Metabolic syndrome and cardiovascular risk among patients with schizophrenia receiving antipsychotics in Malaysia

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INTRODUCTION This study aimed to determine the prevalence of metabolic syndrome and risk of coronary heart disease (CHD) in patients with schizophrenia receiving antipsychotics in Malaysia.

METHODS This cross-sectional study, conducted at multiple centres, involved 270 patients who fulfilled the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR diagnostic criteria for schizophrenia, were on antipsychotic medications for at least one year, and were screened for metabolic syndrome. Patients receiving mood stabilisers were excluded. Metabolic syndrome was defined according to the National Cholesterol Education Program ATP III criteria modified for Asian waist circumference. Risk for cardiovascular disease was assessed by using Framingham function (all ten-year CHD events).

RESULTS The prevalence of metabolic syndrome was 46.7% (126/270). Among all the antipsychotics used, atypical antipsychotics (monotherapy) were most commonly used in both the metabolic and non-metabolic syndrome groups (50.8% vs. 58.3%). The ten-year risk for CHD was significantly higher in patients with metabolic syndrome. The proportion of patients with high/very high risk for CHD (Framingham ≥ 10%) was greater in patients with metabolic syndrome than in those with non-metabolic syndrome (31.5% vs. 11.0%, odds ratio 3.9, 95% confidence interval 2.0–7.6; $p < 0.001$). The mean body mass index was higher in patients with metabolic syndrome than in those without (29.4 ± 5.1 kg/m^2 vs. 25.0 ± 5.6 kg/m^2; $p < 0.001$).

CONCLUSION Patients with schizophrenia receiving antipsychotics in Malaysia have a very high incidence of metabolic syndrome and increased cardiovascular risk. Urgent interventions are needed to combat these problems in patients.

Keywords: body mass index, cardiovascular risk, metabolic syndrome, prevalence, schizophrenia
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INTRODUCTION

Metabolic syndrome comprises a spectrum of medical disorders associated with an increased risk of developing type 2 diabetes mellitus and cardiovascular disease (CVD).[1] Metabolic syndrome affects a great number of people and it is estimated that approximately 20%–25% of the world's adult population suffers from it.[2] The reported prevalence of metabolic syndrome in Asians is lower (5%–16%).[3-5] However, the incidence of metabolic syndrome in Malaysia is much higher compared to other Asian countries.[6] According to the World Health Organization, National Cholesterol Education Program (NCEP) ATP III, International Diabetes Federation and Harmonized metabolic syndrome definitions, the overall crude prevalences of metabolic syndrome in Malaysia are 32.1%, 34.3%, 37.1% and 42.5%, respectively.[6] Metabolic syndrome not only entails serious health complications but also places individuals at a greater risk of other serious medical conditions such as CVD.[7]

The pathophysiology of metabolic syndrome is extremely complex and is not fully understood. Insulin resistance and central obesity are considered to be important underlying causes of metabolic syndrome.[8,9] Some individuals may be at greater risk of developing metabolic syndrome due to medications that cause weight gain or changes in blood pressure, cholesterol and blood sugar levels.[10] Atypical antipsychotics have been reported to be associated with the increased risks of hyperglycaemia and impaired glucose levels, and consequently, an increased risk of developing metabolic syndrome.[11] It has also been shown that psychiatric disorders, including schizophrenia, are associated with an elevated risk of developing diabetes mellitus regardless of antipsychotic use.[12] Patients with schizophrenia are at a greater risk for metabolic dysfunctions than other individuals due to a number of reasons, including an inactive lifestyle, poor dietary choices as well as the side effects of antipsychotic medications.[13]

Cohn et al used the NCEP ATP III criteria to assess metabolic syndrome in 240 patients with schizophrenia or schizoaffective

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disorder, and reported a gender-based prevalence of 42.6% in men and 48.5% in women.[14] They also reported comparable incidence among patients under (43.8%) and over (45.8%) 45 years of age. Using the same definition of metabolic syndrome, studies have described the prevalence of metabolic syndrome in inpatients with schizophrenia to range between 27%–29%[15,16] and in outpatients to be between 25%–35%.[17,18]

In Southeast Asia, especially in Malaysia, there is a paucity of data on the prevalence of metabolic syndrome and cardiovascular risk among patients with schizophrenia. A local study on 51 patients with primary psychotic and mood disorders by Rahman et al found the prevalence of metabolic syndrome to be 37.2% in these patients.[19] In the present study, we aimed to determine the prevalence of metabolic syndrome in patients with schizophrenia receiving antipsychotics in Malaysia as well as the risk of coronary heart disease (CHD) in these patients.

METHODS

The study was conducted at four mental institutions (Hospital Bahagia Ulu Kinta, Perak; Hospital Permai Johor Bahru, Johor; Hospital Sentosa Kuching, Sarawak; Hospital Mesra Kota Kinabalu, Sabah), two army hospitals (Terendak Army Hospital, Melaka; Navy Hospital Lumut, Perak) and two general hospitals (University Malaya Medical Centre [UMMC], Kuala Lumpur; Hospital Sg Petani, Kedah) from June 2008 to September 2011.

The study population comprised patients with schizophrenia between 18–65 years of age who fulfilled the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR diagnostic criteria for schizophrenia. The patients must have received antipsychotic treatment for at least one year. Patients receiving mood stabilisers were excluded from the study, as it could have confounded the parameters of weight gain and metabolic syndrome.[20,21] One patient on lithium and three others on sodium valproate were excluded. Out of 527 patients who were screened during the study period, 485 patients fulfilled the DSM-IV-TR criteria for schizophrenia. 325 patients with schizophrenia agreed to be interviewed and underwent part assessment for metabolic syndrome parameters. However, only 270 patients gave final consent for fasting blood investigations and full metabolic syndrome profile. All participants were outpatients. There was no difference between the group of patients who consented to participation and those who did not, in terms of sociodemographics or diagnosis.

The prevalence of metabolic syndrome was estimated using the NCEP criteria (the 2001 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) modified for the Asian waist circumference[22] based on the presence of three or more of the following components – abdominal obesity (waist circumference: men ≥ 90 cm; women ≥ 80 cm), hypertriglyceridaemia (fasting triglyceride concentration > 150 mg/dL), dyslipidaemia (fasting high-density lipoprotein [HDL] cholesterol: men < 40 mg/dL; women < 50 mg/dL), hypertension (systolic/diastolic blood pressure, > 130/85 mmHg) and hyperglycaemia (fasting glucose concentration > 100 mg/dL).

Waist circumference was measured at the midpoint between the lower rib margin (12th rib) and the iliac crest. Participants were asked to stand with feet together and arms in a relaxed position at either side during measurement. A tape was then held in a horizontal position and wrapped around the waist, loose enough for the recorder to place one finger between the tape and the participant's body. Patients were asked to breathe normally and measurements were taken to the nearest 0.1 cm at the end of a normal exhalation. It was ascertained that participants did not contract the abdominal muscles during measurements.

Blood pressure was measured using a digital sphygmomanometer (Omron Digital Automatic Blood Pressure Monitor Model HEM-907, Omron Healthcare Co Ltd, Kyoto, Japan) on both the right and left arms following a rest of five minutes in a seated position, with the arm supported at heart level. Each arm was measured twice and measurements from the arm with the highest readings were used to calculate the average systolic and diastolic blood pressures. To minimise variability in anthropometric measurements between recorders and study centres, the main investigators from each institution attended an investigators meeting, held prior to the start of the study. Procedures were standardised and appropriate training was provided as part of the meeting. Training for the remaining members of the research team was subsequently carried out by the main investigators at their respective institutions. All anthropometric measurements for the duration of the study were carried out by these trained team members.

The Framingham[23] function was used to estimate the overall risk of fatal or nonfatal CHD (including any type of angina, myocardial infarction, other types of coronary ischaemia, congestive heart failure, intermittent claudication or peripheral arterial ischaemia) over ten years. The Framingham function is a mathematical probability model obtained using multivariate analysis from follow-up studies of individuals in the general population, in which the incidence of a fatal or nonfatal CHD event is related to the individual risk factors of each participant. Risk of CHD was calculated from the values meant for age, gender, total cholesterol, HDL cholesterol, blood pressure, diabetes mellitus status and smoking status. Patients were classified according to the probability of presenting a high/very high risk for fatal or nonfatal CHD (Framingham ≥ 10%) within ten years.

Sociodemographic and clinical data were recorded for all participants in addition to detailed information on lifestyle, smoking and occupational status. Patients were classified into two groups – metabolic syndrome and non-metabolic syndrome – according to the criteria mentioned above. The mean, standard deviation, median and interquartile range were calculated for continuous variables, and the frequency and percentage of patients were used to estimate the prevalence of cardiovascular risk factors and the components of metabolic syndrome. Individual

Table I. Characteristics of patients with schizophrenia (n = 270).

Characteristic	No. of patients (%)		p-value*
	Metabolic disease (n = 126)	Non-metabolic disease (n = 144)	
Mean age ± SD (yrs)	40.5 ± 11.3	39.5 ± 11.8	0.472§
Age group (yrs)			
< 20†	2 (1.6)	2 (1.4)	0.500
20–29	18 (14.3)	34 (23.6)	
30–39	44 (34.9)	40 (27.8)	
40–49	29 (23.0)	32 (22.2)	
50–59	26 (20.6)	27 (18.8)	
≥ 60	7 (5.6)	9 (6.2)	
Mean BMI ± SD (kg/m²)	29.4 ± 5.1	25.0 ± 5.6	< 0.001§,¶
BMI group (kg/m²)			
Underweight‡ (< 18.5)	0 (0)	14 (9.7)	
Normal weight† (18.5–24.9)	25 (19.8)	70 (48.6)	< 0.001¶
Overweight (25–29.9)	50 (39.7)	35 (24.3)	
Obese (≥ 30)	51 (40.5)	25 (17.4)	
Gender			
Male†	74 (58.7)	100 (69.4)	0.747
Female	52 (41.3)	44 (30.6)	
Occupation			
Employed†	33 (26.1)	55 (38.2)	0.003¶
Unemployed	83 (65.9)	67 (46.5)	
Housewife	6 (4.8)	5 (3.5)	
Not specified	4 (3.2)	17 (11.8)	

*Chi-square test. †Reference group.‡Patients who were underweight (BMI < 18.5 kg/m²) were excluded, and only the data of those categorised as normal, overweight and obese were used for chi-square analysis. §*t*-test. ¶p < 0.05 was statistically significant.
BMI: body mass index; SD: standard deviation

prevalence of cardiovascular risk factors and the prevalence of metabolic syndrome components were estimated by calculating the corresponding 95% confidence intervals. Framingham risk scores in the metabolic syndrome and non-metabolic syndrome patient groups were compared using parametric (Student's *t*-test) or nonparametric (Mann-Whitney U test) tests, according to the distribution of variables. The risk score of patients were further classified as low (Framingham < 10%) or high/very high (Framingham ≥ 10%) ten-year risk of CHD. The categorical risk scores were compared using chi-square test. A p-value < 0.05 was considered statistically significant.

The least squares mean of Framingham risk scores were also compared according to patient age groups with and without metabolic syndrome. The multiple comparisons were analysed using two-way interaction in three-way analysis of variance (ANOVA), with Bonferroni correction and adjustment for gender. Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 16.0 (SPSS Inc, Chicago, IL, USA). Ethics approval for the study was obtained in advance from the Medical Research and Ethics Committee, Ministry of Health Malaysia, and University Malaya Medical Centre Ethics Committee.

RESULTS

The prevalence of metabolic syndrome in patients with schizophrenia was 46.7% (126/270). The mean body mass index (BMI) showed a statistically significant difference between patients with metabolic syndrome and non-metabolic syndrome. The mean BMI for metabolic syndrome patients was higher than that for the non-metabolic syndrome group (29.4 ± 5.1 kg/m² vs. 25.0 ± 5.6 kg/m²). A majority of patients with metabolic syndrome were overweight (39.7% vs. 24.3%) and obese (40.5% vs. 17.4%) compared to those in the non-metabolic group (Table I).

Table II presents the antipsychotics and other concomitant medications that were given to patients during the study. Among all antipsychotics used, atypical antipsychotics (monotherapy) were used the most in both metabolic syndrome and non-metabolic syndrome group patients (50.8% vs. 58.3%), followed by typical antipsychotics (monotherapy), also in both patient groups (21.4% vs. 20.8%). Among patients receiving typical antipsychotics (monotherapy) treatment, chlorpromazine (33.3%) was given the most to patients in the metabolic syndrome group, followed by sulpiride and perphenazine (18.5% each). Among patients receiving atypical antipsychotics (monotherapy) treatment, olanzapine (42.2%) was given most frequently to patients in the metabolic syndrome group followed by risperidone (32.8%). None of the patients on amisulpride had metabolic syndrome (Table II).

Table III shows statistically significant differences for all metabolic syndrome components, except low-density lipoprotein (LDL) cholesterol, between patients in the metabolic syndrome and non-metabolic syndrome groups. The median values of fasting blood glucose, triglycerides and glycated haemoglobin were also significantly different between patients in the metabolic syndrome and non-metabolic syndrome groups (Mann-Whitney U test). Among all the metabolic syndrome components, abnormal waist circumference was the commonest among patients in the metabolic syndrome and non-metabolic syndrome

Table II. Treatment with antipsychotics and other medications in patients with schizophrenia.

Treatment	Patients No. (%)		p-value*
	Metabolic disease (n = 126)	Non-metabolic disease (n = 144)	
Current antipsychotics			
Atypical antipsychotics (monotherapy)†	64 (50.8)	84 (58.3)	0.339
Typical antipsychotics (monotherapy)	27 (21.4)	30 (20.8)	
Combination of typical and atypical antipsychotics	15 (11.9)	11 (7.7)	
Combination of typical antipsychotics	14 (11.1)	9 (6.2)	
Combination of atypical antipsychotics	6 (4.8)	10 (7.0)	
Typical antipsychotics (monotherapy)			
Chlorpromazine	9 (33.3)	10 (33.3)	
Sulpiride	5 (18.5)	6 (20.0)	
Perphenazine	5 (18.5)	5 (16.7)	
Haloperidol†	3 (11.2)	5 (16.7)	0.960
Stelazine	2 (7.4)	1 (3.3)	
Intramuscular fluanxol	2 (7.4)	1 (3.3)	
Intramuscular modecate	1 (3.7)	2 (6.7)	
Atypical antipsychotics (monotherapy)			
Olanzapine†	27 (42.2)	26 (31.0)	0.390
Risperidone	21 (32.8)	29 (34.5)	
Paliperidone	11 (17.2)	16 (19.0)	
Clozapine	2 (3.1)	1 (1.2)	
Quetiapine	1 (1.6)	2 (2.4)	
Aripiprazole	2 (3.1)	6 (7.1)	
Amisulpride	0 (0)	4 (4.8)	
Concomitant medication			
Anticholinergics	41 (32.5)	44 (30.6)	0.726
Benzodiazepine	25 (19.8)	22 (15.3)	0.324
Antidepressants	16 (12.7)	19 (13.2)	0.904
Other medication			
Antidiabetic medication	8 (6.3)	5 (3.5)	0.271
Blood pressure-lowering medication	6 (4.8)	6 (4.2)	0.813
Lipid-lowering medication	6 (4.8)	10 (6.9)	0.449

*Chi-square test. †Reference group.

groups (98.4% vs. 50.7%), followed by HDL cholesterol (72.6% vs. 30.9%); fasting blood glucose was the least common in the two patient groups (51.6% vs. 6.2%) (Table III).

31.5% of patients in the metabolic syndrome group had a high/very high ten-year risk of CHD, while the corresponding figure for patients in the non-metabolic syndrome group was 11.0%. The difference in incidence of high/very high ten-year risk of CHD was statistically significant between the two groups ($p < 0.001$). Also significant was the difference in the median Framingham risk scores of the two patient groups ($p < 0.001$). The mean Framingham risk score for the metabolic syndrome group was 7.6 (i.e, 8/100 people with this level of risk were likely to have a heart attack in the next ten years) while that for the non-metabolic syndrome group was 5.0 (i.e. 5/100 people with this level of risk might have a heart attack in the next ten years) (Table IV).

There was a greater increase in the mean scores of CHD risk for patients of all age groups in the metabolic syndrome group compared to those in the non-metabolic syndrome group. There was a significant difference in the mean score of CHD risk for patients of all age groups except those over 60 years of age (Fig. 1).

DISCUSSION

Our study was aimed at estimating the prevalence of metabolic syndrome in patients with schizophrenia in the local population who were being treated with antipsychotic medications for at least one year. Our results showed that 46.7% of patients fulfilled the criteria for metabolic syndrome, as defined by NCEP ATP III guidelines. This incidence is considerably higher than the reported prevalence of metabolic syndrome in both the general Malaysian (34.3%)[6] and Asian populations (5%–16%).[3-5]

The higher prevalence of metabolic syndrome in patients with schizophrenia has frequently been reported.[14,24] For instance, a study by Cohn et al[14] 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.[24]

The reasons for a higher rate of metabolic syndrome being associated with schizophrenia are many. Certain lifestyles (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.[25,26] 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.[27,28] Some antipsychotics are associated with a high occurrence of the development of metabolic syndrome. These medications may cause weight gain or changes in blood pressure, cholesterol and blood sugar levels.[10]

Table III. Metabolic syndrome components according to metabolic syndrome status in patients with schizophrenia.

Component	Metabolic disease (n = 126)		Non-metabolic disease (n = 144)		Total (n = 270)		p-value*
	No. (%)	95% CI	No. (%)	95% CI	No. (%)	95% CI	
Waist circumference (men ≥ 90 cm; women ≥ 80 cm)	124 (98.4)	94.4–99.6	73 (50.7)	42.6–58.7	197 (73.0)	67.4–77.9	< 0.001‡
HDLC† (men < 40 mg/dL; women < 50 mg/dL)	90 (72.6)	64.1–79.7	42 (30.9)	23.7–39.1	132 (50.8)	44.7–56.8	< 0.001‡
Triglyceride† (≥ 150 mg/dL)	84 (67.7)	59.1–75.3	21 (15.4)	10.3–22.5	105 (40.4)	44.7–56.8	< 0.001‡
BP (≥ 130/85 mmHg)	77 (61.1)	52.4–69.2	36 (25.0)	18.6–32.7	113 (41.9)	36.1–47.8	< 0.001‡
Fasting blood glucose (≥ 100 mg/dL)	65 (51.6)	42.9–60.1	9 (6.2)	3.3–11.5	74 (27.4)	22.4–33.0	< 0.001‡
Laboratory test parameter							
Fasting blood glucose (mg/dL)							
Mean ± SD	110.5 ± 37.9	103.9–117.2	89.2 ± 21.3	85.7–92.7	99.2 ± 31.9	95.3–103.0	
Median (IQR)	100.8 (88.2–113.4)		86.4 (81.0–91.8)		90.0 (82.8–100.8)		< 0.001‡,§
Triglycerides (mg/dL)							
Mean ± SD	214.1 ± 57.0	185.5–242.6	116.9 ± 57.0	107.2–126.6	163.2 ± 127.9	147.6–178.9	
Median (IQR)	171.8 (125.8–245.3)		113.8 (81.5–138.2)		132.9 (97.4–186)		< 0.001‡,§
HbA1c (%)							
Mean ± SD	6.4 ± 1.7	6.1–6.7	5.5 ± 0.7	5.4–5.6	5.9 ± 1.3	5.8–6.1	
Median (IQR)	5.9 (5.6–6.5)		5.4 (5.2–5.8)		5.6 (5.3–6.1)		< 0.001‡,§
Mean TC ± SD (mg/dL)	216.1 ± 46.5	207.8–224.3	202.2 ± 41.3	195.2–209.2	208.8 ± 44.3	203.4–214.2	0.011‡,¶
Mean LDLC ± SD (mg/dL)	136.6 ± 40.4	129.1–144.0	131.1 ± 40.4	124.2–138.0	133.6 ± 40.4	128.6–138.6	0.287¶
HDLC ± SD (mg/dL)							
Men	37.9 ± 6.8	36.3–39.5	46.0 ± 13.0	43.3–48.6	42.5 ± 11.5	40.7–44.2	< 0.001‡,¶
Women	44.5 ± 10.7	41.5–47.5	52.8 ± 13.6	48.5–57.1	48.2 ± 12.7	45.5–50.8	0.001‡,¶
Other parameters							
Mean waist circumference ± SD (cm)							
Men	102.4 ± 9.8	100.1–104.7	87.5 ± 13.8	84.7–90.2	93.9 ± 13.9	91.9–95.8	< 0.001‡,¶
Women	96.7 ± 10.8	93.7–99.7	88.6 ± 13.7	84.4–92.8	91.7 ± 13.1	89.4–94.0	0.002‡,¶
Mean systolic BP ± SD (mmHg)	127.0 ± 16.7	124.0–130.0	117.4 ± 17.4	114.5–120.2	121.6 ± 18.2	119.7–123.6	< 0.001‡,¶
Mean diastolic BP ± SD (mmHg)	83.8 ± 12.7	81.6–86.1	77.1 ± 11.9	75.1–79.1	80.7 ± 13.0	79.3–82.1	< 0.001‡,¶

*Chi-square test. †For triglycerides and HDLC (n = 260). ‡p < 0.05 was statistically significant. §Mann-Whitney U test. ¶t-test.
CI: confidence interval; BP: blood pressure; HbA1c: glycated haemoglobin; IQR: interquartile range; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; LDLC: low-density lipoprotein cholesterol; SD: standard deviation

Table IV. Cardiovascular risk factors and coronary heart disease risk (Framingham) according to metabolic syndrome status in patients with schizophrenia.

Variable	Metabolic disease (n = 126)		Non-metabolic disease (n = 144)		Total (n = 270)		p-value*
	No. (%)	95% CI	No. (%)	95% CI	No. (%)	95% CI	
Cardiovascular risk factors							
Age (men ≥ 40 years; women ≥ 45 years)	58 (46.0)	37.6–54.7	64 (44.4)	36.6–52.6	122 (45.2)	39.4–51.2	0.794
Smoker	29 (23.0)	16.5–31.1	47 (32.6)	25.5–40.7	76 (28.1)	23.1–33.8	0.079
Diabetes mellitus (known diagnosis or glucose ≥ 126 mg/dL)	26 (20.6)	14.5–28.5	6 (4.2)	1.9–8.8	32 (11.9)	8.5–16.3	< 0.001§
TC† (≥ 200 mg/dL)	80 (64.5)	55.8–72.4	68 (50.0)	41.7–58.3	148 (56.9)	50.9–62.8	0.018§
HDLC† (men < 45 mg/dL; women < 50 mg/dL)	99 (79.8)	71.9–86.0	78 (57.4)	49.0–65.4	177 (68.1)	62.2–73.4	< 0.001§
Mean systolic BP‡ ± SD (men ≥ 140 mmHg; women ≥ 130 mmHg)	28 ± 22.2	15.9–30.2	22 ± 15.3	10.3–22.1	50 ± 18.5	14.3–23.6	0.143
Mean diastolic BP‡ ± SD (men ≥ 90 mmHg; women ≥ 80 mmHg)	42 ± 33.3	25.7–42.0	20 ± 13.9	9.2–20.5	62 ± 23.0	18.4–28.3	< 0.001§
Ten-year risk of CHD (Framingham)							
Mean ± SD	7.6 ± 6.4	6.5–8.8	5.0 ± 4.4	4.3–5.8	6.3 ± 5.6	5.6–7.0	
Median (IQR)	6.5 (2.5–11.0)		4.0 (1.0–7.0)		4.0 (1.0–9.0)		< 0.001§,¶
Patients with high/very high (Framingham ≥ 10%) ten-year risk of CHD (Framingham)	39 (31.5)	23.9–40.1	15 (11.0)	6.8–17.4	54 (20.8)	16.3–26.1	< 0.001§

*Chi-square test. †For total and HDLC (n = 260). ‡In patients with diabetes mellitus, cardiovascular disease or kidney disease. §p < 0.05 was statistically significant. ¶Mann-Whitney U test.
CI: confidence interval; BP: blood pressure; CHD: coronary heart disease; IQR: interquartile range; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; SD: standard deviation

Studies have shown that atypical antipsychotics are associated with an increased risk of hyperglycaemia and impaired glucose levels, which consequently increase the risk of metabolic syndrome.[11,29,30] Among the patients in our study who had metabolic syndrome, 42% of them were on olanzapine, 32.8% were on risperidone and 17.2% were on paliperidone.

We found that the presence of metabolic syndrome in schizophrenic patients was associated with CHD 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,[17] 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.[31] Similarly, Holt el al found that 12% of patients in their study with serious mental illness had a > 20% ten-year risk of CHD.[32]

We observed a statistically significant difference in all metabolic syndrome components, except LDL cholesterol, between patients in the metabolic syndrome and non-metabolic syndrome groups. The mean fasting blood sugar level in the metabolic syndrome group was clearly impaired (110.5 mg/dL) although it was normal in the non-metabolic syndrome group (89.2 mg/dL). Men in the non-metabolic syndrome group had normal mean HDL cholesterol levels compared to those in the metabolic syndrome group. Furthermore, the mean triglyceride level in the metabolic syndrome group was nearly double that in the non-metabolic syndrome group (214.1 mg/dL vs. 116.9 mg/dL).

The most common findings in our patients with metabolic syndrome were abnormal waist circumference (98.4%), low HDL cholesterol (72.6%), raised triglycerides (67.7%) and elevated blood pressure (61.1%). Elevated fasting blood glucose was the least frequent abnormality. Our results substantiate those by Kato et al, who found that the most common metabolic syndrome criteria were abnormal waist circumference, dyslipidaemia and elevated blood pressure, while the least prevalent metabolic component was elevated fasting blood glucose.[33]

The mean BMI was significantly higher in patients with metabolic syndrome (29.4 ± 5.1 kg/m^2) in our study than those with non-metabolic syndrome (25.0 ± 5.6 kg/m^2; $p < 0.05$). When patients were categorised according to weight, a significantly higher proportion of overweight (39.7% vs. 24.3%) and obese (40.5% vs. 17.4%) patients were seen in the metabolic syndrome group than in the non-metabolic syndrome group. Our results were similar to that of the CLAMORS study, where general obesity and abdominal adiposity were high in outpatients with schizophrenia who had metabolic syndrome.[17] The study by Bobes et al recorded a two-fold higher rate of obesity in outpatients with metabolic syndrome when compared to those with non-metabolic syndrome (55.2% vs. 22.7%).[17] The high prevalence of obesity and abdominal adiposity among patients with schizophrenia who had metabolic syndrome in our study was also in agreement with the results of the CATIE study.[34]

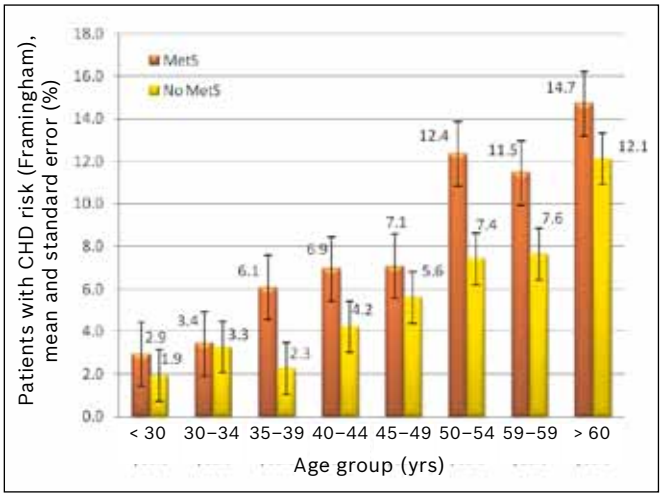

Fig. 1 Risk of coronary heart disease (Framingham) according to patients' age group and metabolic syndrome (MetS) status.

Despite finding higher rates of metabolic syndrome in patients with schizophrenia, the present study is not without limitations. First, as this was a cross-sectional study, the causal pathway of metabolic syndrome in patients with schizophrenia could not be inferred from our study even though it was frequent in our population. Second, a reference population without psychopathology was not to be found although the incidence of metabolic syndrome in adult Malaysians was available from a nationwide survey.[6]

In conclusion, we found that the prevalence of metabolic syndrome in patients with schizophrenia receiving antipsychotic therapy in Malaysia is very high. Our data adds to the mounting body of evidence that suggests that patients with schizophrenia are at an increased risk of developing metabolic syndrome. Our findings highlight the need for urgent formulation of comprehensive interventional measures aimed at combating problems faced by this patient cohort.

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