IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
August 2022 Vol.:25, Issue:1

Incidence and Risk of Hyperglycemia in Psychiatric Population on Atypical Antipsychotics

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Prudence A Rodrigeus, Yogavadula.S.S*, Vijay.R, Vinitha.B, Ummay Salma

Department of Pharmacy Practice, PSG college of Pharmacy, Coimbatore, India

Submitted: 25 July 2022
Accepted: 31 July 2022
Published: 30 August 2022

Keywords: Atypical Antipsychotics, schizophrenia, hyperglycemia, blood glucose levels, risk factors.

ABSTRACT

BACKGROUND: Antipsychotics are associated with an increased risk of adverse metabolic outcomes, including weight gain, dyslipidaemia, and hyperglycaemia. Increases in adiposity and disturbances in glucose and lipid metabolism represent a serious health risk in a patient that may be predisposed to these metabolic conditions. The increased risk for diabetes with certain antipsychotics may be associated with the risk of treatment-induced weight gain. OBJECTIVE: To assess whether antipsychotics causes hyperglycaemia, to monitor the patient's blood glucose levels and predisposing risk of diabetes in non-diabetic psychiatric patients. METHODOLOGY: A total of 52 psychiatric inpatients recently diagnosed with psychiatric illness and taking atypical antipsychotics for the first time were included in the study. Their FBS and RBS levels were monitored at baseline (Day1) and followed up at Day 15. From these values the incidence rate of hyperglycaemia in psychiatric population in drug naïve patients taking atypical antipsychotics was determined. American Diabetes Association risk assessment tool was used to test the predisposing risk in these patients. RESULTS: In this study, 76 psychiatric inpatients who were prescribed with atypical anti-psychotics were screened among which 52 patients were monitored for glucose levels at day 1(baseline) and day 15(follow-up) based on the length of required hospital stay. RBS and FBS levels were documented during the study to assess whether atypical anti-psychotics induced hyperglycaemia. Only 8 patients developed hyperglycaemia within 15days of hospital stay as a result of atypical anti-psychotics. CONCLUSION: In the present study, it was confirmed that occurrence of hyperglycaemia within 15days secondary to atypical antipsychotics use in drug naïve patients was found to be rare. The incidence of atypical antipsychotics induced hyperglycaemia from our study showed the need to monitor the blood glucose levels in patients taking atypical antipsychotics.

INTRODUCTION

Psychiatric disorders have a potential impact on health and major social, human rights, and economic consequences around the world.[1] Only a significant fraction of the world's 400 million people with the psychiatry disease receive competent psychiatric care. [2] The discipline of psychiatry is in serious need of a therapy breakthrough, as most psychiatric drugs are over 40 years old.[3] Antipsychotics are the first line of treatment for schizophrenia and other primary psychotic illnesses, according to literature. Antipsychotics medications have various side effects, ranging from minor tolerability issues (e.g., mild sedation or dry mouth) to extremely unpleasant (e.g., constipation, akathisia, sexual dysfunction) to painful (e.g., acute dystonia) to disfiguring (e.g., weight gain, tardive dyskinesia) to life-threatening (e.g., myocarditis, agranulocytosis).[4] ADRs are common in these individuals who are taking antipsychotic medications, which are usually moderate. As a result, recognizing and managing these side effects can help to ensure that the patient receives the best possible care. [5] Weight gain, decreased glucose metabolism, worsening of existing type 1 and type 2 diabetes, new occurrence of type 2 diabetes mellitus and diabetic ketoacidosis are all linked to antipsychotic drug use. [6,7] Patients with schizophrenia are 2–3 times more likely than individuals in the general community to develop type 2 diabetes, even if they are medication naive. Furthermore, diabetes is commonly misdiagnosed and undertreated in schizophrenic patients, and screening methods fluctuate greatly between clinical investigations. Also, atypical antipsychotics have been linked to a greater increase in weight gain than traditional antipsychotics. The amount of weight gain caused by atypical antipsychotics varies from patient to patient. Compared to other treatments, clozapine and olanzapine-treated patients had the highest maximum weight gain and gained weight for a longer period. Intermediate amounts of weight gain were found in Risperidone-treated patients. [8] Hyperglycemia was usually reversed when therapy discontinued and resurfaced when treatment was resumed in the majority of cases. [9, 10] So, it is necessary to monitor the blood glucose level of patient taking second generation anti-psychotics to prevent ADR like weight gain and diabetes mellitus.

MATERIALS AND METHODS

A prospective observational study was conducted in the department of psychiatry in PSG hospitals after obtaining the ethical approval from IHEC. The sample size was calculated using rao soft sample size calculator. Patients were selected based on inclusion and exclusion

criteria. Psychiatric inpatients of age greater than 18years prescribed with atypical anti-psychotics, both male and female patients and who are adherent to medications with at least use of one atypical antipsychotic not less than 15days of hospital stay were included. Patients below 18years of age with medical history of diabetes mellitus or CAD related co-morbidities, pregnant women's and patients who are not willing to participate were excluded. Informed consent form was provided to each patient or to the patient's legal representative depending on their preferable language. Patient information was collected from inpatient files where information of admission date, IP/OP number, age, sex, weight, height, occupation, medical history and medication history, family history, allergies, social history, complaints on admission, diagnosis, vital signs, drugs prescribed, dose and frequency were collected.

In the initial visit (Day1) base line blood glucose values were assessed by collecting Fasting Blood Sugar (FBS) and after one hour Post Prandial Blood Sugar (PPBS) values using Accu-check glucometer. In the follow up visit (Day15) FBS value and PPBS value were assessed. According to WHO, FBS values >100mg/dl and PPBS values >200mg/dl were considered as hyperglycemia in this study.

The patients FBS and PPBS values are compared and assessed for any change in the basal glucose values after the intake of atypical antipsychotics. American diabetes association Risk assessment tool given to the Patients legally accepted representative, the questions to be answered are patients age, sex, weight, history of gestational diabetes, family history of diabetes mellitus, blood pressure status and status of physical activity. Each category was given a score and the total score added to obtain the final score. Patients with a total score of score 5 or above are at higher risk for developing type 2 diabetes mellitus. Thus, the patients at higher risk are excluded from this study and it confirms that only SGA are responsible for causing hyperglcemia other than any other factors. Statistical analysis was done using IBM SPSS statistical software version 26 gratis. A significance level of 0.05 was used. The probability risk of hyperglycemia was statistically analyzed using the Chi-Square test.

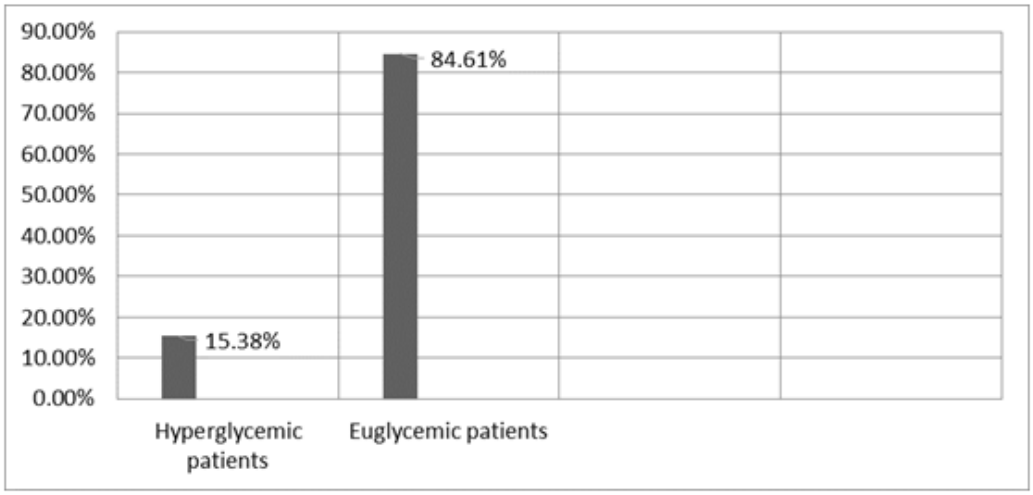

FIGURE I: INCIDENCE OF HYPERGLYCEMIA

RESULTS

Between May 2021 and Oct 2021 52 psychiatric patients with no previous history of any psychiatric disorders were admitted in department of Psychiatry in PSG hospitals. A total of 76 drug naive psychiatry in patients were screened. Of these 52 patients were recruited for the assessment of hyperglycaemia induced by atypical anti psychotics.

TABLE I: HYPERGLYCEMIC INCIDENCE OF PATIENTS

PARAMETERS	HYPERGLYCEMIC INCIDENCE
Male	16.6%
Female	20%
Age	
<20	1.9%
21–40	9.6%
41–60	1.9%
>60	1.9%
Family history	
Yes	11.5
No	3.8%
Weight status	
Over-weight	1.9%
Normal	13.4%
Physical activity	
Yes	9.6%
No	5.7%

DEMOGRAPHIC CHARACTERISTICS

Among 52 psychiatric patients 24 were male (46.2%) and 28 were female (53.8%). Mean age was 33.67 years. Out of 52 patients 13.4% were aged less than 20, 63.8% were between 21 and 40, 17.1% were between 41, and 60 and 5.7% were greater than 60%.The diagnosis and treatment varies for each patient (Table III). On examining the FBS and PPBS values on Day 1 and Day 15, 8 drug-naïve psychiatric patients were found to be hyperglycemic on Day 15. The incidence of hyperglycemia was 15.38%. (Figure I) The study population was divided into eight broad categories of psychiatric illness, out of which schizophrenia had the highest incidence (n=3) compared to other conditions like depression, anxiety disorder, personality disorder, OCD, BPAD and psychosis. OLANZAPINE was commonly prescribed at different doses [46.1 %(n=24)] and the same has exhibited higher incidence of hyperglycemia (16.6%) in patients, followed by OLANZAPINE and RISPERIDONE combination which was 5.8% (n=3) and all 3 exhibited hyperglycemia (100%).The difference was seen within 15 days. Among 8 patients who developed hyperglycemia, 4 were male (20%) and 4 were female (16.6%) which was not significant. Mean of FBS is 93.21mg/dl and PPBS is 119.13mg/dl on Day1 whereas FBS and PPBS values on Day 15 were found to be 95.83mg/dl and 125mg/dl respectively. Therefore, the increase in FBS and PPBS values within 15days was not significant. Cumulative values are given in figures II and III.

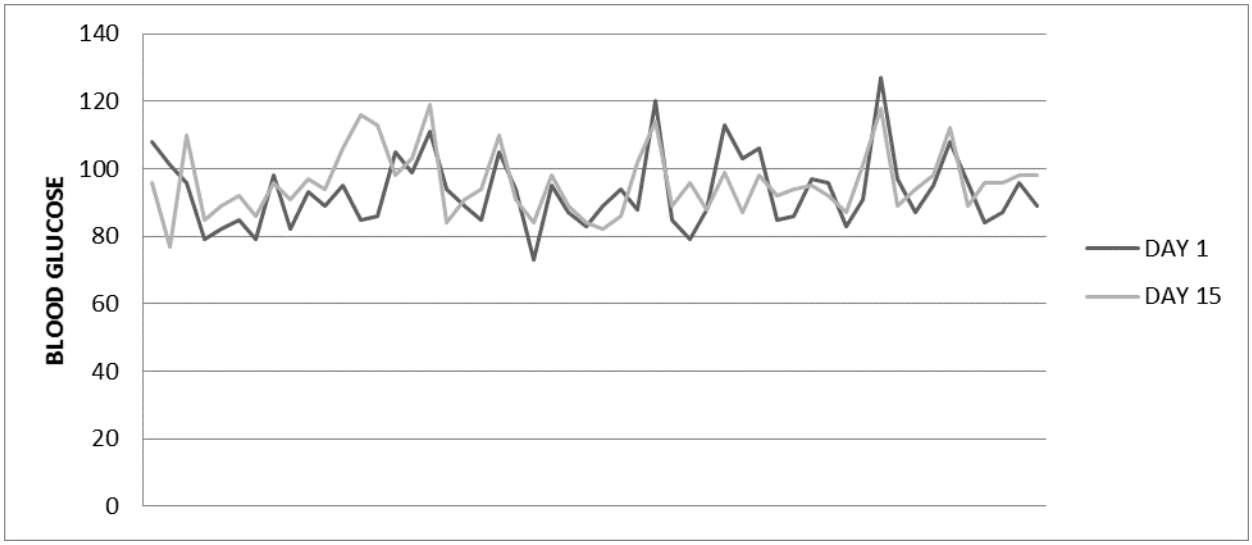

FIGURE II: FBS VALUES OF PATIENTS

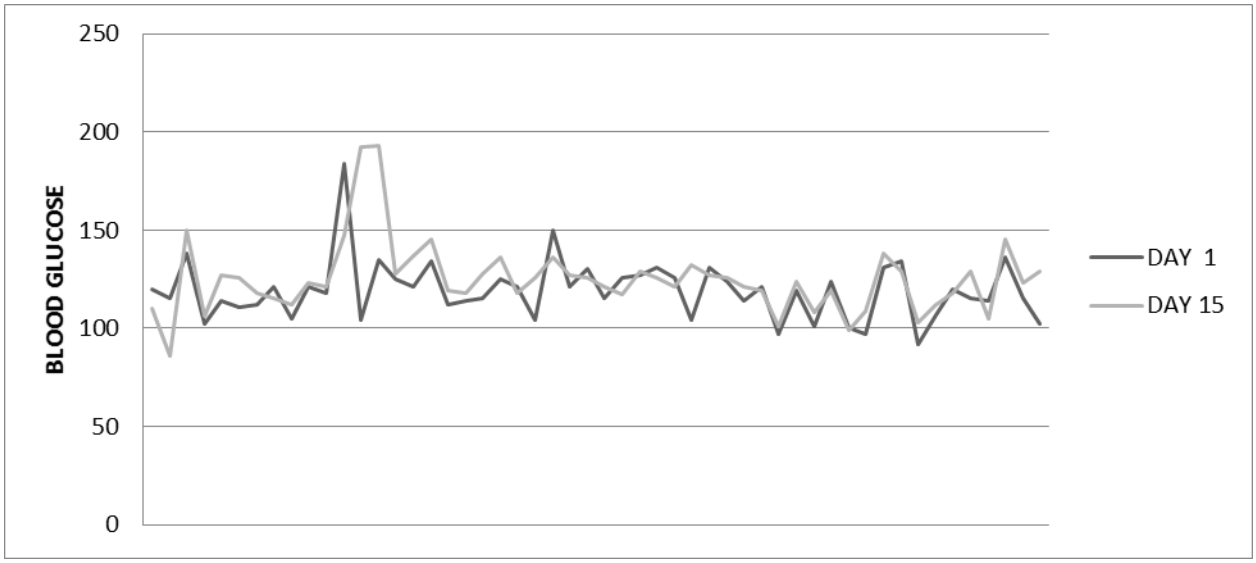

FIGURE III: RBS VALUES OF PATIENTS

The American Diabetic Association risk assessment tool was used to assess the risk of type-2 diabetes mellitus in patients taking atypical antipsychotics. The factors included were age, weight, gender, BMI, family history, gestational diabetic history, physical activity and previous history of high blood pressure. The risk score of greater than 5 is considered a high risk for Type 2 diabetes mellitus. Even though the psychiatric patient showed increased FBS and PPBS values, hyperglycemic symptoms were absent.

TABLE II: PROFILE OF PATIENTS DEVELOPED HYPERGLYCEMIA

S.NO	GENDER	AGE	FAMILY HISTORY	WEIGHT STATUS	PHYSICAL ACTIVITY	DRUG THERAPY	DIAGNOSIS	RISK SCORE
1	Male	32	Yes	No	Yes	Risperidone 2mg	Schizophrenia	3
2	Female	62	No	No	Yes	Risperidone 2mg+Olanzapine 5mg	Schizophrenia	4
3	Male	40	Yes	Yes	Yes	Olanzapine 10mg	Mania	4
4	Male	34	Yes	Yes	No	Olanzapine 10mg	Bipolar affective disorder-current episode of mania	4
5	Female	42	Yes	Yes	No	Olanzapine 5mg	Depression	5
6	Female	29	No	Yes	No	Olanzapine 10mg	Schizophrenia	2
7	Female	19	Yes	No	No	Risperidone 4mg+olanzapine 10mg	Severe depression	2
8	Male	26	Yes	Yes	Yes	Risperidone 4mg+olanzapine 10mg	Bipolar maniac episode	3

TABLE III: INCIDENCE OF DISEASE AND DRUGS AMONG SUBJECTS

	PARAMETERS	INCIDENCE AMONG SUBJECTS
DISEASE	Schizophrenia	32.7%
	Depression	25%
	BPAD	23.1%
	Psychosis	9.6%
	Personality Disorder	3.8%
	Anxiety Disorder	3.8%
	OCD	1.9%
DRUGS	Olanzapine	46.2%
	Quetiapine	9.6%
	Risperidone	26.9%
	Risperidone + Olanzapine	11.5%
	Risperidone + Quetiapine	5.8%

DISCUSSION

This study tried describing the association between atypical antipsychotics and risk of hyperglycemia within 15days in drug naïve psychiatric patients. Various studies in animal models have proved that atypical anti-psychotics cause hyperglycemia in short duration (1month) but there were very limited human studies that have evaluated this effect so it is a fummox to declare a conclusion. Even though the results of this study didn't show the risk of developing hyperglycemia within 15days of treatment initiation, the study emphasis the need for blood glucose monitoring in psychiatric patients taking atypical anti-psychotics.

Hyperglycaemia results from either impaired ability of insulin to stimulate glucose uptake into peripheral tissues or reduced ability of insulin to suppress glucose production by the liver coupled with inappropriate insulin secretion. Bergman et al demonstrated that metabolic side effects seen with some atypical antipsychotic medications could be amplified by, or caused by, pharmacological effects on one or more of these target organs. [11] Antipsychotics have been linked to weight gain, dyslipidemia, and diabetes, according to growing data. [10] Weight gain was not found in the study population because of the antipsychotic medication. Weight gain-independent hyperglycemia does occur, too, and can be reversed by switching to another antipsychotic, according to previous epidemiological evidence. [12] Houseknecht et al. reported the first proof that OLAN and CLOZ create severe whole-body insulin resistance after a single dose, with no changes in weight or body composition. [13] Although various animal models have shown that atypical antipsychotics promote hyperglycemia in the near term, there have been few human trials to back up these findings.

The incidence rate of hyperglycemia induced by atypical antipsychotics was estimated to be 15.38 percent in the current study, and this was confirmed. Males (20%) were found to have a greater rate of atypical antipsychotic-induced hyperglycemia in the acute phase than females (16.6 percent). Men, according to the research, are at a higher risk of hyperglycemia than women. [14] The insignificance of the incidence rate could be due to the small sample size (n=52).

Meyer et al. and McEnoy et al. determined that schizophrenia has an impact on the pathophysiology of diabetes, which is 1.5–2 times more prevalent in schizophrenic patients than in the normal population. [15,16] According to the existing evidence, persons with

schizophrenia are more likely to acquire diabetes mellitus, and taking antipsychotic medication increases the risk of developing non-insulin-dependent hyperglycemia. [17]

Not all the second generation drugs cause hyperglycemia but the most common drugs are **OLANZAPINE, RISPERIDONE, and QUETIAPINE**. Among the atypical antipsychotics administered, the combination of Olanzapine-Risperidone had the highest incidence followed by olanzapine monotherapy followed by Risperidone monotherapy. Quetiapine and Risperidone-Quetiapine combination was not associated with hyperglycemia. Olanzapine is becoming increasingly popular as a first line agent for treating psychosis and in mood disorders, therefore proper guidelines must be established for monitoring blood glucose levels and determination of risk factors for diabetes mellitus.

All the drugs were given in different doses depending upon individual patient conditions. The increased dose was found to have higher incidence of hyperglycemia in patients. Occurrence of hyperglycemia was found for Olanzapine 10mg monotherapy, Olanzapine 10mg plus Risperidone 4mg , Olanzapine 5mg plus Risperidone 2mg and even for Risperidone 2mg monotherapy (n=2). Among this group the patients who developed hyperglycemia were also predisposed to any one the factors influencing i.e., age, weight, family history. Some studies show that the incidence of hyperglycemia due to atypical antipsychotic dose independent. [18] However, this study shows higher dose of olanzapine and combination of olanzapine and risperidone is associated with higher incidence of hyperglycemia.

The study also assessed risk factors for type 2 diabetes mellitus using American Diabetes Association Risk Assessment Tool for Type 2 Diabetes Mellitus that included factors such as age, weight, gender, BMI, family history, gestational diabetic history, physical activity and previous history of high blood pressure. The risk score performed with reasonable sensitivity and specificity, and it could therefore form part of a strategy for early detection of type 2 diabetes. [19] This study compared the risk scores with incidence of hyperglycaemia to find the patients who were predisposed to type 2 diabetes. Since most of patients were between the age group of 21–40 years the risk score was not more than 5 except for 1 patient. Therefore, there were no high-risk patients in our study population. Some patients were found to predispose diabetes based on their family history, physical activity and weight status.

CONCLUSION

In this study, we confirmed that the incidence is less hence the risk of hyperglycemia within a period of 15days is limited and largely dependent upon the individual characteristics. Therefore, this study warrants the healthcare professionals of psychiatry department to monitor the glycemic profile of the psychiatric population receiving certain atypical antipsychotics(ie., drugs observed in this study) to prevent hyperglycemia and further complications that may occur when this goes unnoticed.

REFERENCES

1. Mental health- WHO 28 Nov 2019 Available from: https://www.who.int/news-room/fact sheets/detail/mental-disorders
2. CDC [online database] Mental Health. Atlanta, GA. (accessed 2015 August). Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5434a1.htm.
3. Krystal JH, State MW. Psychiatric disorders: diagnosis to therapy. Cell. 2014 Mar 27;157(1):201-14.
4. Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry. 2018 Oct;17(3):341-56.
5. Angadi NB, Mathur C. Prevalence and Severity of Adverse Drug Reactions Among Patients Receiving Antipsychotic Drugs in a Tertiary Care Hospital. International Journal of Nutrition, Pharmacology, Neurological Diseases. 2020 Jul 1;10(3):144.
6. Haupt DW, Newcomer JW. Hyperglycemia and antipsychotic medications. Journal of Clinical Psychiatry. 2001 Jan 14;62(27):15-26.
7. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ. Antipsychotic-induced weight gain: a comprehensive research synthesis. American journal of Psychiatry. 1999 Nov 1;156(11):1686-96.
8. Wirshing DA, Wirshing WC, Kysar L, Berisford MA, Goldstein D, Pashdag J, Marder SR. Novel antipsychotics: comparison of weight gain liabilities. The Journal of clinical psychiatry. 1999 Jun 30;60(6):12925.
9. Rouillon F, Sorbara F. Schizophrenia and diabetes: epidemiological data. European Psychiatry. 2005 Dec 1;20: S345-8.
10. Holt RI, Bushe C, Citrome L. Diabetes and schizophrenia 2005: are we any closer to understanding the link? Journal of Psychopharmacology. 2005 Nov;19(6_suppl):56-65.
11. Bergman RN, Hope ID, Yang YJ, Watanabe RM, Meador MA, Youn JH et al (1989). Assessment of insulin sensitivity in vivo: a critical review. Diabetes/Metab Rev 5: 411–429.
12. Koller EA, Doraiswamy PM (2002). Olanzapine-associated diabetes mellitus. Pharmacotherapy 22: 841–852.
13. Houseknecht KL, Robertson AS, Zavadoski W, Gibbs EM, Johnson DE, Rollema H. Acute effects of atypical antipsychotics on whole-body insulin resistance in rats: implications for adverse metabolic effects. Neuropsychopharmacology. 2007 Feb;32(2):289-97.
14. Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. Endocrine reviews. 2016 Jun 1;37(3):278-316.
15. Meyer JM, Nasrallah HA, McEvoy JP, Goff DC, Davis SM, Chakos M et al (2005). The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial: clinical comparison of subgroups with and without the metabolic syndrome. Schizophrenia Res 80: 9–18.
16. McEvoy JP, Meyer JM, Goff DC, Nasrallah HA, Davis SM, Sullivan L et al (2005). Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of

Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III B. Schizophrenia Res 80: 19–32.
17. Lambert MT, Copeland LA, Sampson N, Duffy SA. New-onset type-2 diabetes associated with atypical antipsychotic medications. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2006 Jul 1;30(5):919-23.
18. Lindenmayer JP, Nathan AM, Smith RC. Hyperglycemia associated with the use of atypical antipsychotics. J Clin Psychiatry. 2001; 62 Suppl 23:30-8.
19. Park PJ, Griffin SJ, Sargeant L, Wareham NJ. The performance of a risk score in predicting undiagnosed hyperglycemia. Diabetes care. 2002 Jun 1;25(6):984-8.

Image *Author -1*	***YOGAVADULA.S.S*** *DEPT. OF PHARMACY PRACTICE* *PSG COLLEGE OF PHARMACY, COIMBATORE*
Image *Author -2*	***VIJAY.R*** *DEPT. OF PHARMACY PRACTICE* *PSG COLLEGE OF PHARMACY, COIMBATORE*
Image *Author -3*	***UMMAY SALMA.F*** *DEPT. OF PHARMACY PRACTICE* *PSG COLLEGE OF PHARMACY, COIMBATORE*
Image *Author -4*	***VINITHA.B*** *DEPT. OF PHARMACY PRACTICE* *PSG COLLEGE OF PHARMACY, COIMBATORE*
Image *Author -5*	***PRUDENCE A RODRIGUES*** *DEPT. OF PHARMACY PRACTICE* *PSG COLLEGE OF PHARMACY, COIMBATORE*