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Metabolic Syndrome and Cardiovascular Disease Risk in Schizophrenic Patients

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Abstract:

Background: *The schizophrenic patients are at higher risk for cardiovascular disease. This study aimed to determine the prevalence of metabolic syndrome and to measure cardiovascular disease (CVD) risk parameters in patient group and compare it with normal population.*

Methodology*: We recruited 74 patients meeting ICD-10 criteria for schizophrenia and 25 healthy controls from general population. The body mass index, blood sugar, lipid parameters and high sensitive C-reactive protein (hs-CRP) were measured in both groups. Metabolic syndrome and dyslipidemia prevalence were assessed based on International Diabetes Federation (IDF) guidelines.*

Results: *The schizophrenia subjects showed statistically significant increased Sugar, triglycerides and decreased HDL cholesterol values. The subjects also showed statistically significant increased hs-CRP values. The prevalence of metabolic syndrome and dyslipidemia were 52% and 57% respectively, which were higher compared to control group.*

Conclusion: *Schizophrenia patients are at higher risk for cardiovascular disease due to high prevalence of metabolic syndrome and dyslipidemia. These patients should be regularly monitored for CVD risk factors.*

Key words: Metabolic syndrome, Dyslipidemia, High sensitive C-Reactive proteins

Introduction:

Schizophrenia, a debilitating mental illness characterized by hallucinations, delusions and in many cases impaired cognitive and occupational functioning, is a life-shortening disease.[1] Schizophrenics have shorter life period than the general population[2-4] and are associated with higher risk of respiratory, infectious and cardiovascular disease.[5] Different factors related to the underlying pathology, antipsychotic medications and lifestyle (e.g. smoking, general neglect of health, poor diet and decreased access to health care services) may contribute to the increased mortality in these patients.

The World health Organization as identified the top six modifiable risk factors worldwide for early mortality as hypertension, smoking, raised glucose, physical inactivity, obesity and dyslipidemia.[6] All of these risk factors occur at higher rates in people with schizophrenia than in the general population and hypertension, hyperglycemia and dyslipidemia, being less 'visible' than the others, tend to not be identified and/or not treated. A combination of decreased access to general health care, a lack of awareness, and the nature of mental illness itself in terms of social marginalization and impaired cognitive and social functioning, are all contributing factors to this.[7] However, even when these conditions are identified and treated, adding antihypertensive, hypoglycemic agents and /or statins to an often already complex regime compounds the 'pill burden', potentially lowering compliance rates.[8]

In recent studies, schizophrenic patients are reported to have higher risk for cardiovascular disease[9, 10] and this risk is shown by presence of metabolic syndrome characteristics and dyslipidemia.

Metabolic syndrome is identified by coincidence of elevated waist circumference, impaired lipid metabolism, hypertension and/or hyperglycemia. This cluster is a well- accepted risk factor for cardiovascular morbidity and mortality.[11]

hs-CRP is a sensitive marker for low-grade systemic inflammation and raised levels in blood independently predicts the future risk of CVD.[12-14]

In this study, we aimed to measure the CVD risk in schizophrenic subjects in terms of metabolic syndrome characteristics, dyslipidemia, body mass index and hs-CRP.

Material and methods:

A total of seventy four (74) patients suffering from schizophrenia (54 males, 20 females between ages of 20 and 60 years) were recruited from Psychiatry centre, SMS Medical College, Jaipur Rajasthan. Patients were interviewed and diagnosed by the psychiatrist as per ICD-10 (International Classification of Mental disorders) criteria of mental disorders. The patient's sociodemographic profile and history of illness was recorded in self designed semi-structured proforma. The severity of illness was assessed by the psychiatrist using "Positive and Negative syndrome scale (PANSS)". The exclusion criteria were mental retardation, chronic inflammatory conditions, treatment with mood stabilizers, pregnant or lactating women. A total 25 age and sex matched controls were psychiatrically evaluated and enrolled in the study with no past history of psychiatric illness. Institutional ethical committee approval was obtained before the commencement of the study. Informed consent was obtained from guardians and families of the subjects.

Assessment:

Height (in meters) and weight (in kg.) of subjects was measured and Body mass index was calculated by formula BMI=

weight/(Height)^2 The blood pressure was measured using sphygmomanometer. Fasting serum glucose, serum lipid parameters and hs-CRP were measured.

International Diabetes Federation (IDF) guideline criteria was used for defining metabolic syndrome. According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have central obesity (defined as waist circumference with ethnicity specific values) plus any two of the following four factors[15]

Raised triglycerides	≥ 150 mg/dl (1.7 mmol/l)
Reduced HDL cholesterol	<40 mg/dl (1.03 mmol/l) in males <50mg/dl (1.29 mmol/l) in females
Raised Blood pressure	Systolic BP≥130 or diastolic BP ≥85 mm
Raised fasting serum glucose	FS ≥100 mg/dl (5.6 mmol/dl)

If BMI is >30 kg/m^2, central obesity can be assumed and waist circumference does not need to be measured.

hs-CRP assay: Serum hs-CRP was measured by an enzyme-linked immune sorbent assay or sandwich type assay. The assay makes use of two highly specific monoclonal antibodies: A monoclonal antibody specific for CRP is immobilized on to the microwell plate and another monoclonal antibody specific for a different region of CRP was conjugated to horse raddish peroxidase (HRP). CRP from the sample and standards were allowed to bind to the plate, washed and subsequently incubated with HRP conjugate. After second washing enzyme substrate was added. The enzymatic reaction was terminated by addition of the stop solution. The absorbance was measured on a microtitre plate reader. The intensity of the colour formed by the enzymatic reaction was directly proportional to the concentration of CRP in the sample.

Statistical Analysis:

The numerical data was presented as mean ±standard deviation (mean±SD). Independent t-test was used for comparison of both the groups. The level of significance was $p \leq 0.05$.

Results:

The socio-demographic characteristics of the study groups are presented in Table-1.

The statistical comparison of physical and laboratory parameters are shown in Table-2. Difference in body mass index of patients and control groups was not statistically significant.

Among metabolic syndrome parameters fasting glucose levels, the increase in triglycerides and decrease in HDL level were significant in patient group. The systolic and diastolic BP showed no difference. hs-CRP was significantly high in patient group.

Table 1. Socio-demographic characteristics of Schizophrenic patients and Controls

Variable	Patients (74)	Controls (25)
Age	38.31±11.39	35.64±10.51
Marital Status		
1. Single	12 (16.21%)	8 (32%)
2. Married	56 (75.6%)	17 (68%)
3. Widower/Divorced/ Separated	6 (8.10%)	-
Employment		
1. Employed	26 (35.13%)	10 (40%)
2. Unemployed	48 (64.86%)	15 (60%)
Education		
1. Secondary completed	61 (82.43%)	19 (76%)
2. University completed	13 (17.56%)	6 (24%)
Family Type		
1. Nuclear	18 (24.32%)	8 (32%)
2. Joint	56 (75.67%)	17 (68%)

Locality		
1. Urban	9 (12.1%)	7 (28%)
2. Rural	65 (87.8%)	18 (72%)

Both Groups were comparable on socio-demographic variable

Table 2: Statistical comparison of physical and biochemical parameters in schizophrenic patients and controls

Parameter	**Subjects (74)** Mean±SD	**Controls (25)** Mean±SD	p-**value**
BMI weight/(height)^2	29.2±4.7	26.9±5.2	NS
Waist circumference (cm)	96.4±11.1	87.5±12.3	0.01*
Fasting glucose (mg/dl)	102.51±41.10	82.5±20.50	0.02*
Systolic BP	123.5±9.4	121.4±8.7	NS
Diastolic BP	83.8±10.4	79.2±8.9	NS
Total cholesterol (mg/dl)	181.7±33.7	149.5±25.4	0.001*
Triglycerides (mg/dl)	126.2±58.1	90.2±31.3	0.001*
HDL (mg/dl)	38.5±2.7	42.9±4.14	0.001*
LDL (mg/dl)	118.2±30.8	88.6±16.3	0.001*
hs-CRP (mean±SD)	7.63±6.3	1.96±0.70	0.000*

*****p value statistically significant (<0.05)

Discussion:

The mean age of schizophrenic patients was 38.31±11.39 (20-60) years and of control subjects was 35.64±10.51 (20-60) years. Most of subjects included in our study were married (study group 75.6%, control 68%), joint families (study group 75.6%, control 68%) and of rural background (study group 87.8%, control 72%). The mean age of onset was 30.48 ±11.83 (8-50) years and the total duration of illness was 7.66 ± 4.91(1-20) years. There was no statistically significant difference in the two groups with respect to socio-demographic variables.

We found that 52% of our samples fulfilled the IDF criteria for metabolic syndrome. Our finding is similar to previous reports.[16] The higher prevalence of metabolic syndrome in patients with schizophrenia has frequently been reported.[17] For instance a study by Cohn et al[17] found that the prevalence of metabolic syndrome in men and women with schizophrenia was 42.6% and 48.5% respectively using the

same criteria. Similarly a Japanese study by Sugawara et al reported a 48.1% incidence of metabolic syndrome in outpatients with schizophrenia.[16] The reasons for a higher rate of metabolic syndrome being associated with schizophrenia are many. Certain lifestyle (such as sedentary habits and intake of high Fat and high carbohydrate diets) that are frequently seen in people with severe mental illness are associated with metabolic syndrome.[18,19] Schizophrenia may predispose individuals to physiological changes that increase the risk of metabolic syndrome. For instance, abnormalities in glucose regulation along with a pattern of insulin resistance have been described in schizophrenic patients even prior to the development of illness or the use of antipsychotic agents.[20,21]

Many of the antipsychotic drugs used to treat schizophrenia are associated with the emergence of cardiovascular risk factors. Antipsychotic-induced weight gain occurs in at least 50% of patients treated with antipsychotics[22] and impacts on cardiovascular risk, self esteem and adherence to treatment. Individual antipsychotic drugs have differing effects on weight gain as well as on glucose and lipid metabolism.[23]

We found that the presence of metabolic syndrome in schizophrenic patients was associated with CVD risk. A significant difference was observed in the cardiovascular risk of patients with and without metabolic syndrome. Our results were similar to a study in Spain by Bobes et al[24] which reported high cardiovascular risk, as defined by the Framingham score, in patients treated with antipsychotic drugs. Correll et al, who studied 367 adult patients being treated with atypical antipsychotics, found that metabolic syndrome was present in 137 (37.3%) patients and it was significantly associated with a ten-year risk of CHD.[25] Similarly, Holt et al found that 12% of patients in their study with serious mental illness had a >20% ten-year risk of CHD.[26]

Dyslipidemia is one of the most significant risks for cardiovascular disease.[27] Prevalence rates in the US general population are as high as 35% in people aged over 20 years.[28] (centres for disease control and prevention, 2011). In people with severe mental illness, the figures are much higher; baseline data on 1460patients from the Clinical Antipsychotic trials of Intervention Effectiveness (CATIE) study showed that 998 (68.4%) had dyslipidemia, only 12% of whom were receiving treatment.[29] In the UK, even though patients with mental illness may visit their GP on a regular basis, few are screened for diabetes or have had lipid profiles done.[30]

High sensitive CRP is a well-established sensitive marker which indicates low-grade systemic inflammation. Raised levels of CRP in blood independently predict the future risk of cardiovascular disease.[31] There are increasing evidence in literature which emphasize immune activation and raised CRP levels in schizophrenia cases.[32, 33] This study found significant increase in blood CRP levels in schizophrenia subjects. The study also suggests that CRP may play a role in underlying inflammation and inflammation is a possible contributing factor in disease pathogenesis.

Limitations:

Type of antipsychotic drug was not taken into account, hence effect of drugs could not be evaluated. Also, for patient population, the factors like physical activity or dietary habits were not controlled hence, effect of these factors on CVD risk could not be described.

Conclusion:

The study concludes that the prevalence of metabolic syndrome and cardiovascular disease risk is very high. This study underlines the importance of timely referral of patients to

physician for further evaluation. The patients will benefit from timely biochemical evaluation and adequate treatment.

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