INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
Earthjournals Publisher
E-ISSN:2320-3137
www.earthjournals.org

RESEARCH ARTICLE

PREVALENCE OF METABOLIC SYNDROME AMONG ADOLESCENTS AND YOUNG ADULTS RECEIVING ANTIPSYCHOTICS – A CROSS SECTIONAL STUDY.

Vinoth Kumar M , Meenakshi B ,Abdul Rahuman MB, Ezhil Ramya J

Tirunelveli Medical College, Tirunelveli,Tamilnadu,India,627011

Corresponding author: DR B.MEENAKSHI M.D., Associate Professor, Department of Pharmacology, Tirunelveli Medical College, Tirunelveli-627011, Tamil Nadu, INDIA

ABSTRACT:

Objectives: To find out the prevalence of Metabolic Syndrome (MS) in adolescents and young adults who were on antipsychotics for more than six months.Participants and Methods: Young out-patients (16- 30 years) on antipsychotics (chlorpromazine or risperidone or both) for more than 6 months attending the psychiatry outpatient department were included. Patients with the history of diabetes, hypertension and dyslipidemia even before starting the drug were excluded from the study. Total study population was 101. Their waist circumference and blood pressure were measured .Fasting blood sugar and serum lipid profile was done and they were used to assess the presence of metabolic syndrome. Results: Among 101 patients, 25 had metabolic syndrome. The prevalence of metabolic syndrome was 24.8%. Prevalence in females (44.1%) was 3 times more than males (14.9%). Prevalence of MS was the highest with combination of drugs (30.4%) followed by risperidone (25%) and chlorpromazine (19.2%). Conclusion: The prevalence of metabolic syndrome in young patients receiving antipsychotics was 24.8%. It was more in females ($p<0.05$), in patients with polypharmacy and with second generation antipsychotic drugs. The prevalence of impaired fasting glucose, diabetes, prehypertension, hypertension and dyslipidemia were also higher in patients on antipsychotic drugs.

KEY WORDS: Antipsychotic drugs, Chlorpromazine, Metabolic Syndrome, Prevalence, Risperidone

INTRODUCTION

The metabolic syndrome is a cluster of the most dangerous heart attack risk factors: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure.[1-4]The Metabolic Syndrome is a risk factor for thromboembolism.[5]In addition, people with metabolic syndrome have a fivefold greater risk of developing type 2 diabetes. It is estimated that around 20-25 per cent of the world's adult population have the metabolic syndrome and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome. [6]

Cardiovascular disease (CVD) is the leading cause of death globally. It is also the most common cause of natural mortality in psychotic patients [7], accounting for 34% of deaths in male patients and 31% of deaths in female patients. [8]

Over the last decades there is a dramatic increase in the use of antipsychotic drugs in young patients. They are commonly prescribed not only for psychotic disorders but also prescribed off-label for a variety of paediatric and adult disorders like pervasive developmental disorders, tic disorders, severe Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive

Compulsive Disorders (OCD).[9] Children and adolescents are highly vulnerable for Drug Induced Metabolic Syndrome (DIMS).

Thus the management of Metabolic Syndrome and its risk factors should be targeted in the same way as we treat mental disorders. Hence patients on antipsychotic drugs require regular monitoring with simple laboratory and clinical measures for prevention or early detection of Metabolic Syndrome.

Metabolic Syndrome as per New International Diabetes Federation is defined as central obesity (Waist circumference > 90 cm for South Asian men > 80 cm for South Asian women) plus any two of the following

- ✓ Fasting triglyceride level > 150 mg/dL
- ✓ HDL < 40 mg/dL for men; < 50 mg/dL for women
- ✓ BP > 130 mm Hg systolic or > 85 mm Hg diastolic
- ✓ Fasting blood sugar > 100 mg/dL [10, 11]

This above criterion is applicable for subjects more than 16 years old only. We included adolescents more than 16 years and adults less than 30 years who had been taking antipsychotic drug (either chlorpromazine or risperidone or both) for more than six months.

MATERIALS AND METHODS

OBJECTIVES

- To find out the prevalence of Metabolic Syndrome in adolescent and young adults who are on antipsychotics for more than six months.
- To find out the prevalence of Diabetes & hypertension irrespective of the presence or absence of metabolic syndrome.
- To compare the prevalence of metabolic syndrome among patients taking chlorpromazine or Riperidone or both.

Clinical significance

The results may help to devise guidelines for screening and regular monitoring of Metabolic Syndrome in patients receiving antipsychotics.

Methodology:

After getting approval from the Institutional Ethical Committee the study was conducted in the Out Patient Department of Psychiatry, Tirunelveli Government Medical College, Tirunelveli. Written informed consent was obtained from the patients or from their caretakers. Demographic details were recorded. History of present illness, past history and family history of obesity, diabetes, hypertension and dyslipidemia were elicited from the patient or anybody who accompanied the patient. Medication history was taken from the medical records. The antipsychotic drugs available in the Psychiatry Department of Tirunelveli Government Medical College Hospital are chlorpromazine and risperidone and hence the patients who had been taking these drugs either singly or in combination were considered for the study.

Study Design:

Cross sectional study.

Study Population:

Young out-patients (16- 30 years) on antipsychotics for more than 6 months attending the psychiatry outpatient Department.

Number of Subjects: 101 patients

Duration of Study:

2 months. (From 1st May 2013 to 30th June 2013)

Inclusion Criteria:

1. Age of the patients 16 – 30 years
2. Both sex
3. Patients on chlorpromazine or risperidone or both for not less than 6 months irrespective of their primary psychiatric diagnosis.

Exclusion Criteria:

1. Patients < 16 years and > 30 years
2. Patients with the history of diabetes, hypertension or dyslipimedia even before starting antipsychotics.
3. Patients who are on steroids.
4. Patients who are on adjunctive drugs that pose risk for Metabolic Syndrome like Tricyclic antidepressants.

Parameters Assessed:

1. On the first day of visit

Weight, height, BMI were assessed

- Waist circumference was measured with a measuring tape in centimetres at the level of midway between the lowest rib and iliac crest. Patients were asked to stand with their feet together with arms in relaxed posture. The measuring tape was held in horizontal position and wrapped around the waist. They were asked to breathe normally and measurements were taken to the nearest 0.1 cm at the end of inhalation after ensuring that they did not contract the abdominal muscles during measurements.
- Blood pressure - The patients were asked to sit in the chair comfortably for 5 minutes and the arms barred and supported at heart level with his/her back supported. BP was recorded twice at the interval of at least two minutes and average of the two readings was taken.

2. On the next day of visit

The patients were asked to come with empty stomach on the next day and the venous blood was taken and analyzed for fasting blood sugar and complete lipid profile.

3. Diagnosis of Metabolic Syndrome

The reports of the investigations were collected on the next day and assessed for the presence or absence of Metabolic Syndrome.

The patient was considered to have Metabolic Syndrome if there is central obesity (waist circumference >90 cm for male and >80 cm for female) plus any two of the following:

- Fasting triglyceride level ≥ 150 mg/dL
- HDL < 40 mg/dL for men; < 50 mg/dL for women.
- BP ≥ 130 mmHg systolic or ≥ 85mmHg diastolic
- Fasting blood sugar ≥ 100 mg/dL

The results of the study were statistically analyzed.

For patients who were identified to have metabolic syndrome Therapeutic Lifestyle Changes were advised by the psychiatrist. Patients with severe metabolic derangement, frank Diabetes Mellitus, Hypertension, and Hypertriglyceridemia were referred to the Medicine

Department for further evaluation and treatment. The Patients who didn't have Metabolic Syndrome were advised to have a periodical health check up.

OBSERVATION AND RESULTS

Table1. Mean distribution of each parameter assessed

	N	Minimum	Maximum	Mean (Standard Deviation)
Age	101	17	30	27.0 (3.0)
BMI	101	13.8	44.6	23.6 (5.8)
Waist Circumference	101	48	129	83.9 (13.3)
Fasting Blood Sugar	101	52	385	93.8 (39.7)
Triglycerides	101	55	515	146.4 (75.4)
HDL	101	13	58	32.6 (8.8)
Systolic BP	101	90	160	118.6 (10.6)
Diastolic BP	101	60	110	79.0 (8.4)

Table 1 shows the mean age, BMI, Waist Circumference (WC), Fasting Blood Sugar (FBS), Triglycerides (TGL), HDL, and Systolic BP (SBP) & Diastolic BP (DBP) of all the 101 patients (adolescents and young adults) included in the study.

Table2. Gender Distribution

	Total n=101	Male n=67	Female n=34	Chi square value	p-value
Metabolic Syndrome, according to IDF criteria	25 (24.8%)	10 (14.9%)	15 (44.1%)	10.3195	**0.001***

Table 2 shows that the prevalence of metabolic syndrome is significantly increased in females.

Table3. Distribution of risk factors

	Metabolic Syndrome	n=25
1.	Central Obesity + 2 risk factors	19 (76%)
2.	Central Obesity + 3 risk factors	5 (20%)
3.	Central Obesity + 4 risk factors	1 (4%)

IDF criteria for diagnosis of metabolic syndrome involve central obesity + any 2 of 4 risk factors. Out of 25 patients having metabolic syndrome, 19 patients (76%) had central obesity with 2 risk factors; 5 patients (20%) had central obesity with 3 risk factors; only one patient (4%) had central obesity with all the four risk factors (Table3).

Table4. Prevalence of Diabetes in young adults taking antipsychotics

	Metabolic Syndrome n=25	No Metabolic Syndrome n=76	Total n=101
Normal Fasting Glucose (FBS < 100mg %)	12 (48%)	62 (81.6%)	74(73.3%)
Impaired Fasting Glucose (FBS 100 – 125mg %)	8 (32%)	12 (15.8%)	20(19.9%)
Diabetes Mellitus (FBS ≥ 126mg %)	5 (20%)	2 (2.6%)	7(6.9%)

Among patients who didn't have metabolic syndrome (n=76), 15.8% had impaired fasting glucose (they are more prone to develop type 2 diabetes mellitus) and 2.6% were diabetic. Among all the 101 subjects 19.9% had impaired fasting glucose and 6.9% had their FBS more than 126 mg %.

Table5. Prevalence of Hypertension in young adults taking antipsychotics

According to Joint National Committee (JNC) VII criteria	Metabolic Syndrome n=25	No Metabolic Syndrome n=76	Total n=101
Normotensive *(systolic <120mmHg and diastolic<80mmHg)*	6 (24%)	19 (25%)	25 (24.8%)
Prehypertensive *(systolic 120-139mmHg or diastolic 80-89mmHg)*	17 (68%)	45 (59.2%)	62 (61.4%)
Stage I Hypertension *(systolic 140-159mmHg or diastolic 90-99mmHg)*	2 (8%)	7 (9.2%)	9 (8.9%)
Stage II Hypertension *(systolic ≥160mmHg or diastolic ≥100mmHg)*	2 (8%)	3 (3.9%)	5 (5%)

Table5 shows that among patients with metabolic syndrome (n=25), 68% were prehypertensive; 8% were found to have stage I Hypertension; and another 8% were found to have stage II hypertension. Even though there is no metabolic syndrome as per the criteria, among the people without metabolic syndrome 59.2% had prehypertension 9.2% had stage I and 3.9% had stage II hypertension. The overall prevalence of prehypertension, stage I and stage II Hypertension were found to be 61.4%, 8.9% and 5% respectively.

Table6. Prevalence of Metabolic Syndrome in relation to various antipsychotics used

	Chlorpromazine n=26	Risperidone n=52	Both n=23
Metabolic syndrome	5 (19.2%)	13 (25.0%)	7 (30.4%)

Table 6 shows that the prevalence of metabolic syndrome was 19.2% with chlorpromazine & 25% with risperidone. Among patients who were taking both the drugs the prevalence was 30.4%.

DISCUSSION

Prevalence of metabolic Syndrome

The prevalence rate varied largely among studies. The lowest prevalence rate reported was 3.9% and the study was conducted in unmedicated, *drug naïve young out-patients (mean age 26.9)* with chronic schizophrenia in Indian population by Padmavathi et al.[(12)] The highest prevalence rate reported was 68%, in patients treated with a combination of first generation and second generation antipsychotics.[(13)]Our study conducted in south Tamil Nadu, involved only young patients *(mean age 27.0)* taking either a first or a second generation antipsychotic (monopharmacy) or both (polypharmacy) irrespective of the primary psychiatric illness.

As the consequences of metabolic syndrome are well known, essential steps must be taken to screen all the patients receiving antipsychotics periodically, for early detection of components of metabolic syndrome and dietary and life style modifications should be advised.

Gender Distribution

Numerous studies compared the prevalence rates between men and women and most studies revealed substantially increased prevalence of metabolic syndrome in women.[(14)] Similar to the prevalence of metabolic syndrome in general population our study also shows the female preponderance. According to our study approximately there was a threefold increase in the prevalence of metabolic syndrome in women when compared to men.

Distribution of risk factors

IDF criteria for diagnosis of metabolic syndrome involve central obesity plus any 2 of 4 risk factors. About 20% of the patients had 3 risk factors in addition to the central obesity. A 25 year old female patient had central obesity with all the components of metabolic syndrome according to IDF criteria. She was found to be diabetic with a fasting blood glucose level of 385mg% and hypertensive with a blood pressure of 150/95mmHg. She was taking chlorpromazine for the past 8 years which could be attributed to be the cause of these metabolic derangements, as she did not have any family history of diabetes or hypertension. She was referred to General Medicine Department for control of diabetes and hypertension. She was referred to the Departments of Cardiology, Nephrology, Ophthalmology and Neurology for the expert opinions and further management.

Metabolic Syndrome and Diabetes

Regardless of the presence of any abnormalities of glucose metabolism, individuals with metabolic syndrome are at increased risk of type II diabetes. [(15)] Some studies point out that the

prevalence of diabetes and obesity to be two to four times higher in people with schizophrenia than in general population and the overall prevalence of diabetes among patients with schizophrenia range from 16 – 25%.[16]

Only the fasting blood glucose levels were measured and the postprandial blood sugar estimation was not done. Hence here the diagnosis of DM is based only on the fasting blood sugar value. If it was ≥ 126 mg. the patient was considered to be a diabetic. It was observed in our study that 32% of patients with metabolic syndrome and 15.8% of individuals without metabolic syndrome had impaired fasting glucose (FBS 100-125mg). Similarly, 20% of the study subjects with metabolic syndrome had diabetes (FBS ≥ 126mg). These young patients are prone for the diabetes-related micro and macro vascular complications. A study conducted elsewhere in psychiatric patients (mean age 37.6) who were on antipsychotic drugs reported 37.0% of prediabetes and 10.2% of diabetes mellitus.[17] In contrast to the mean age of patients included in that study (37.6), the mean age of our subjects was 27. The overall prevalence of IFG and DM in our study irrespective of the presence of metabolic syndrome was 19.95 % and 6.9% respectively. (Table 4)

Metabolic syndrome and hypertension

In our study we observed that among the 101 individuals who had been on antipsychotics, 61.4% had prehypertension, 8.9% had stage I hypertension and 5% had stage II hypertension (Table 8). This is according to the Joint National Committee VII criteria.[18] According to this criteria, <120mmHg systolic and <80mmHg diastolic BP is defined as normal; 120-139mmHg systolic or 80-89mmHg diastolic BP is considered as prehypertension; 140-159mmHg systolic or 90-99mmHg diastolic BP is defined as Stage I and ≥160mmHg systolic and ≥100mmHg diastolic BP is stage II hypertension. This prevalence is really too high for the mean age (27) of the patients involved in the study.

Hypertension is an important risk factor for atherosclerosis [19] and stroke. [20] There is a greater agreement that prehypertension is a precursor of hypertension and there is a potential for its association with an excess morbidity and mortality from cardiovascular disease (CVD). One study suggested that 47% of all heart attacks might be prevented by eliminating prehypertension.[21] Early detection of prehypertension in individuals getting antipsychotics by periodical screening may help in reducing morbidity and mortality. Dietary salt and fat restriction, increased physical activity and appropriate antihypertensive drugs in patients will help in bringing down their blood pressure as well as the cardiovascular and cerebrovascular complications.

Metabolic Syndrome and Dyslipidemia

Low HDL values were observed in 78.2% of the study subjects and TGL was found to be elevated in 36.6% of the patients irrespective of the presence or absence of metabolic syndrome. This type of lipid phenotype is defined as *Atherogenic Dyslipidemia* which is an important risk factor for cardiovascular disease (CVD). [22] Available prospective studies in Western populations consistently indicate moderate and highly significant associations between triglyceride values and coronary heart disease risk. [23]

Prevalence of Metabolic Syndrome in relation to various antipsychotics used

Consistent findings across these studies found that metabolic syndrome was more likely with SGAs over FGAs, polypharmacy over monotherapy and high-potency over low-potency

agents. [24-26] In our study we observed that 19.2% of patients receiving Chlorpromazine and 25% of patients on Risperidone had metabolic syndrome. Among patients receiving both chlorpromazine and risperidone 30.4% were found to have metabolic syndrome. The prevalence of metabolic syndrome was the highest with polypharmacy, followed by second generation antipsychotic drug risperidone monotherapy and the least with chlorpromazine monopharmacy.

We can prevent or reduce the incidence of cardiovascular and cerebrovascular mortality and morbidity by periodical screening of the patients for hypertension, dyslipidemia, diabetes and for metabolic syndrome. Caregivers can be educated about the disadvantages of weight gain in patients taking antipsychotics. Physical activity must be promoted in these patients. Dietary modifications are essential to keep the blood sugar, blood pressure and lipids within normal limits.

CONCLUSION

The prevalence of metabolic syndrome in young patients receiving antipsychotics was 24.8%. It was more in females ($p<0.05$), in patients with polypharmacy and with second generation antipsychotic drugs. The prevalence of impaired fasting glucose, DM, prehypertension, hypertension and dyslipidemia were also found to be higher in patients on antipsychotic drugs. Due steps must be taken to screen the patients periodically and treat the individuals accordingly.

ACKNOWLEDGEMENT:

We sincerely thank Indian Council of Medical Research (ICMR) for the financial support.

CONFLICTS OF INTEREST

No conflict of interest

REFERENCES

1. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome a new worldwide definition. Lancet 2005; 366:1059-62.
2. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome-a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med 2006 May; 23(5):469-80.
3. www.idf.org/metabolic_syndrome, website of the International Diabetes Federation
4. The metabolic syndrome, Diabetes Voice special issue, May 2006, 51.
5. Borch KH, Braekkan SK, Mathiesen EB, Njolstd I, Wilsgaard T, Stormer J, Hansen JB. "Abdominal obesity is essential for the risk of venous thromboembolism in the Metabolic Syndrome: The Tromso study." *J Thromb Haemost* 7.5 (2009):739-745.
6. Stern M, Williams K, Gonzalez-Villalpando C et al. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? Diabetes Care 2004; 27(11):2676-81
7. Tandon, Rajiv, Henry A. Nasrallah, and Matcheri S. Keshavan. "Schizophrenia, “just the Facts” 4. Clinical Features and Conceptualization." *Schizophrenia Research* 110.1-3 (2009): 1-23.
8. Brown S. "Excess Morality of Schizophrenia: A Meta Analysis" *Br. J. Psychiatry* 171(1997): 502-508.
9. Henry J, Paola Antonini, Michael F.M. "Atypical Antipsychotics and Metabolic Implications." *Am Health Drug Benefits* 2011: 292-302.
10. The IDF consensus world-wide definition of Metabolic Syndrome, www.idf.org
11. The IDF consensus worldwide definition of Metabolic Syndrome in children and adolescents 2005, www.idf.org
12. Padmavathi R, McCreadie R, Tirupati S. "Low Prevalence of obesity and metabolic syndrome in never-treated chronic schizophrenic." *Schizophr Res* 121(2010): 199-202. [PubMed]
13. Tirupati S, Chua L. "Obesity and Metabolic syndrome in a psychiatric rehabilitation service." *Aust N ZJ Psychiatry* 41(2007): 606-610. [PubMed]

14. Evangelos papanastasiou. "The prevalence and mechanisms of Metabolic Syndrome in schizophrenia: a review." *Ther Adv Psychopharmacol* 3.1(2013 Feb): 33-51. [PubMed]
15. Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. "The Metabolic Syndrome as Predictor of Type II Diabetes." *Diabetes Care* (2003):3153-3159.
16. Dixon L, Weiden P, Delahanty J, Goldberg R, Postrado L, Lucksted A, et al. "Prevalence and correlation of diabetes in national schizophrenia samples." *SchizophrBull* 26(2000): 903-12.
17. Manu P, Correll CU, van Winkel R, Wampers M, De Hert M. "Prediabetes in patients treated with antipsychotic drugs." *J Clin Psychiatry* 73.4(2012 April): 460- 466.
18. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, et al. "The seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure: the JNC7 report." *JAMA* 21:289.19(2003 May): 2560-2572.
19. Riccioni G, De Santis A, Cerasa V, et al. "Atherosclerotic plaque formation and risk factors." *Int J Immunopathol Pharmacol* 13(2003): 25-35. [PubMed]
20. Yu JG, Zhou RR, Cai GJ. "From hypertension to stroke: mechanism and potential prevention statergies." *CNS Neurosci Ther* 13(2011): 577-584. [PubMed]
21. Qureshi A, Suri MFK, Kirmani JF, Divani AA, Mohammad Y. "Prehypertension triples heart attack risk. Health and Medicine." Science Daily. Fromhttp://www.sciencedaily.com/releases/2005/08/050805110759.htm
22. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-3142. [PubMed].
23. Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, et al. "Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in western prospective studies." *Circulation* 115.4(2007 Jan 30): 450-8.
24. Hagg S., Lindblom Y., Mjorndal T., Adolfsson R. "High prevalence of the metabolic syndrome among a Swedish cohort of patients with schizophrenia." *Int Clin Psychopharmacol* 21(2006): 93–98. [PubMed]
25. Cerit C., Ozten E., Yildiz M. "The prevalence of metabolic syndrome and related factors in patients with schizophrenia." *Turk Psikiyatri Derg* 19(2008): 124– 132. [PubMed]
26. Lee N., Kim S., Jung D., Kim E., Yu H., Sung K., et al. "The prevalence of metabolic syndrome in Korean patients with schizophrenia receiving a monotherapy with aripiprazole, olanzapine or risperidone." *Prog Neuropsychopharmacol Biol Psychiatry* 35(2011): 1273–1278. [PubMed]