Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Prevalence and predictors of metabolic syndrome in patients with schizophrenia and healthy controls: A study in rural South Indian population

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ARTICLE INFO

Article history:
Received 4 January 2017
Received in revised form 19 April 2017
Accepted 22 April 2017
Available online xxxx

Keywords:
Metabolic syndrome
Schizophrenia
Prevalence
Antipsychotics

ABSTRACT

Introduction: Metabolic syndrome (MetS) has been extensively studied as a co-morbidity in patients with schizophrenia. A disparity is noted between hospital and community based estimates in India. We aimed to examine the prevalence and predictors of MetS in schizophrenia patients and general population controls in a rural population in South India.
Methods: Patients (n = 157) and general population controls (n = 263) were recruited from a rural area in South India. Diagnosis of MetS was established using International Diabetes Federation (IDF) criteria. Patients were also assessed on clinical parameters, treatment details, dietary and physical activity patterns. Predictors of MetS were estimated based on subgrouping of patients with and without MetS.
Results: 50 (31.8%) of the patients and 76 (28.9%) of the controls were diagnosed to have MetS. Female gender and ongoing antipsychotic exposure were noted to be significant predictors of MetS with odds ratio (95% confidence interval) of 2.87 (1.2–6.86) and 4.42 (1.37–14.25) respectively. Three empirically defined treatment groups 'never treated', 'ever treated' and 'continuous treatment' groups had odds ratios (95% CI) of 0.53 (1.68–6.58), 0.92 (0.5–1.69) and 3.33 (1.68–6.58) when compared to the control group.
Conclusions: Patients who were naïve to antipsychotics had a significantly lower prevalence of MetS compared to general population. This finding doesn't support the antipsychotic independent risk for MetS in patients with schizophrenia. Female gender and regular antipsychotic exposure predicted MetS.

1. Introduction

The turn of twenty-first century has seen a major transition in public health indicators of mortality and disability from communicable to non-communicable disorders, and, this is particularly so for low and middle income countries (LAMICs) (Murray et al., 2012). According to Global Burden of Disease report, mental health disorders and other non-communicable disorders account for >40% of years of life lost (YLL) and 70% of years lived with disability (YLD) (University of Washington, Institute for Health Metrics and Evaluation, 2013). Schizophrenia being one of the severe mental disorders, results in an average reduction of longevity of fifteen years in men and twelve years in women compared to those who do not suffer this illness (Crump et al., 2013). While suicide and homicide account for only 15% of this reduction, more than one third of reduced longevity is attributable to cardiovascular diseases (Crump et al., 2013; Lawrence et al., 2013).

Metabolic syndrome (MetS) comprises of core components of central obesity, insulin resistance, dyslipidemia and hypertension across all the expert panel consensus statements *viz.*, World Health Organization (WHO), National Cholesterol Education Program – Adult Treatment Panel III (NCEP ATP III) and International Diabetic Federation (IDF). (WHO, 1999; Grundy et al., 2005; Alberti et al., 2005). Each of the individual components of metabolic syndrome and their combination significantly contribute mortality due to cardiovascular events (Pouliot et al., 1994; Robins et al., 2003; Hu et al., 2004). Patients with schizophrenia have been noted to be at higher risk of developing metabolic syndrome (Mitchell et al., 2013a, 2013b) and its individual components like insulin resistance (Holt et al., 2005), central obesity (Coodin,

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http://dx.doi.org/10.1016/j.schres.2017.04.039
0920-9964/

2001) and hypertension (De Hert et al., 2011), explaining the high proportion of increased risk for cardiovascular mortality. Though the second-generation anti-psychotics significantly increase the prevalence of this co-morbidity (Mitchell et al., 2013a, 2013b; Saddichha et al., 2007) even un-medicated patients and their first-degree relatives are noted to be at higher risk in individual studies (Ryan et al., 2003). These findings have resulted in speculations for shared etiological pathways for the two disorders independent of antipsychotic exposure (Venkatasubramanian et al., 2007).

The prevalence of MetS varies widely among studies from different populations and countries. Though this could be partly attributed to variability in the definitions used across studies the variation remains even among studies which have used uniform definitions with race and ethnicity specific diagnostic criteria (Cameron et al., 2004; O'Neill and O'Driscoll, 2015). A recent systematic review and meta-analysis on the subject which included studies from twelve countries reported a varying pooled prevalence ranging from 25.4% in Brazil to 50.2% in Australia (Vancampfort et al., 2015). The same study also included 16 studies from India of which 14 included patients with schizophrenia and one study each in Bipolar Disorder and Majar Depressive Disorder. The pooled prevalence of MetS from Indian studies was 26.3% which was lower than the rates noted from high income countries. Of these fourteen studies twelve were from studies conducted in urban hospital settings and two were based on community samples.

Studies on MetS in patients with schizophrenia from India conducted in hospitals report a prevalence rate ranging from 11% to 45% (Grover et al., 2014; Meena and Gautam, 2011). A systematic review examined the urban and rural prevalence of MetS in schizophrenia in India found a pooled prevalence of 33.05% among the studies conducted in hospital setting while a significantly lower pooled prevalence of 10.81% in community based studies. (Ganesh et al., 2016). This highlights an evident disparity in the prevalence of MetS between and hospital and community studies but the data from the community is limited to only two studies. (Ganesh et al., 2016).

In this study, we examined the prevalence of MetS in a mixed group of treated and untreated patients with schizophrenia and controls in a rural community. Secondarily, we examined the determinants of metabolic syndrome accounting for dietary and lifestyle factors.

2. Methods

Patients and controls were recruited for the study after written informed consent. The study was approved by institutional ethics committee of National Institute of Mental Health and Neurosciences, Bengaluru.

2.1. Samples

Patients were recruited from a community intervention program for schizophrenia at Turuvekere taluk (an administrative block) in the state of Karnataka. The health assistants in each village were sensitized for case identification. The cohort of patients was established by house to house survey of entire administrative block in the first phase. Incident cases were contacted by health assistants by collaborating with key informants from the villages. Diagnosis of schizophrenia was established by clinical interview and Mini International Neuropsychiatric Interview (MINI) by an experienced psychiatrist (Sheehan et al., 1998).

All patients with diagnosis of schizophrenia established by expert clinician and confirmed by MINI were eligible to participate in the study. There were 236 diagnosed patients in the program at the time of intake for the study. 40 patients refused to consent for blood sampling, 39 patients were not visiting the clinic and could not be assessed. We could collect complete data for the remaining 157 patients after obtaining informed consent.

Population control sample was collected across the administrative block divided across 11 primary health centers (PHC). The villages were stratified on the population size and two random villages from each stratum in each PHC area was identified. Based on baseline prevalence and accounting for 25% non-response rate total sample size required was estimated to be 540. Controls were identified as per the electoral census out of which 40 were not located and 50 were not found at the initial contact, 55 refused for the study and 70 agreed initially and later refused to take part in the study, totalling of refusal rate of 25%. Of the 325 controls enrolled for the study 263 consented to give blood sample and undergo anthropometric assessments. Once the control participant reached the study centre, they were administered MINI screening (by the staff of the research team) to rule out psychiatric disorders.

2.2. Assessments

Physical parameters of height, weight, waist circumference, hip circumference, blood pressure were measured in accordance to recommendations in IDF consensus (The IDF consensus, 2006). Biochemical parameters of fasting blood sugar, lipid profile including triglycerides were assessed by standardized procedures in a single laboratory with prescribed quality controls. History of lifetime and current substance use was obtained for both the groups.

Patients were additionally interviewed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Clinical details of duration, course of illness and treatment details were collected using a checklist. Indian Disability Evaluation Assessment Scale (IDEAS) (Rehabilitation Committee of Indian Psychiatric Society, 2002) was used to quantify the level of disability in four domains of functioning. Evidence suggests that patients with schizophrenia engage in significantly less moderate and vigorous physical activity compared to controls (Stubbs et al., 2016). As exercise levels and calorie intake can have direct implication on metabolic status they were measured as covariates. Daily exercise pattern was measured Physical Activity Questionnaire standardized to our population (Bharathi et al., 2000). This questionnaire measures the number of hours spent in a day at work, hours spent standing, sitting walking and at sleep. It also accounts for hours spent in rigorous physical activity. Daily calorie intake was approximated using daily food intake records and measuring total calories consumed by cereals, pulses, vegetables, meat and other foods as per the guidelines by National Institute of Nutrition, Hyderabad, India.

Diagnosis of MetS was established using International Diabetic Federation consensus criteria with ethnicity specific waist circumference cut-offs for South Asian population defined as waist circumference greater than or equal to 90 cm for men and 80 cm for women (The IDF consensus, 2006).

2.3. Statistical analysis

The individual components for the diagnosis of MetS, *viz.*, waist circumference, blood pressure, fasting blood sugar, HDL cholesterol and triglycerides were compared between cases and controls as dichotomous variables as normal or deranged using Chi square test. This approach was adopted in view of sex specific values for two of the five criteria namely HDL cholesterol and waist circumference. Point prevalence of MetS was determined for each group and compared using Chi square test.

The patient group was divided as subgroups with and without MetS. Demographic, clinical and physical activity parameters were compared between these groups using *t*-test and chi square test for continuous and categorical variables respectively. The variables which significantly differed between these two subgroups and those implicated to influence MetS in previous research, namely, age, gender, calorie intake, duration of illness, physical activity levels, antipsychotic exposure, PANSS and IDEAS scores were used as predictor variables with forced entry in a binary logistic regression model, with presence/absence of metabolic syndrome as the outcome variable.

Please cite this article as: Rawat, V.S., et al., Prevalence and predictors of metabolic syndrome in patients with schizophrenia and healthy controls: A study in rural South Indian..., Schizophr. Res. (2017), http://dx.doi.org/10.1016/j.schres.2017.04.039