in those didn't have metabolic syndrome, 17.2% (24 patients) fulfilled 2 criteria, 18.6% (26 patients) fulfilled 1 criterion and 42.1% (59 patients) not meeting any of the NCEP criteria for metabolic syndrome.

Examining each criteria separately for all the 31 patients with metabolic syndrome, the most deranged parameter was reduced HDL level which was observed in 83.9% patients, closely followed by elevated fasting blood glucose observed in 80.7% patients then elevated blood pressure & triglyceride level seen in 48.4% patients and elevated waist circumference seen in 41.9% patients.

Prevalence of metabolic syndrome according to gender, age and antipsychotic drug therapy

The prevalence of metabolic syndrome in females was 32.4 % which was statistically higher (P value = 0.01) compared to 14.1% observed in the males. It was higher in the patients above 40 years of age with 35.7% and 33.3% in 41 – 50 years and > 50 years age group respectively compared to 14.3% and 18.7% in age groups 21 – 30 years and 31 – 40 years respectively. The association of metabolic syndrome with age was not statistically significant (P value = 0.16).

The prevalence of metabolic syndrome among the various treatment groups was 33.3% (12 patients) with olanzapine, 32.3% (10 patients) with risperidone, 18.5% (5 patients) with quetiapine, 13.3% (2 patients) with amisulpiride, 6.3% (1 patient) with aripiprazole, and 6.7% (1 patient) with haloperidol. The association of metabolic syndrome with the antipsychotic drug was not statistically significant (P value = 0.08).

The highest prevalence of metabolic syndrome was 34.5% (10 patients) seen in the treatment groups treated for eight to nine months, followed by the prevalence of 27% (10 patients) in the treatment groups treated for six to seven months and 14.9% (11 patients) in four to five months respectively. The association of metabolic syndrome with the duration of therapy was not statistically significant (P value = 0.1).

DISCUSSION

In this study, the overall prevalence of metabolic syndrome in patients on antipsychotic drug therapy was observed to be 22.1% compared to 5 - 43% observed in general population (not taking antipsychotic therapy [4,16,17,18] and 11.7 - 48.1% observed in various studies involving patients on antipsychotic therapy. [19-22]

The prevalence of metabolic syndrome observed in this study in males (14.1%) was lower than that in females (32.3%) and is in accordance with prevalence trend observed in other studies involving general population [16,17,18] and patients on antipsychotic therapy.[20.21] The higher prevalence of metabolic syndrome in females may be due to hormonal differences in the two genders especially of leptin, adiponectin and resistin which along with oestrogen, act to regulate energy metabolism. [23]

The prevalence of metabolic syndrome was observed to be higher in patients aged 40 years and above i.e. 33.3 – 35.7% as compared to patients of the younger age group in which the prevalence was ranging between 14.3 – 18.7%. These patterns are comparable to those reported by Deepa, et, al [17] in general population and Karoline et, al [24] in patients on antipsychotic therapy indicating a steady increase in the prevalence with rise in age.

In the present study, the prevalence of metabolic syndrome was highest with olanzapine (33.3%) followed by risperidone (32.3%), quetiapine (18.5%), amisulpiride (13.3%), haloperidol (6.7%) and aripiprazole (6.3%). Higher prevalence of metabolic syndrome with olanzapine as observed in this study is in concurrence with the reports of Gautam S, et al [25], Ozguven HD, et al [26], L'Italien GJ, et al [27]and Goswami N, et al.[28] Aripiprazole group was observed to have the lowest prevalence of metabolic syndrome in this study is in agreement with the reports of Kemp DE, et al [29] who stated the incidence of metabolic syndrome and its components with aripiprazole was similar to placebo. Haloperidol (typical antipsychotic drug) group had prevalence of metabolic syndrome as 6.7% which is lower than in other studies by Said M, et al (11.2%)[19], Ko KY, et al (36.8%)[20] and Shahda M, et al (33.3%)[21], who also reported higher prevalence of metabolic syndrome even with other antipsychotic drugs.

The prevalence of metabolic syndrome was highest in the treatment group treated for eight to nine months (34.5%) followed by the group which received treatment for six to seven months (27%) and group treated for four to five months (14.9%) suggesting that prevalence of metabolic syndrome is treatment duration dependent.

Though the overall prevalence of metabolic syndrome was not observed to be higher than the general population but the prevalence of deranged individual parameters viz. low HDL, hypertriglyceridemia and elevated fasting blood glucose was higher in the study population.

The prevalence of low HDL cholesterol of 83.9% observed in this study was higher compared to 46.9 to 63.5% in the general population [4,16,17,18] and 23.6 to 72.6% in patients receiving antipsychotic drug therapy in other studies [19,20,22]

The prevalence of hypertriglyceridemia of 48.4% observed in this study was higher than 25.2 – 38.1% in the general population [4,16,17,18] and was comparable to 39.3 – 67.7% observed in patients on antipsychotic therapy in other studies. [19,20,22]

The elevated fasting blood glucose was observed in 80.7% of patients which is higher compared to 14.7 – 39.9% in the general population [4,16,17,18] and 24.6 – 51.6% observed in patients on antipsychotic therapy in other studies.[19-22] A recent systematic review and meta-analysis concluded that all atypical antipsychotic drugs (excluding aripiprazole, ziprasidone and amisulpride for which there was insufficient data to be included in the analysis) were associated with a 30% increased risk of

diabetes as compared to typical antipsychotic drugs in people with schizophrenia. [30]

Prevalence of hypertension in the present study was 48.4% compared to 31.2 – 63.1% [4,16,17,18] observed in general population and 40 - 61.1%[19-22] in patients on antipsychotic therapy.

Prevalence of elevated waist circumference was observed in 41.9% patients compared to 9.6 – 48.9%[4,16,17,18] in general population and 61.6 – 98.4[19-22] on patients taking antipsychotic therapy in other studies. Our findings for hypertension and obesity in patients on antipsychotic therapy agree with Saddichha S, et al [31] who stated that the use of antipsychotic drugs in the long run may be associated with a significant greater risk of developing obesity with moderate influence on the development of diabetes but minimal or no risk for hypertension.

Contrary to reports that prevalence of metabolic syndrome increases with antipsychotic therapy, the prevalence observed in our study was not higher than general population, however low HDL, hypertriglyceridemia and elevated fasting blood glucose were observed to be individually higher in the study population. The possible reasons for not observing higher prevalence in the study population may be inclusion of younger study population, shorter exposure to antipsychotic therapy, differences in genetic profile, level of urbanization, lifestyle and socioeconomic status compared to other studies in existing literature.

CONCLUSION

The metabolic syndrome is a well described cluster of interrelate risk factors for development of cardiovascular disease, type 2 diabetes, stroke and death. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia, and hypertension.[1]

Patients of schizophrenia and bipolar disorders have been reported to have higher prevalence of metabolic syndrome compared to the general population[12] due to unhealthy lifestyles, poor accessibility & quality of physical health care and adverse effects of drug treatment. [13,14] However, there is limited literature on the prevalence of metabolic syndrome in Indian patients receiving antipsychotic drugs and it may be different from their counterparts in other regions of the world. Hence, the present study was planned to find the prevalence of metabolic syndrome in Indian patients on antipsychotic drug therapy. The association of this syndrome with gender, age groups, antipsychotic drugs and treatment duration was also assessed.

In this study, a total of 140 patients receiving antipsychotic therapy for at least 4 months duration were screened for the presence of metabolic syndrome as per NCEP ATP III criteria. The prevalence of metabolic syndrome observed in this study was 22.1% which was not higher than 5 – 43% in general population [4,16,17,18] and 11.7 – 48.1% in patients on antipsychotic drugs in other studies.[19-22]

In this study, the prevalence of metabolic syndrome was observed to be higher in females compared to males and in those aged 40 years and above. Among the drug groups, olanzapine group had highest prevalence of metabolic syndrome while aripiprazole group had lowest. Prevalence of metabolic syndrome was highest in patients who received treatment for eight to nine months followed by those treated for six to seven months and group treated for four to five months suggesting that prevalence is treatment duration dependent.

Though the overall prevalence of metabolic syndrome was not observed to be higher than the general population but the prevalence of deranged individual parameters viz. low HDL, hypertriglyceridemia and elevated fasting blood glucose was higher in the study population.

Our findings of higher prevalence of metabolic syndrome in female patients, those aged 40 years & above, those on olanzapine & receiving longer duration of antipsychotic drug treatment are in accordance with other studies on similar patients. However, overall prevalence of metabolic syndrome was not observed to be higher than general population probably due to inclusion of younger study population, shorter duration of exposure to antipsychotic therapy, differences in genetic profile, level of urbanization, lifestyle and socioeconomic status compared to other studies.

It is concluded from our findings that studies with larger sample size, longer duration of drug exposure with a control group from the same population (who is not exposed to antipsychotic drug therapy) be conducted in future to confirm the increase in risk of metabolic syndrome with the use of antipsychotic drug therapy.

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