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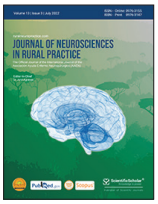

Brief Report

Vascular age, cardiovascular disease risk factors, and hematological parameters in patients with Schizophrenia: An exploratory study

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ABSTRACT

Objectives: Patients with schizophrenia have shortened life expectancy due to greater cardiovascular disease (CVD) risk. Due to sparse data, index study was planned to assess the CVD risk factors, vascular age (VA), and hematological parameters in patients with schizophrenia and the concordance between Framingham Risk Score (FRS) for lipids and body mass index (BMI) (FRS_{LIPIDS} and FRS_{BMI}).

Materials and Methods: Patients with schizophrenia (n = 53) were evaluated for the presence of metabolic syndrome (MS) using the modified NCEP ATP III criteria, along with their functionality, illness severity, physical activity and nutritional score, FRS_{LIPIDS} and FRS_{BMI}, and hematological parameters.

Results: Prevalence of MS was 39.6%; in addition, 47% of patients were at risk for developing MS as they fulfilled one or two components of MS criteria and 56% of patients were obese. BMI, obesity, and RBC count were found as significant correlates for MS. CVD risk (FRS) median score (3.10) was comparable for BMI and lipid criteria along with significant correlation for FRS_{LIPIDS} and FRS_{BMI} ($r = 0.555$, $P < 0.001$).

Conclusion: VA and 10-year CVD risk (FRS for BMI and lipid criteria) represent easier way to communicate with the patients and caregivers and also to guide for comprehensive treatment plan, appropriate nutrition, physical activity, and cardiometabolic screening.

Keywords: Cardiovascular disease risk factors, Hematological parameters, Schizophrenia

INTRODUCTION

Patients with schizophrenia have shortened life expectancy and higher mortality than general population with major contributor being cardiometabolic disorders, including metabolic syndrome (MS). A systematic review and meta-analysis reported pooled MS prevalence of 33.4% in patients with schizophrenia, with relative risk of 1.87 compared to healthy individuals.[1] The prevalence of MS in drug naïve Indian patients with schizophrenia is 19%,[2] which suggests the role of illness, lifestyle factors, and psychotropic medications in developing MS.

A multivariable risk factor algorithm, the Framingham risk score (FRS), is used to estimate 10-year cardiovascular disease (CVD) risk.[3] Patients with schizophrenia have significantly greater CVD risk (FRS), compared to healthy population.[4] CVD risk (FRS) is generally calculated on lipid parameters, but it can also be calculated on body mass index (BMI) parameter for the ease and logistics. Vascular age (VA) or heart age depicts the age of the vascular system of an individual with regard to cardiovascular risk factors.[5]

Grover *et al.*[6] reported 36% prevalence of MS, with 1.65% CVD risk in 10 years in patients with schizophrenia in Northern India. Rekhi *et al.*[4] reported higher CVD risk and VA difference on lipids as well on BMI in patients with schizophrenia in Singapore, compared to healthy controls, with correlation between FRS for lipids and BMI (FRS_{LIPIDS} and FRS_{BMI}).

In a longitudinal cohort study, Wu *et al.* reported association of RBC and hemoglobin with MS in general population.[7] Similarly, positive association of RBC count was reported with higher odds of having MS, abnormal triglyceride, and high-density lipoprotein (HDL) levels in patients with schizophrenia.[8]

In view of sparse data from India and magnitude of cardiometabolic disorders in patients with schizophrenia, index study was planned to assess the CVD risk factors, VA, and hematological parameters in patients with schizophrenia

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and to examine their association and the concordance between FRS_{LIPIDS} and FRS_{BMI}.

MATERIALS AND METHODS

After obtaining approval from our Institutional Ethics Committee, the study was carried out at psychiatry outpatient setting of tertiary care center in Northern India. Patients with schizophrenia (diagnosed by Consultant Psychiatrist as per International Classification of Diseases, 10th revision),[9] aged between 30 and 60 years (since the FRS calculator is validated for individuals between the ages of 30–74),[3] were recruited through purposive sampling after obtaining written informed consent. Patients with comorbid chronic physical disorders, psychiatric disorders, and substance use disorders (other than nicotine) were excluded from the study.

Modified NCEP ATP-III criteria were used to diagnose MS, for which the presence of three out of following five abnormalities were required: High waist circumference (≥80 cm for females and ≥90 for males of Asian origin), systolic blood pressure ≥130 and/or diastolic blood pressure ≥85 mm of Hg, triglyceride levels ≥150 mg/dl, HDL cholesterol <40 mg/dl for male and <50 mg/dl for females, and fasting blood sugar ≥100 mg/dl (or on treatment for hypertension, diabetes, or dyslipidemia).[10]

Demographic and clinical details were ascertained on structured pro forma and following tools with high reliability and construct validity were used to assess the patients:

Global assessment of functioning scale provided the functionality score in relation to psychiatric disorder and associated disturbances.[11]

Positive and negative syndromes scale (PANSS) was used to assess the severity of schizophrenia on positive, negative, and general psychopathology subscales.[12]

Health promoting lifestyle profile-II assessed their physical activity and nutritional scores with using two subscales on physical activity and nutritional habit. Higher score depicted better physical activity and nutritional habits.[13]

FRS and VA calculators were used to calculate FRS and VA based on BMI by including the age, systolic blood pressure, treatment for hypertension, cigarette smoking, diabetes, and BMI into gender-specific Cox regression models.[3] FRS and VA based on lipids were calculated similarly with including total cholesterol and HDL cholesterol instead of BMI. The difference between VA and actual age (VAdiff_lipids, VAdiff_BMI) was also calculated.

Statistical analysis

Analysis was done using the Statistical Package for the Social Sciences (SPSS) version 21.0 for Windows (Chicago, Illinois, USA). After descriptive analysis, correlational analysis was used to find the correlates of MS.

RESULTS

Demographic and clinical profile

A total of 53 patients with schizophrenia were recruited and their mean age was 40 years. Males and females were nearly equal and about one-third of them were employed. Mean duration of illness was 12 years (details are depicted in [Table 1]).

Hematological parameters

About 20% of patients (five males and six females) had anemia, two patients had thrombocytopenia, and none of the patient had leukocytopenia (<4000/microliter). Mean RBC count was 4.96 (Standard deviation [SD] 0.53) million cells per microliter, platelet count was 3.08 (SD 0.82) lac per microliter, white blood count was 7414 (SD 1771) cells per microliter, and differential leukocyte count was neutrophil 59.1% (SD 8.26), lymphocyte 30.44% (6.46), monocytes 7.07% (SD 2.92), eosinophil 2.73% (SD 2.34), and basophil 0.56% (SD 0.29).

Table 1: Demographic and clinical profile.

Variable	Mean (SD)
Age (years)	40.62 (9.51)
Education (years)	11.75 (4.13)
Monthly family income (INR)	5245.25 (10727.67)
Duration of illness (months)	145.83 (10.2.41)
Global assessment of functioning score	70.07 (15.04)
Illness severity (PANSS) score	50.07 (16.72)
	Frequency (%)
Sex	
Male	27 (50.9)
Female	26 (49.1)
Marital status	
Currently Single	11 (20.8)
Married	42 (79.2)
Occupation	
On paid jobs	18 (34)
Home makers/Not on paid jobs	35 (66)
Locality	
Urban	37 (69.8)
Village	16 (30.2)
Religion	
Hindu	47 (88.7)
Non-Hindu	6 (11.3)
Family	
Nuclear	38 (71.7)
Extended/Joint	15 (28.3)

Cardiometabolic profile

As depicted in [Table 2], the most common metabolic abnormality was hyperglycemia (50.9%), followed by abnormal waist circumference, hypertriglyceridemia, lower HDL level, and hypertension was the least common (24.5%). About half of the patients (56%) were obese and one-sixth of them were smokers (17%). About two-fifth of the patients had MS (39.6%), and in addition, half of the patients (47.2%) had one or two metabolic abnormalities. Mean physical activity score and nutritional score were 1.50 and 10.52, respectively.

Mean VA was 41.30 years as per lipid criteria and 42.98 years as per BMI criteria. Difference in actual age and VA was 0.68 years and 2.35 years, respectively, as per lipid and BMI criteria. Median FRS was 3.10% as per lipid and BMI criteria. FRS score was greater in males compared to females, but difference was not statistically significant. Significant association was found among VA difference and FRS as per lipid criteria (r = 0.738, $P < 0.001$), VA difference and FRS as per BMI criteria (r = 0.437, $P < 0.001$), and FRS as per lipid and BMI criteria (r = 0.555, $P < 0.001$).

Correlates of MS

Physical activity and nutritional scores were lesser, while illness severity PANSS score was greater in patients with MS, compared to in patients without MS. However, these differences were statistically not significant.

Patients residing in urban locality had greater rate of MS (48.6%) than patients residing in rural locality (18.7%) (X^2 4.17, P = 0.041). Patients with MS had greater BMI (28.63 ± 6.38 vs. 24.60 ± 4.26, t = −2.76, P = 0.008), obesity (BMI ≥25) (56.6% vs. 17.39%, X^2 8.39, P = 0.004), and RBC count (5.20 ± 0.60 vs. 4.79 ± 0.41 million cells per microliter, t = −2.91, P = 0.005), compared to patients without MS. RBC count was positively correlated with metabolic abnormalities (number of fulfilled MS criteria) (r = 0.318, P = 0.020) and presence of MS (r = 0.378, P = 0.005).

Table 2: Cardiometabolic profile.

Variable	Frequency (%)
Abnormal waist circumference (≥90M, ≥80 F)	23 (43.4)
Systolic blood pressure ≥130 mm Hg	9 (17)
Diastolic blood pressure ≥85 mm Hg	8 (15.1)
Hypertension (blood pressure ≥130/≥85 mmHg)	13 (24.5)
Hypertriglyceridemia (TG ≥150 mg/dl)	21 (39.6)
Lower HDL (<40 mg/dl M, <50 mg/dl F)	19 (35.8)
Hyperglycemia (FBS ≥100 mg/dl)	27 (50.9)
Obesity (as per Asian Indian cut off BMI ≥25)	30 (56.6)
Metabolic syndrome	21 (39.6)
Smokers	9 (17)
MS criteria fulfilled	
0	7 (13.2)
1	16 (30.2)
2	9 (17)
3	16 (30.2)
4	4 (7.5)
5	1 (1.9)
	Mean/Median
VA (Lipid) (Mean [SD])	41.30 (14.07)
VA (BMI) (Mean [SD])	42.98 (14.52)
FRS (Lipid) (Median [IQR])	3.10 (1.45–4.95)
FRS (BMI) (Median [IQR])	3.10 (1.60–5.95)

M: Male, F: Female, TG: Triglycerides, HDL: High-density lipoprotein cholesterol, FBS: Fasting blood sugar, BMI: Body mass index, MS: Metabolic syndrome, VA: Vascular age, FRS: Framingham risk score

DISCUSSION

Index study assessed CVD risk and hematological parameters in 53 outpatients with schizophrenia. Hyperglycemia was most common metabolic abnormality followed by abnormal waist circumference. About half of the patients were obese as per Asian Indian cutoff (BMI ≥25).[14] Earlier studies[6,15] have reported abnormal waist circumference/abdominal obesity as most common abnormality and similar rates of obesity in patients with schizophrenia. One-sixth of the patients were smokers, which are similar to figures reported in earlier study from northern India (18%),[6] but relatively half as compared to the study from Singapore (33%).[4]

MS prevalence was 39.6% in index study, which is close to figures reported in earlier studies from same center (34.5%),[15] other center of Northern India (36.4%),[6] and systematic review and meta-analysis (33.4%).[1] In addition, about half of the patients had metabolic abnormalities (fulfilled one or two components of MS criteria), which depicts their greater vulnerability to develop MS.

Index study on patients receiving antipsychotic medications reported almost double MS prevalence (39.6%) compared to drug naïve patients from India (19%).[2] It, further, highlights that illness related, lifestyle related (e.g., nutrition, physical activity, and substance use), and medications related factors attributing to MS risk. Although due to smaller sample, we could not find association of MS with nutritional score, physical activity score, and smoking, other studies have proven their association with MS.[1]

In index study, RBC count was positively associated with presence of number of metabolic abnormalities and MS. Similar trends were reported earlier in general population[7] and patients with schizophrenia.[8] In line with earlier studies,[8,15] we also found BMI, obesity, and RBC count as significant correlates for MS.

Rekhi *et al*.[4] reported greater difference in the actual age and VA of patients with schizophrenia as per lipid and BMI criteria, and similarly, Ratliff *et al*.[16] found significant VAdiff for lipids in obese patients with schizophrenia as compared

to obese controls. Compared to index study, these studies had larger sample, greater smoking rates[4] (double to our sample) and ethnic variations.

Several studies have reported significant risk of CVD in patients with schizophrenia than the general population.[4,17] In index study, median FRS was 3.10% as per lipid and BMI criteria. Our figures were greater than earlier study from northern India (1.65%)[6] and lesser than study from Singapore (4.5–5%).[4] These differences might be due to substantially lower age of patients and duration of illness in study by Grover *et al*.[6] and due to ethnic variations, greater smoking rates in study by Rekhi *et al*.[4] Similar to Rekhi *et al*.,[4] we also found significant associations among VA difference, FRS_{LIPIDS} and FRS_{BMI}.

Index study has limitations such as small sample from single-center, cross-sectional design, and lack of controls and assessment regarding effects of medications (dosage and duration of use) on developing MS. Future prospective studies should assess CVD risk in larger sample, with comprehensive evaluation of lifestyle factors attributing to CVD risk and should also guide for effective preventive strategies.

FRS_{BMI} is more convenient, as BMI is feasible to measure than blood lipids in low resource setting including rural or peripheral locations with lack of laboratory support. Clinicians should educate the patients about the risk of CVD with sedentary lifestyle and should emphasize on the need of cardiometabolic screening, and proper nutrition and physical activity.

CONCLUSION

To conclude, two-fifth of the patients had MS, in addition, about half of the patients fulfilled one or two components in MS criteria and half of the patients were obese. BMI, obesity, and RBC count were found as significant correlates for MS. CVD risk (FRS) median score was comparable for BMI and lipid criteria.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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