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ORIGINAL ARTICLE

Prevalence of Metabolic Syndrome among Bahraini Patients with Schizophrenia

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Abstract

Background and objectives: Metabolic syndrome comprise of a few cardiovascular risk factors that increase morbidity and mortality. To evaluate the prevalence of metabolic syndrome among Bahraini schizophrenia patients.

Methods: Using a case-control design, 50 patients with schizophrenia (cases) were compared to 50 age- and sex-matched healthy controls for the prevalence of metabolic syndrome. The workout included: anthropometric measurements, such as weight, height, and waist and hip circumferences, fasting blood glucose, lipid profile, blood pressure, and past medical history. Descriptive statistics such as mean and standard deviations for continuous variables and frequency counts and proportions for categorical variables were used to summarize the demographic characteristics and the different variables of the metabolic syndrome. Odds ratio (OR) was computed to measure the levels of association between exposure (schizophrenia) and outcomes (metabolic syndrome).

Results: Based on the International Diabetes Federation criteria, 48% cases had metabolic syndrome in comparison to 34% controls. A statistical difference was observed among the cases and controls with respect to three metabolic abnormalities i.e., central obesity (OR, 4.5; 95% confidence interval (CI), 1.6–13.1), raised triglyceride level (OR, 2.5; 95% CI, 0.9–7.3), and reduced level of high-density lipoprotein cholesterol (OR, 0.4; 95% CI, 0.2–1.1).

Conclusion: The prevalence of metabolic syndrome is extremely high among the Bahraini patients with schizophrenia. Clinicians are encouraged to monitor the physical health and physical components in patients with schizophrenia to detect metabolic syndrome and reverse it. Further, studies need to merit racial variability in metabolic syndrome among patients with schizophrenia due to the difference in the predisposing factors.

Keywords: Syndrome X; schizophrenia; metabolic syndrome; insulin resistance syndrome

Introduction

The rates of premature mortality in patients with schizophrenia have reached an alarming level.[1, 2] Standardized mortality rate (SMR) reveals that schizophrenic patients are approximately four times more likely to have premature deaths.[3] The magnitude of shortened life expectancy among patients with schizophrenia has reached to 20 years. Two-thirds of these deaths are due to physical health comorbidities, particularly cardiovascular disease.[4]

Metabolic syndrome is defined by a constellation of variables, including central obesity, high blood pressure, low levels of high-density lipoprotein (HDL) cholesterol, elevated triglycerides levels, and raised plasma glucose levels.[5]

Many published studies have reported the prevalence of metabolic syndrome among patients with schizophrenia. A recent meta-analysis and a systematic review show that at least 77 previous studies were dedicated to the topic.[1] The meta-analysis concluded that the overall rate of metabolic syndrome in patients with schizophrenia was 32.5% and that studies were extremely scarce.[1] There is a dearth of research to review the prevalence of metabolic syndrome among patients with schizophrenia in Bahrain and the neighboring Gulf Cooperation Council countries. In the absence of local research studies, the use of pooled data from meta-analyses is less feasible to plan and conduct clinical interventions to reduce the impact of metabolic syndrome in this vulnerable population.

Thus, investigating the prevalence of metabolic syndrome in specific contexts are essential to reduce physical health comorbidities and associated premature deaths. Recent clinical studies indicated that metabolic syndrome is associated with cognitive and functional impairments.[6, 7] Furthermore, metabolic syndrome also has a sizable effect on quality of life[8] and treatment compliance.[9] Predisposing risk factors of metabolic syndrome in patients with schizophrenia include long-term use of antipsychotic medications, poor diet, and low levels of physical activity.[1, 2] Recent research in the general population on metabolic syndrome has concluded the necessity to develop ethnic-/race-specific criteria for the syndrome.[10]

The research hypothesis is that there is a higher prevalence of metabolic syndrome among patients with schizophrenia in Bahrain as compared to healthy controls. Accordingly, the current epidemiological case-control study was designed to evaluate the prevalence of metabolic syndrome among the Bahraini patients with schizophrenia using the International Diabetes Federation (IDF) criteria.[10]

Materials & methods

Research design

The research was planned and executed using the best practice guidelines of the STrengthening the Reporting of OBservational studies in Epidemiology: STROBE statement.[11] In this case-control design, data were collected between June 2016 and June 2017. Enrolment stopped during the holy month of Ramadan to avoid any confounding effect of intermittent fasting on metabolic syndrome. The study was reviewed and approved by the Secondary Health Research Ethics Committee, Ministry of Health, Kingdom of Bahrain. A written informed consent was obtained from the participants before commencing data collection. Participation was voluntary; no incentives were offered for participation in the study.

Participants and sample size

Enrollment of patients with schizophrenia was conducted in the Outpatient department (OPD) at the Psychiatric Hospital, Ministry of Health in Bahrain. The psychiatric hospital is considered the national center for diagnosis and treatment of patients with severe and persistent psychiatric illness.

Cases

Patients with schizophrenia included in the study were termed as 'cases'. The inclusion criteria were patients aged 20–60 years, diagnosed as schizophrenia of any type according to the diagnostic criteria of the International Classification of Disease 10th Revision (ICD-10),[12] attending the OPD of the Psychiatric Hospital, being treated with the same antipsychotic medication for the past 12 months, and those willing to participate in the research. Pregnant or lactating women, patients with dual psychiatric diagnosis, and those enrolled in lifestyle interventions or randomized controlled trials were excluded from the study.

Controls

Healthy individuals from the general population were termed as 'controls', and the sex- and age-matched healthy individuals with three years variance comprised of the control group. Pregnant or lactating women and individuals with a positive history of psychiatric illness were excluded from the study.

Sample size

The sample size was determined by using the data of National Non-Communicable Diseases Survey, Bahrain.[13] Metabolic syndrome is diagnosed with abdominal obesity and the presence of two or more clinical features (i.e., elevated triglycerides,

low HDL cholesterol, high blood pressure, and increased plasma glucose). Abdominal obesity was selected for sample size calculation due to its critical importance in defining metabolic syndrome.[14, 15] To estimate the prevalence of metabolic syndrome with scientific precision, the prevalence rate of abdominal obesity was hypothesized to be 30%. During sample size calculation, the statistical power was set to 80%, beta 20%, and 5% two-sided significance alpha levels. Sample size calculation for the case-control design suggested a minimum of 45 subjects per group for viable analysis. Hence, 50 cases of schizophrenia and 50 sex- and age-matched healthy controls were included in the study.

Assessments and data collection

Trained research assistants collected data from the participants, which included anthropometric measurements, blood pressure, and biochemical analysis.

Anthropometric measurements

Anthropometric measurements included weight, height, waist circumference (WC) and hip circumference (HC). Weight was measured using digital scales with height rod attachment that was kept on a hard, horizontal floor. Participants were in light clothing, stood upright without shoes, and weight was recorded to the nearest 0.1 kg. Height was measured with the rod attached to the weighing scale to the nearest 1 cm. Body mass index (BMI) was calculated using weight-to-height ratio and categorized into underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2). WC and HC were measured using a standard tape meter on a hard, horizontal floor and were recorded to the nearest 0.1 cm. Anthropometric measurements for all participants were taken by the same data collector to avoid errors. Abdominal obesity was defined in this research according to the IDF criteria of WC≥94 cm for men and ≥80 cm for women taking into consideration that the European values are recommended for Eastern Mediterranean, Middle East, and Arab populations until more specific data are available.[15]

Blood pressure

After the participant rested for 10 min, blood pressure was measured using a clinically validated digital sphygmomanometer in a sitting position. Measurements were taken twice, and arithmetic mean was computed accordingly for data analysis (Hypertension: elevated systolic blood pressure ≥130 mm Hg or elevated diastolic blood pressure ≥85 mm Hg, or treatment of previously diagnosed hypertension).[15]

Fasting blood glucose

Fasting blood was collected from the participants after 12h of overnight fast. Blood collection and blood biochemical analysis were done in an independent laboratory of the department of Pathology at the Salmaniya Medical Complex, Ministry of Health, Kingdom of Bahrain (Type 2 diabetes mellitus: fasting blood glucose ≥5.6 mmol/L, or previously diagnosed type 2 diabetes mellitus).[15]

Lipids

Medical information about the participant's prescriptions for metabolic abnormalities or their treatments were collected from the electronic health record, Bahrain. We focused on the treatment of previously diagnosed hypertension and raised triglyceride [≥1.7 mmol/L or specific treatment for this lipid abnormality]/reduced HDL cholesterol levels (<1.03 mmol/L in men and <1.29 mmol/L in women, or specific treatment for this lipid abnormality), and previously diagnosed as type 2 diabetes mellitus).[15]

Based on the IDF criteria metabolic syndrome was defined as central obesity plus any two of the metabolic abnormalities, including raised triglycerides level, reduced HDL cholesterol, raised blood pressure, and raised fasting plasma glucose.

Statistical analysis

Descriptive statistics were used to summarize the demographic characteristics and the different components of the metabolic syndrome. The arithmetic means and standard deviations (SD) were reported for continuous variables, whereas counts and percentages were reported for categorical variables. The 95% CI was reported for points estimate of a population parameter. The focus of the analysis was case-control, and OR was computed to measure the levels of association between binary exposure (schizophrenia) and binary outcome variables (metabolic syndrome).

Pearson chi square test or Fisher's exact test and independent sample t test were used to analyze the

differences between the two groups. Significance was set at 5% level; all statistical analyses were performed using Stata 13.1 software.

Results

A total of 50 cases and 50 age- and sex-matched controls were recruited in the study. Descriptive statistics of the study participants are shown in Table 1. Significant difference was observed among the cases and controls with respect to the following variables: body weight, BMI, HDL, WC, HC, and waist to hip ratio. All the cases with schizophrenia were regularly attending the OPD clinics with a median of one visit per month. At the time of the study, all cases were on second-generation antipsychotic treatment.

Based on odds ratio, central obesity appeared to be the major metabolic abnormality as shown in Table 2. Cases showed higher body weight than controls with an average difference of 8.0 kg. It was observed that the frequency of males and females in both the groups was similar with respect to overweight (cases, 31.4% vs. controls, 25%) and obesity (cases, 45.7% vs. controls, 50%).

Table 1: Demographic characteristics of the case and control groups

Variable	Cases (mean±SD)	Controls (mean±SD)	*P* value
Gender (male)	35 (70%)	35 (70%)	1.0
Age (years)	41.3±10.7	38.9±10.9	0.273
Body weight (kg)	83.6±21.7	75.1±18.8	0.039*
Height (cm)	165.4±10.0	166.3±8.7	0.666
BMI	30.4±6.6	27.1±6.3	0.012*
Systolic BP (mm Hg)	131.9±16.0	129.1±18.6	0.422
Diastolic BP (mm Hg)	76.7±10.3	78.7±11.3	0.354
HDL (mmol/L)	1.1±0.2	1.3±0.4	0.002*
LDL (mmol/L)	2.9±0.8	2.8±0.7	0.436
Triglyceride (mmol/L)	1.8±1.4	1.5±1.1	0.206
Cholesterol (mmol/L)	5.8±7.9	5.7±6.9	0.943
Fasting blood sugar (mmol/L)	5.2±1.1	5.4±1.2	0.398
Waist circumference (cm)	103.8±14.1	91.6±15.3	0.001*
Hip circumference (cm)	108.1±13.3	100.9±13.4	0.008*
Waist hip ratio	1.0±0.1	0.9±0.1	0.003*

**Significant, P < 0.05*; *BMI*, Body mass index; *BP*, Blood Pressure; *HDL*, High-density lipoprotein; *LDL*, Low-density lipoprotein; *SD*, Standard deviation

Table 2: Prevalence of metabolic syndrome in the case and control groups

Variable	Cases, n (%)	Controls, n (%)	OR (95% CI)	*P* value
Central obesity	42 (84)	24 (54)	4.5 (1.6–13.1)	0.001*
Raised triglyceride level	18 (36)	9 (18)	2.5 (0.9–7.3)	0.04*
Reduced HDL cholesterol	24 (48)	34 (68)	0.4 (0.2–1.1)	0.04*
Raised blood pressure	30 (60)	28 (56)	1.2 (0.5–2.8)	0.7
Raised fasting plasma glucose	16 (32)	15 (30)	1.1 (0.5–2.8)	0.8
Metabolic syndrome	24 (48)	17 (34)	1.8 (0.7–4.4)	0.1

**Significant, P < 0.05; HDL*, High-density lipoprotein; *OR*, Odds ratio; *CI*, Confidence interval

Table 3: Gender difference in the prevalence of metabolic syndrome among cases

Variable	Males, n (%)	Females, n (%)	*P* value
Central obesity	28 (80)	14 (93.3)	0.23
Raised triglyceride level	15 (42.9)	3 (20)	0.12
Reduced HDL cholesterol	20 (57.1)	4 (26.7)	0.04*
Raised blood pressure	24 (68.6)	6 (40)	0.06
Raised fasting plasma glucose	15 (42.9)	1 (6.7)	0.01*
Metabolic syndrome	20 (57.1)	4 (26.7)	0.048*

**Significant, P < 0.05*; *HDL*, High-density lipoprotein

According to the IDF criteria, 84% of the cases with schizophrenia had central obesity when compared to 54% of the controls. The prevalence rates of metabolic syndrome were 48% and 34% in cases and controls, respectively.

Table 3 shows the differences in the prevalence rates of metabolic abnormalities and metabolic syndrome between males and females. Prevalence of metabolic syndrome was higher in males when compared to females in the case group (57.1% vs. 26.7%, $P=0.048$). Females (93.3%) with schizophrenia had higher prevalence of central obesity as compared to males (93.3% vs. 80%, $P=0.23$). However, males showed a higher prevalence of raised triglyceride level ($P=0.12$), reduced HDL cholesterol ($P=0.04$), raised blood pressure ($P=0.06$), and raised fasting plasma glucose ($P=0.01$) when compared to females, which contributed to increased rates of metabolic syndrome.

Discussion

The focus of this study is to examine the prevalence of metabolic syndrome among the Bahraini patients with schizophrenia in the outpatient settings. The expected results were an overall prevalence rate of 33% for metabolic syndrome; this was projected based on the pooled results from recent meta-analysis.[1] The prevalence rates of the specific metabolic abnormalities, including central obesity (45%), raised blood pressure (40%), raised fasting plasma glucose (20%), raised triglyceride levels (40%), and reduced HDL cholesterol levels (40%) were also expected.[1]

The prevalence of four out of five IDF diagnostic criteria for metabolic syndrome including central obesity, raised fasting plasma glucose, raised blood pressure, and reduced HDL cholesterol levels was higher in the Bahraini cases as compared to the previous studies.[1]

According to the IDF diagnostic criteria, prevalence rate of central obesity was extremely high in the Bahraini cases with schizophrenia. This translates to central obesity having a 50% higher magnitude compared to ranges of previously reported studies.[1] In addition, the prevalence of raised fasting plasma glucose was 32% in the Bahraini cases with schizophrenia, which is 10–15% higher as compared to the range of previously reported studies.[1] One possible explanation for the increased prevalence of raised fasting plasma glucose in the Bahraini cases with schizophrenia compared to earlier reports is the low screening and treatment of diabetes. Historically, patients with psychiatric illnesses have low rates of screening and treatment for metabolic conditions such as diabetes.[16]

The prevalence of raised blood pressure was 60% in the Bahraini cases with schizophrenia, which is approximately 20% higher than the pooled rate of previous studies.[1] A higher prevalence rate (48%) of reduced HDL cholesterol level was observed in the present study, which is approximately 10% higher than ranges of the previous studies.[1] Results from the current investigation for the remaining diagnostic criterion (raised triglyceride level) showed that the Bahraini cases with schizophrenia fall in the range of the previous studies.[1] Studies reporting the prevalence of metabolic syndrome in Arabic cases with schizophrenia are scarce. A cross-sectional design conducted in 63 cases in Egypt revealed 38% prevalence of metabolic syndrome, according to the IDF diagnostic criteria.[17]

A multicentric research in the Kingdom of Saudi Arabia including 992 cases with various psychiatric

illnesses concluded a 41.2% prevalence of metabolic syndrome, according to the IDF diagnostic criteria.[18] Prevalence of specific metabolic abnormalities was evaluated in the Saudi sample, including central obesity (42.2%), raised blood pressure (42.5%), raised fasting blood glucose (47.8%), and low HDL cholesterol levels (52.5%).[18] A Palestinian study focused on 250 cases with schizophrenia and determined a 43.6% prevalence rate of metabolic syndrome.[19] It is therefore evident that there is a notable variation in the research methodology such as sample size and sampling techniques, as well as the difference in the diagnostic criteria used among published research; the finding from the current research consistently shows higher rates in comparison with the international and regional literature.

The high prevalence of metabolic syndrome among the Bahraini cases with schizophrenia has several clinical implications. First, there is an urgent need to develop clinical interventions including diet and physical activity to reverse and control metabolic abnormalities among cases with schizophrenia. Second, to establish a system for continuous monitoring and surveillance of metabolic abnormalities among cases with schizophrenia. These implications require collaboration between the mental health institutions and other physicians, particularly family physicians. Third, to increase the awareness about metabolic syndromes and encourage mental health staff to acknowledge the physical health of patients with schizophrenia and related disorders. Future research needs to focus on investigating the causes of metabolic syndrome to prevent them.

The current study is not epidemiologically powered to examine the association between metabolic syndrome and other factors such as the use of antipsychotics, physical activity, diet, and further on. Nonetheless, all the cases with schizophrenia enrolled in the study were on second-generation antipsychotics. More than 300 randomized controlled trials have concluded that given the lifelong exposure to antipsychotic medication, fundamentally all antipsychotic medications are associated with central obesity.[20] However, antipsychotic medications are essential in the management of schizophrenia and their benefits are more pronounced than the risk associated with their use.

The main strength of the current research is contributing to the data on metabolic syndrome in cases with schizophrenia from Bahrain, where rates of obesity and type 2 diabetes mellitus[21] are generally high compared to Western and North American countries.[13]

The study has two main limitations. First, the study enrolled cases with schizophrenia attending the outpatient clinics, and therefore, assumed to be in the stable state. The results are not generalizable to the inpatient cases or noncompliant cases, who do not attend their follow-up visits. Second, risk factors for the development of metabolic syndrome are not assessed due to the small sample size and nature of research design—case-control study. Future research is encouraged to adopt prospective research design to follow large cohorts of cases with schizophrenia, in order to assess the relative risk associated with metabolic syndrome.

Conclusion

The present research reveals that the prevalence of metabolic syndrome is extremely high in the Bahraini cases with schizophrenia. Prevalence rates vary across research methodologies and diagnostic criteria for metabolic syndrome. The research suggests that the IDF criteria are most comprehensive and inclusive for diagnosing cases with this syndrome. Clinicians are encouraged to monitor the physical health and physical components in cases with schizophrenia to detect metabolic syndrome and reverse it. Future studies also need to merit racial variability in metabolic syndrome among cases with schizophrenia due to the difference in predisposing factors to metabolic syndrome.

Conflicts of interest

The authors of the study have no conflict of interest to declare.

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