The Pharma Innovation Journal 2019; 8(4): 21-29

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2019; 8(4): 21-29

www.thepharmajournal.com
Received: 14-02-2019
Accepted: 18-03-2019

B Jahnavi
Pharm D Interns, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

Mullapudi Veda Ishwarya
Pharm D Interns, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

Siddyreaddy Manasa
Pharm D Interns, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

Susmita
Pharm D Interns, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

Apoorva Dev
Assistant Professor, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

P Lokeswara Reddy
M.D., Associate Professor of Psychiatry, Government General Hospital, Guntur Medical College, Guntur, Andhra Pradesh, India

Correspondence
Apoorva Dev
Assistant Professor, Department of Pharmacy Practice, PES College of Pharmacy, Bengaluru, Karnataka, India

A study on prescription patterns and prevalence of metabolic syndrome with anti-psychotic therapy

B Jahnavi, Mullapudi Veda Ishwarya, Siddyreaddy Manasa, Susmita, Apoorva Dev and P Lokeswara Reddy

Abstract
Back ground: Metabolic syndrome refers to the co-occurrence of several known cardiovascular risk factors, including insulin resistance, obesity, atherogenic dyslipidemia and hypertension. This review includes the prevalence of metabolic syndrome in patients receiving atypical antipsychotics by checking the parameters like abdominal girth, body mass index (BMI), blood sugar levels and cholesterol levels.
Aim: To study the prescription patterns and prevalence of metabolic syndrome with anti-psychotic therapy.
Objective: To assess the prevalence of metabolic syndrome associated with the use of anti-psychotic drugs and the duration of the therapy, and creates awareness among patients and clinicians.
Method: All patients who were under antipsychotic therapy for more than six months were included in the study. Patient data was collected in a well-designed patient profile form. This study was conducted for a period of six months.
Results: The overall prevalence of metabolic syndrome was 43.11%. The prevalence was higher in females (25.73%) than males (17.26%). Among the diagnostic subgroups, the prevalence was highest among patients with schizophrenia (22.5%), while it was lesser in the patients with bipolar disorders (17%) and psychotic disorders (3.58%). Prevalence of metabolic syndrome was significantly higher (39.24%) among patients taking second-generation antipsychotics, followed by those on the combination of first generation and second-generation antipsychotics (28.01%).
Conclusion: Our study shows that prevalence of metabolic syndrome is very high in patients with schizophrenia and among patients receiving second-generation anti-psychotics. We also identified the important risk factors for metabolic syndrome in these patients. Screening and monitoring of metabolic syndrome is strongly recommended for these patients. To further assess the pattern of onset and risk for metabolic complications, studies are needed to evaluate second-generation anti-psychotics treatment in larger sample size.

Keywords: metabolic syndrome, anti-psychotics, prevalence, prescription pattern, schizophrenia

Introduction
Anti-psychotics are usually effective in relieving symptoms of psychosis in the short term. The long-term use of antipsychotics is associated with side effects such as involuntary movement disorders, gynecomastia and metabolic syndrome. They are also associated with increased mortality in elderly people with dementia. The use of anti-psychotic medications entails a difficult trade-off between the benefit of alleviating psychotic symptoms and the risk of troubling, sometimes life-shortening adverse effects [1]. There is more variability among specific anti-psychotic medications than there is between the first- and second-generation antipsychotic classes. The newer second generation anti-psychotics, like clozapine and olanzapine, generally tend to cause more problems relating to metabolic syndrome, such as obesity and type II diabetes mellitus. Weight gain is a common adverse effect of using anti-psychotic medications, can be rapid and difficult to control. Weight gain does not seem to be dose dependent within the normal therapeutic range. The effect is worse with clozapine and olanzapine; minimal with aripiprazole and ziprasidone; and intermediate with other antipsychotics, including low potency FGAs (First Generation Anti-psychotics).
Anti-psychotic medications can contribute to a wide range of glycemic abnormalities, from mild insulin resistance to diabetic ketoacidosis, as well as worsening of glycemic control in patients with pre-existing diabetes. Although FGAs and SGAs (Second Generation Anti-psychotics) can cause these problems, risk is variable: the greatest risk is with clozapine and olanzapine. The magnitude of risk is difficult to quantify because so many other diabetic risk factors are present in this population.

Although the weight gain associated with antipsychotics clearly contributes, there appear to be other independent effects as well. Dyslipidemia is also associated with several antipsychotic medications, with increases noted primarily in triglyceride levels. Low-potency FGAs and the SGAs clozapine, olanzapine, and quetiapine are associated with a higher risk of hyperlipidemia. Overall, metabolic disturbances appear to be the greatest with clozapine and olanzapine, intermediate with quetiapine and low-potency FGAs and the lowest with aripiprazole, risperidone, ziprasidone and high-potency FGAs [2].

Anti-psychotics and metabolic syndrome

Notwithstanding the therapeutic effectiveness of anti-psychotic drugs in many illnesses such as schizophrenia, increased attention has turned to the possible deleterious side-effects of these agents. Metabolic derangements associated with antipsychotic agents have been the focus of considerable interest and debate for many years. While metabolic syndrome affects all ages of patients who take anti-psychotic medications, children and adolescents receiving atypical antipsychotic medications are particularly vulnerable to these effects. Notably, obesity-associated metabolic disease short of type 2 diabetes mellitus (i.e. dyslipidaemia and hypertension in the absence of type 2 diabetes mellitus) may be mechanistically linked to lower academic and professional potential in adolescents, as lower cognitive performance and reduction in brain structural integrity among adolescents with metabolic syndrome has been documented in studies. While there appears to be a dose-dependent relationship between the dose of clozapine or olanzapine and metabolic complications, aripiprazole, quetiapine, and ziprasidone do not show a causal relationship, and risperidone has mixed results [3-5].

Metabolic syndrome is a cluster of risk factors comprising obesity (central and abdominal), dyslipidemia, glucose intolerance, insulin resistance (or hyperinsulinaemia), and hypertension, and is highly predictive of type 2 diabetes mellitus and cardiovascular disease. The mean age of death is 61 years for patients with schizophrenia, which is considerably younger than 76 years for the general population. Life expectancy in people with schizophrenia is reduced by 20%, with 60% of the excess mortality due to physical illness. Schizophrenia itself may be a risk factor for metabolic syndrome in addition to many other factors in patients with schizophrenia, and there is also increasing concern that antipsychotic drugs, particularly second-generation antipsychotics (SGAs), have metabolic consequences that contribute to the risk. The precise relationship between antipsychotic drugs and metabolic syndrome remains uncertain, but it is clear that people treated with antipsychotic medications develop individual features of metabolic syndrome, and the syndrome itself, at a higher rate than the general population. Antipsychotic poly pharmacy, which is a common practice in many psychiatric settings, as compared with mono therapy, may be independently associated with increased risk of pre-metabolic syndrome and higher rates of metabolic syndrome and lipid markers of insulin resistance, even after adjusting for patient's lifestyle characteristics. A recent study concluded that switching to mono therapy was appropriate and reasonable as long as patients could return to poly pharmacy when necessary, and switching from a higher- to a lower-risk agent or from poly pharmacy to mono therapy may facilitate metabolic improvement. Many reviews have concluded that there is a need for active routine physical health screening of all individuals receiving treatment with antipsychotic drugs, which is in keeping with the recommendations of the National Institute for Health and Clinical Excellence treatment guidelines for schizophrenia. While many adults with schizophrenia receive little or no medical care, such care is important, given the risk of metabolic abnormalities associated not only with antipsychotic medications, but also with schizophrenia in general [5, 6].

Objectives

- To assess the occurrence of metabolic syndrome associated with the use of antipsychotic drugs.
- To check the metabolic syndrome with the type of anti-psychotic drug and the duration of therapy.
- To create awareness among the patients and clinicians about the metabolic syndrome caused by the use of anti-psychotics.

Materials and Methods

Study site

Psychiatry Department, Government General Hospital, Guntur, Andhra Pradesh, India.

Study design

A Hospital based observational study.

Study duration

The study was conducted for six months.

Study criteria

Inclusion criteria

- Patients who are under anti-psychotic therapy
- Age 16-70 years old only
- Both genders
- Psychotic disorders i.e. schizophrenia, bipolar disorder

Exclusion criteria

- Patients who are not under anti-psychotic therapy
- Clinical trial patients

Source of data

Patient profile form

The patient profile form was self-designed in accordance with the required information for the study. The form consisted of two main categories - patient information and safety monitoring parameters.

- Patient Information - It consists of patient's demographics, diagnosis, duration of disease, family history, past medication history, past medical history, current medication.
- Safety Monitoring Parameters - It consist of physical examination (blood pressure, height, weight, BMI), laboratory investigation required to detect diabetes and hyperlipidemia (FBS, RBS, HBA1C, LDL, HLDL, Triglycerides, VLDL).

Procedure

- Data was collected from patient case files and by interviewing the patients.
- The required information was collected into a self-designed patient profile form.
- The collected data is thoroughly reviewed and the anti-

psychotic therapy administered was compared to the anti-psychotic therapy guidelines (mention any guidelines used).
- After the data collection was complete, the total number of cases was estimated.

Results

A total of 307 subjects were included in the study which was conducted for a period of six months in the psychiatric hospital.

Table 1: Age distribution of the subjects with gender

Age groups in years	Male	Female
16-20	17	13
21-30	43	60
31-40	45	49
41-50	27	24
51-60	15	9
61-70	1	2
71-80	0	2

Table 2: Represents disease status of the subjects

Disease	Male	Female	Total
BPAD	36	53	89
SCHZ	98	91	189
Psychosis	14	15	29

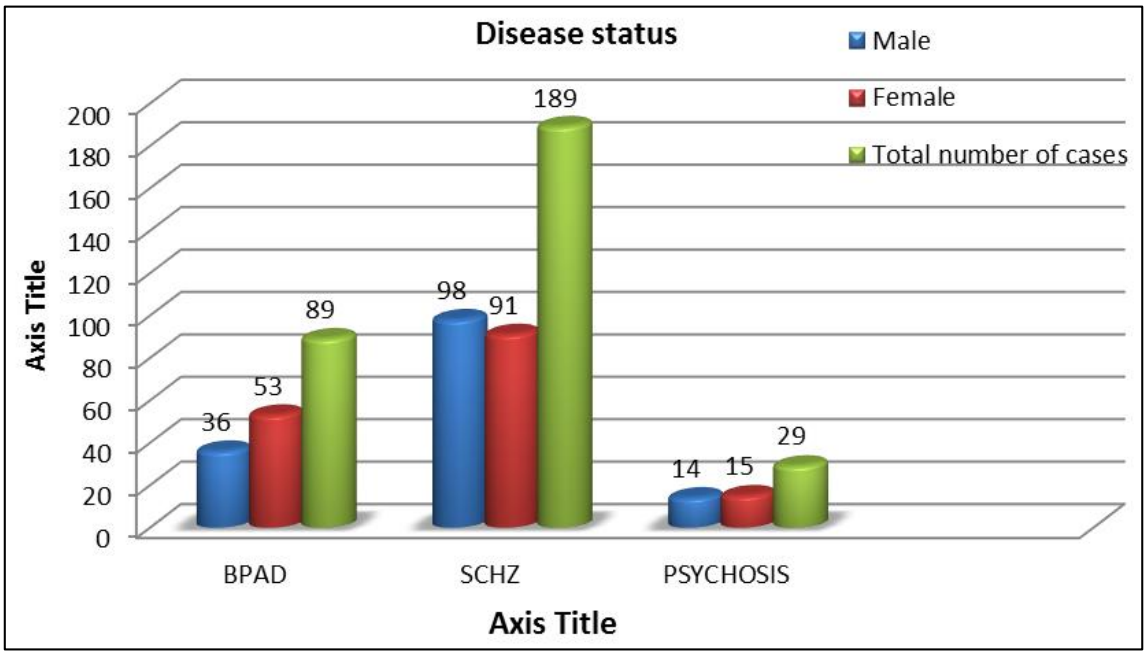

Fig 1: Chart representing disease status of the subjects

Table 3: Family history status of the subjects

Family history	Number of subjects
Yes	57
No	250

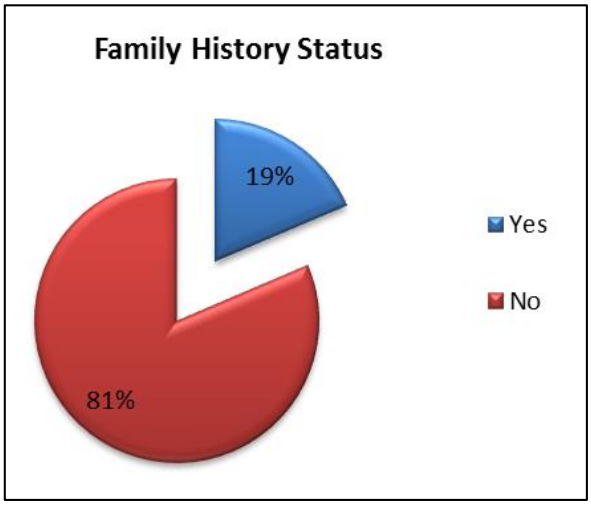

Fig 2: Chart representing family history status of subjects

Table 4: Metabolic syndrome in subjects with duration of disease

Duration of disease	Diabetes mellitus	Weight gain	Hyperlipidemia
6-11 months	1	6	0
1-5 years	13	30	1
6-10 years	7	17	1
11-15 years	3	10	0
16-20 years	9	19	1
21-25 years	2	4	2
26-30 years	0	3	0

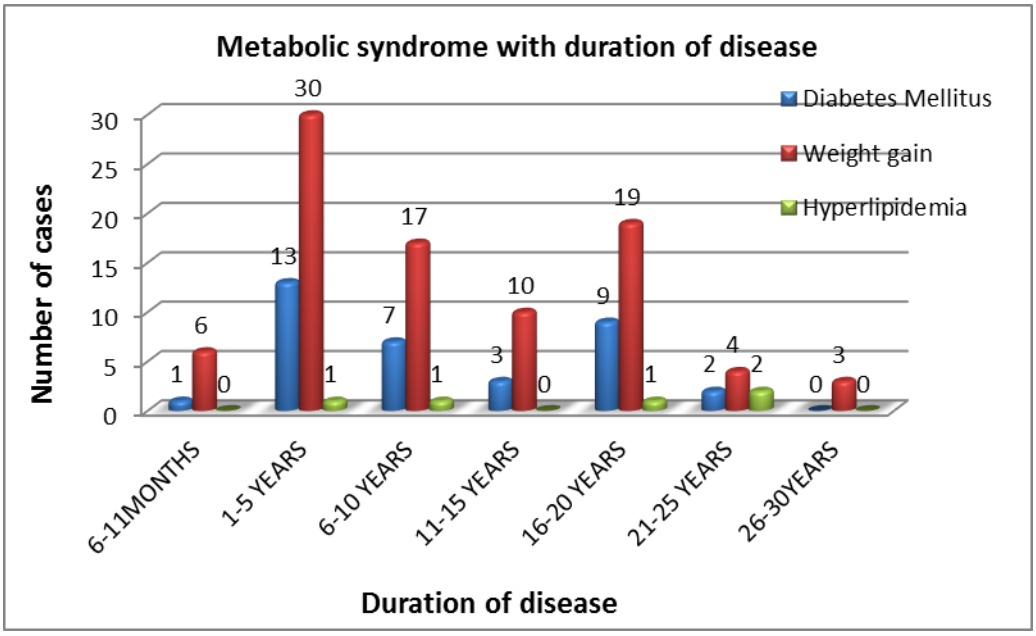

Fig 3: Chart representing metabolic syndrome status with duration of disease

Table 5: Number of cases with metabolic syndrome

Metabolic syndrome	Total cases
DM	36
Lipids	5
BMI	91

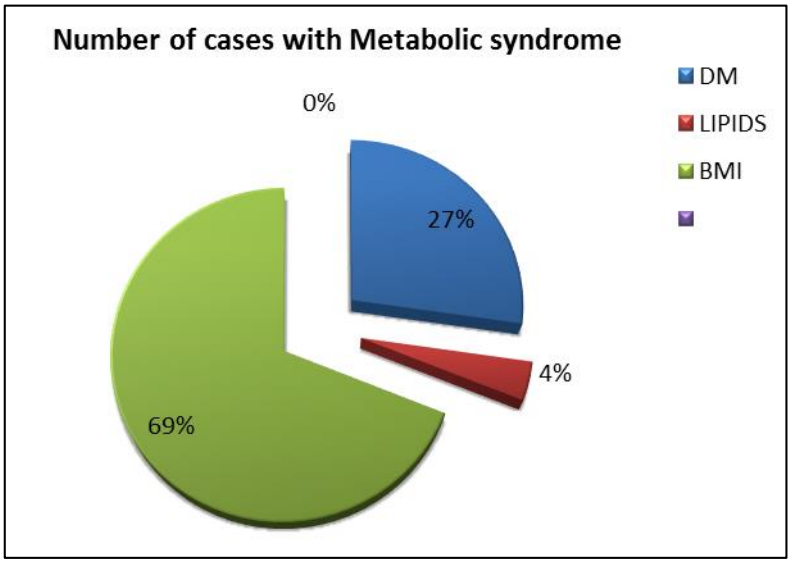

Fig 4: Chart representing number of cases with metabolic syndrome

Table 6: Age of the subjects with the metabolic syndrome

Age in years	Weight gain	Diabetes mellitus	Hyperlipidemia
16-20	5	0	0
21-30	25	10	1
31-40	33	10	2
41-50	18	10	1
51-60	10	6	1

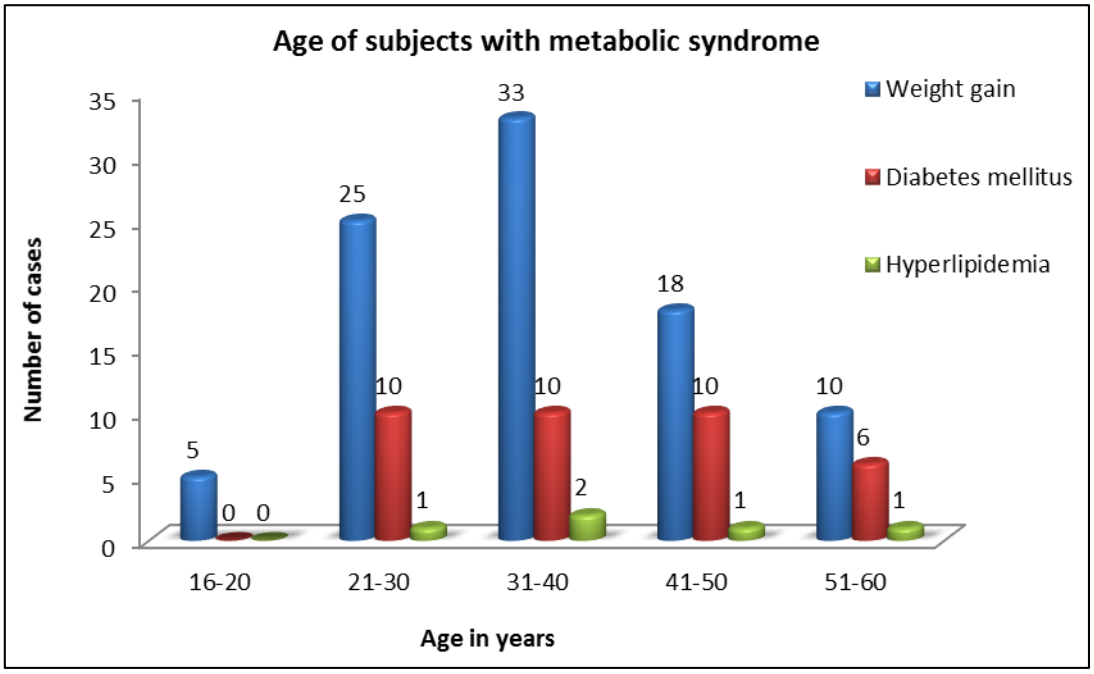

Fig 5: Chart representing age of subjects with metabolic syndrome

Table 7: Metabolic syndrome as per diagnostic groups

Disease	Metabolic syndrome		Total cases
	Present	Absent	
BPAD	52	37	89
SCHZ	69	120	189
Psychosis	11	18	29

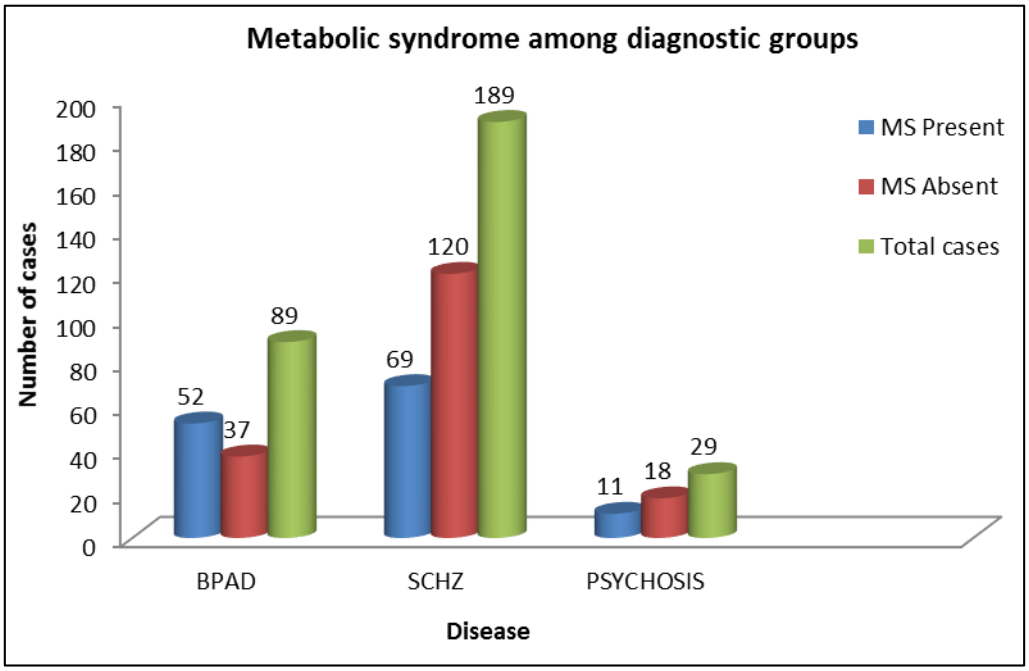

Fig 6: Chart representing metabolic syndrome among diagnostic groups

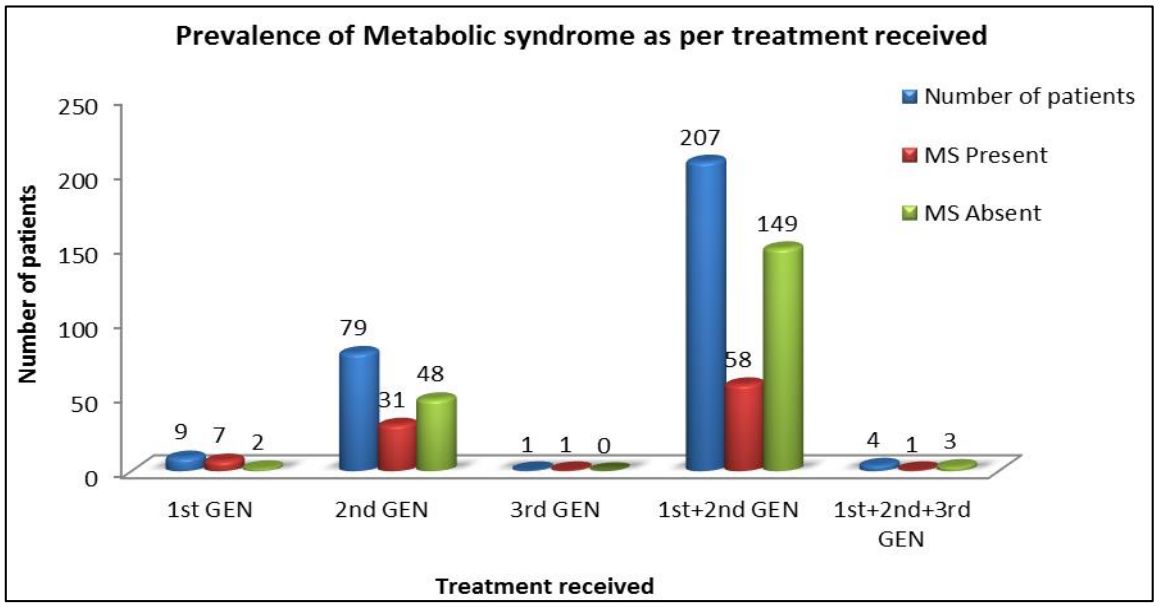

Fig 7: Prevalence of metabolic syndrome as per treatment received

Table 8: Anti-psychotics involved in diabetes mellitus

Drugs received	BPAD	SCHZ	Psychosis
Haloperidol	6	7	0
Chlorpromazine	4	4	0
Flupenthixol	0	1	0
Olanzapine	6	10	1
Risperidone	9	7	1
Qutiapine	3	4	0
Amisulpride	1	4	0
Clozapine	1	2	0
Aripiprazole	0	1	0

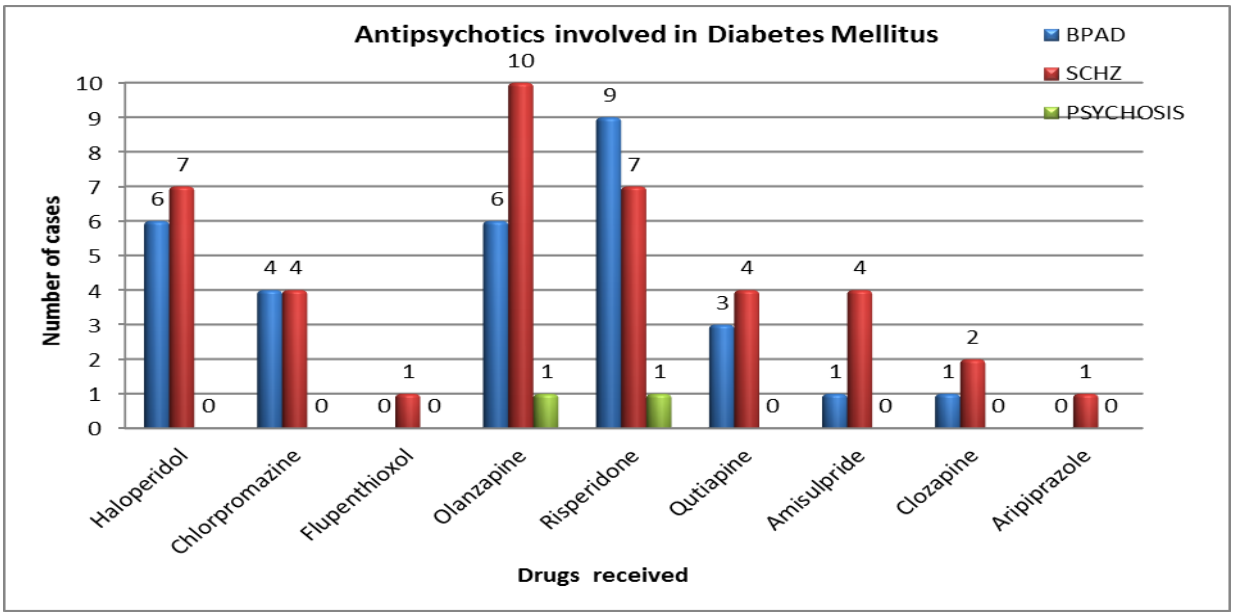

Fig 8: Chart representing antipsychotics involved in diabetes mellitus

Table 9: Antipsychotics involved in weight gain

Drugs received	BPAD	SCHZ	Psychosis
Haloperidol	17	25	5
Chlorpromazine	5	6	0
Flupenthixol	0	2	0
Olanzapine	16	19	4
Risperidone	17	25	3
Qutiapine	3	5	1

Amisulpride	0	6	0
Lurafore	1	0	0
Clozapine	1	0	0
Aripiprazole	1	1	

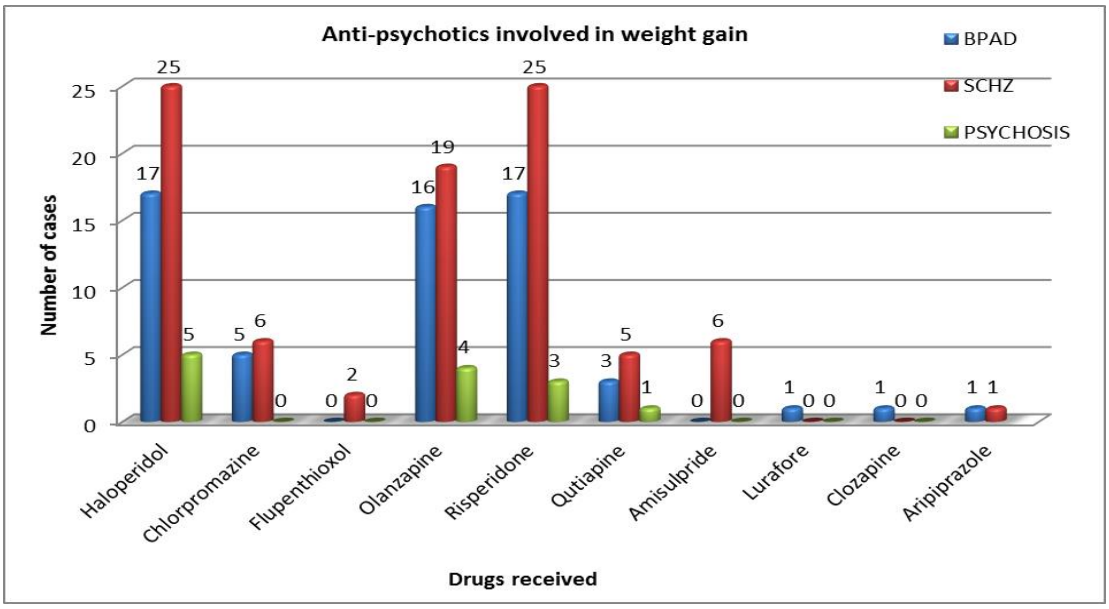

Fig 9: Chart representing antipsychotics involved in Weight gain

Table 10: Anti-psychotics involved in hyperlipidemia

Drugs received	BPAD	SCHZ	Psychosis
Haloperidol	2	2	0
Chlorpromazine	0	1	0
Flupenthixol	0	0	0
Olanzapine	0	1	0
Risperidone	2	1	0
Qutiapine	0	1	0
Amisulpride	0	0	0
Lurafore	0	0	0
Clozapine	0	0	0
Aripiprazole	1	1	0

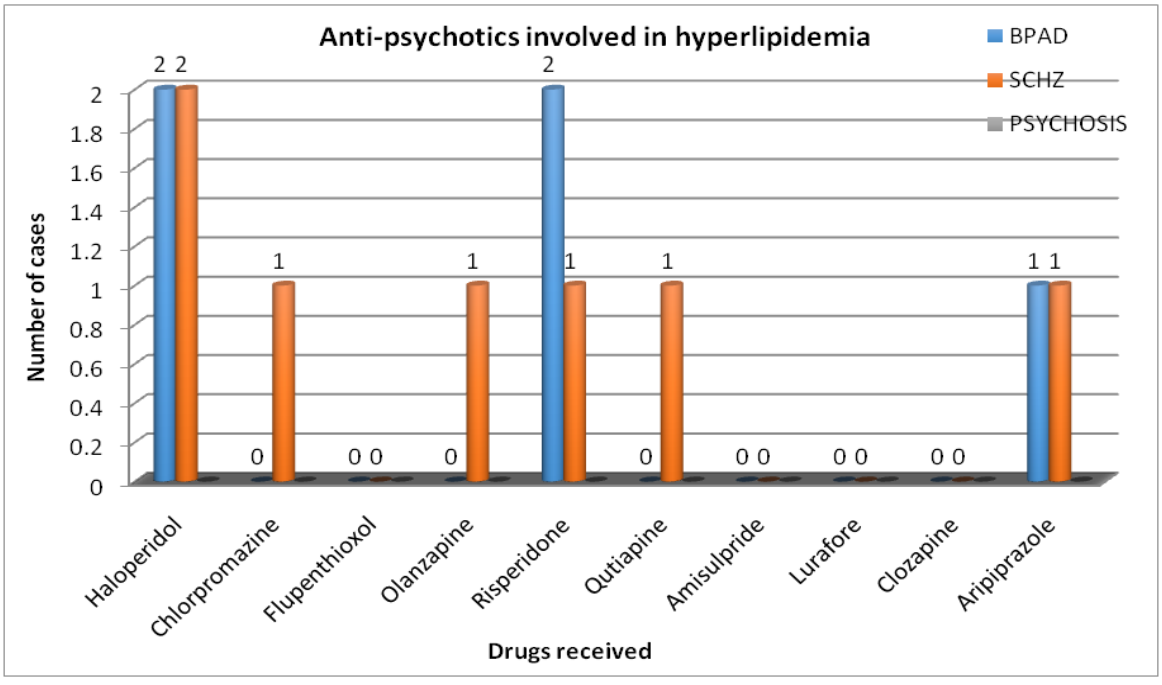

Fig 10: Chart representing Antipsychotics involved in hyperlipidemia

Table 11: Summary of various studies on prevalence of MS in patients with psychiatric disorders

Study	Prevalence of MS
Bipolar disorder	
Teixeira PJR and Rocha FL [7]	38.30%
Chang HH *et al*. [8]	33.90%
Psychotic disorder	
Malhotra N *et al*. [9]	26%
Pallava A *et al*. [10]	27.50%
Sugawara N *et al*. [11]	36%
Medeiros-Ferreira L *et al*. [12]	36.80%

Discussion

The present study was focused on the prescription pattern and prevalence of metabolic syndrome among the psychiatric patients receiving antipsychotics in the government general hospital. Of all the subjects (n=307) included in the study from the psychiatry ward of the hospital 48.20% were male and 51.79% were female. The most commonly found diagnostic category was schizophrenia (61.56%), followed by bipolar disorder (28.99%) and psychotic disorder (9.44%). The overall prevalence of metabolic syndrome in our study was 43.11%. Our results are comparable to the other studies which had similar study design as ours. Prevalence rates of metabolic syndrome have varied from 26% to 52.2% in various cross-sectional studies. The Indian population is heterogeneous. Differences in lifestyle and socio demographic profile may be a reason for dissimilar prevalence of MS across different regions. Although MS is recognized worldwide as a distinct entity, the guidelines for identifying MS by different organizations vary. Using different guidelines in the same sample may yield considerably different estimates for MS prevalence. Hence, to avoid such ambiguities, we used the guidelines issued jointly by different international bodies to unify and harmonize the criteria for MS.

However, one previous study, which assessed some metabolic disturbances associated with MS in schizophrenic outpatients in use of antipsychotics found a high percentage of overweight patients, and increased prevalence of hyperlipidemia. The prevalence of MS stratified by diagnoses was 22.5% (n=69) for schizophrenia, 17% (n=52) for bipolar disorder, 3.58% (n=11) for psychotic disorder. The highest prevalence of MS is seen in schizophrenia, followed by bipolar disorder and psychotic disorder. These results are comparable to numerous studies done across the world as shown in Table12. In the risk factor assessment, female patients exhibited greater risk of developing MS. The female gender was significantly associated with a higher prevalence of MS in our study. Prevalence of MS in females was 25.73% and in males was 17.26%. This result is in accordance with data obtained from the initial assessment of 689 patients included in the Clinical Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial, in the United States. In this study, the prevalence of MS (by NCEP criteria) was 51.5% for women and 36% for men ($p = 0.002$). In our study, the prevalence of metabolic syndrome was highest (39.24%) in patients receiving second generation antipsychotics, followed by those on the combination of first generation and second generation anti-psychotics (28.01%).

The prevalence was lesser in patients on first generation antipsychotics and third generation antipsychotics. Second generation antipsychotic taking patients had significantly higher MS rates ($p=0.002$) than the others. In our study elevated fasting blood sugar level and BMI were highest among patients taking olanzapine and risperidone, followed by haloperidol. Elevated triglyceride levels were highest among patients taking risperidone and haloperidol. In our study, the prevalence of metabolic syndrome was highest (29.64%) in patients with BMI above cut off levels, followed by those with elevated glucose levels (11.72%) and elevated lipid levels (1.62%).

Thus, BMI emerged as the best predictor of metabolic syndrome among various metabolic parameters. All those approaching higher BMIs should be evaluated for MS, advised to increase physical exercise and adopt healthy dietary habits. In our study, the mean value of each metabolic parameter like BMI, triglycerides and fasting blood sugar was significantly higher in patients with metabolic syndrome than those without metabolic syndrome. Moreover, use of atypical antipsychotics produced about four times greater likelihood for developing MS. This is of concern because atypical antipsychotics are the first-choice medications for schizophrenia bipolar disorder and psychotic disorder. Psychiatric patients frequently abandon their psychopharmacological treatment and this is an important cause of hospitalization. Thus, one can suppose that many of the patients evaluated had not been using their medication in the weeks or months that preceded their hospitalization. Length of time since onset of illness and a later onset of illness were significantly associated with MS, indicate that MS may be associated with either or both the chronic mental illness or the long term medication in such subjects.

Conclusion

Our study showed that the prevalence of metabolic syndrome among psychiatric patients was significantly high. The overall prevalence of metabolic syndrome in our study was 43.11%. The prevalence of MS stratified by diagnoses was 22.5% (n=69) for schizophrenia, 17% (n=52) for bipolar disorder, 3.58% (n=11) for psychotic disorder. The prevalence of metabolic syndrome was highest (39.24%) in patients receiving second generation antipsychotics, followed by those on the combination of first generation and second generation antipsychotics (28.01%). Patients with schizophrenia or those on second generation antipsychotics had higher prevalence. Female gender and increasing age were associated with greater risk.

In our study elevated fasting blood sugar level and BMI were highest among patients taking olanzapine and risperidone, followed by haloperidol. Elevated triglyceride levels were highest among patients taking risperidone and haloperidol. In our study, the prevalence of metabolic syndrome was highest (29.64%) in patients with BMI above cut off levels, followed by those with elevated glucose levels (11.72%) and elevated lipid levels (1.62%). All those approaching higher BMIs should be evaluated for MS, advised to increase physical exercise and adopt healthy dietary habits. Although MS is recognized worldwide as a distinct entity, the guidelines for identifying MS by different organizations vary. Using different guidelines in the same sample may yield considerably different estimates for MS prevalence. Prevalence rates of metabolic syndrome have varied from 26% to 52.2% in various cross-sectional studies.

We could hypothesize that these differences in prevalence may be due to different lifestyles and eating habits and the diet. In addition to possible effects due to medications, other factors may be involved in the MS onset, such as biological vulnerability associated with the mental disorder itself and

additional risk factors such as lack of physical activity and unbalanced diet. As these factors were not evaluated in this study, it cannot be excluded a priori that they have influenced the results. Thus, we conclude that the people with major mental disorders are at greater risk of metabolic syndrome that impacts their morbidity and mortality. These patients often receive inadequate medical care and low rates of treatment for co-morbidities like DM, hyperlipidemia and obesity. Health-care providers should be trained and sensitized for monitoring schizophrenic patients for metabolic derangements. Methods to tackle MS and the responsible risk factors should be incorporated as part of the detailed workup and management protocol for schizophrenia and other psychiatric disorders like bipolar disorder and psychotic disorder. In conclusion, treatment of psychiatry patients requires attention to not only their psychiatric conditions but also associated medical conditions by individual health care practitioners and hospital as well as the public health care sector as a whole.

Acknowledgement
The authors wish to thank the management of PES College of Pharmacy, Bengaluru, Karnataka, India for providing necessary equipment for research, constant encouragement, facilities and support. We personally thank to Dr. P Lokeswara Reddy, M.D., Associate Professor of Psychiatry, Government General Hospital, Guntur Medical College, Guntur, Andhra Pradesh, India for his support.

Conflicts of Interest
The author declares that there is no conflict of interest to disclose.

References
1. Alp Ucok, Wolfgang Gaebel. Side effects of atypical antipsychotics: a brief overview. World Psychiatry. 2008; 7:58-62.
2. John W Newcomer. Second Generation (Atypical) Antipsychotics Metabolic Effects: A Comprehensive Literature Review. CNS Drugs 2005, 1-93.
3. Hee-Yun Kim, Hee-Won Lee, Seung-Ho Jung. Prescription Patterns for Patients with Schizophrenia in Korea: A Focus on Antipsychotic Polypharmacy. Clinical Psychopharmacology and Neuroscience 2014; 12(2):128-136.
4. Yogaratnam J, Biswas N, Vadivel R. Metabolic Complications of Schizophrenia and Antipsychotic Medications - An Updated Review. East Asian Arch Psychiatry. 2013; 23:21-8.
5. Guidelines on Choice and Selection of Antipsychotics for the Management of Psychosis and Schizophrenia in Adults, 2019, 1-22.
6. Rebecca Ronsley, Duc Nguyen, Jana Davidson *et al.* Increased Risk of Obesity and Metabolic Dysregulation Following 12 Months of Second-Generation Antipsychotic Treatment in Children: A Prospective Cohort Study. The Canadian Journal of Psychiatry. 2015; 60(10):441-450.
7. Malhotra N, Grover S, Chakrabarti S, Kulhara P. Metabolic syndrome in schizophrenia. Indian Journal of Psychological Medicine. 2013; 35(3):227-40.
8. Pallava A, Chadda RK, Sood M, Lakshmy R. Metabolic syndrome in schizophrenia: A comparative study of antipsychotic-free/naïve and antipsychotic-treated patients from India. Nord J Psychiatry. 2012; 66:215-21.
9. Sugawara N, Yasui-Furukori N, Sato Y, Umeda T, Kishida I, Yamashita H. Prevalence of metabolic syndrome among patients with schizophrenia in Japan. Schizophr Res. 2010; 123:244-50.
10. Medeiros-Ferreira L, Obiols JE, Navarro-Pastor JB, Zúñiga-Lagares A. Metabolic syndrome and health-related quality of life in patients with schizophrenia. Actas Esp Psiquiatr. 2013; 41(1):17-26.
11. John AP, Koloth R, Dragovic M, Lim SC. Prevalence of metabolic syndrome among Australians with severe mental illness. Med J Aust. 2009; 190:176-9.
12. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA *et al*. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009; 120:1640-5.