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# Risperidone versus quetiapine: risk of developing metabolic syndromes in patients suffering from psychiatry disorders of a health care center

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## ABSTRACT

Second generation atypical antipsychotics (SGAAPs) have been used as first-line drugs in psychiatric practice for a wide range of psychotic disorders. These drugs effectively exert therapeutic effects of positive symptoms, negative symptoms, and cognitive impairments. Utilization of SGAAPs in this present scenario has raised questions with respect to their tolerability and adverse drug reactions such as obesity, cardiovascular disorders and other metabolic disorders. The aim of our research project is to compare the risk of metabolic disorders associated with the usage of drugs (Risperidone versus Quetiapine) in psychiatric patients. Our study objective is to assess prognosis reports, compare BMI, FBS, lipid profile and counsel psychiatric patients by providing patient information leaflets. This is a hospital based prospective observational randomized control trial was conducted for a period of 6 months at Government General Hospital (RIMS), Kadapa. 50 patients (25 patients prescribed with Risperidone & 25 patients prescribed with Quetiapine) were recruited based on study criteria. In a total of 50 patients, it was found that 15 patients were males and 35 patients were females. Maximum number of patients (i.e., 17 patients) belonged to 36-50 years' age group. Majority of patients (i.e., 20 patients) receiving SGAAPs had clinical diagnosis as schizophrenia. During 180 to 200 days of study, 3 follow ups were done, with time duration of 30 days between each follow up. The mean value of BMI was 23.46 for Risperidone patients & 22.01 for Quetiapine patients. The mean value of FBS was 90.52 for Risperidone patients & 89.40 for Quetiapine patients. The mean value of total cholesterol was 157.04 for Risperidone patients & 150.32 for Quetiapine patients. The mean value of triglycerides was 123.72 for Risperidone patients & 118.76 for Quetiapine patients. On assessing the above results, we have concluded that Risperidone has increased risk of developing metabolic syndromes when compared to Quetiapine.

## INTRODUCTION

According to World Health Organization (WHO), Health is a state of complete physical, mental and social well-being, and not merely absence of disease or infirmity [1,2]. For better understanding, psychiatric disorder is defined as a disturbance of Thought, Action, Feeling or any imbalance among mentioned three domains. However, this definition does not have much significance in this era. Another way to describe psychiatric disorder or mental disorder is as a clinically significant psychological or behavioral syndrome that causes significant (subjective) distress, (objective) disability, or loss of freedom [3]. Mental status examination is a standardized format that depends on clinical records, signs and symptoms experienced by psychiatric patients. MSE describes relevant information about mental functioning at the time of interview

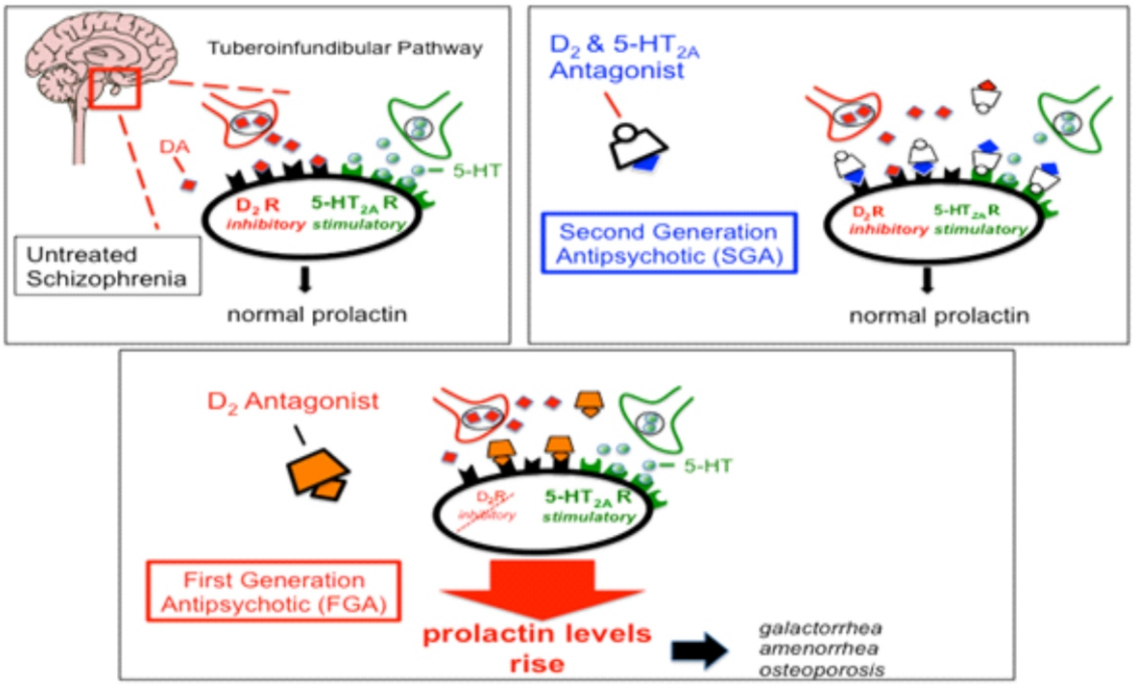


**Fig. 1 :** MOA of FGA & SGA

[4,5]. Most common psychiatric disorders are Anxiety disorders, Personality disorders, Bipolar Disorder, Obsessive Compulsive Disorder, Mood Disorders, Depression, Alcohol dependence disorder, Substance misuse disorder, Eating disorders, Schizophrenia, Delirium, Dementia, Phobias etc. [6] Antipsychotics, also categorized as neuroleptics or major tranquilizers. These drugs belong to class of medications that are primarily used to manage psychosis (including delusions). One of the most significant therapeutic usage is schizophrenia management and other bipolar disorder. Generally, Antipsychotics are effective in relieving symptoms of psychosis in less duration with favorable outcomes. Utilization of antipsychotics for longer durations is associated with certain untoward effects like enlargement of breast (gynecomastia), reduction in testes function (impotence), increased weight (obesity) and other metabolic syndromes [7]. Typical Antipsychotics also known as FGA's (first generation antipsychotics) used to treat psychosis, developed during 1950s. Typical antipsychotics are also being used for mania and agitation treatment. Phenothiazines are the first developed typical antipsychotics in globe. Drowsiness, dry mouth, blurred vision, weight gain, agitation, constipation, dizziness, stuffy nose, breast tenderness, liquid discharge from breasts, missed periods, muscle stiffness and spasms are common side effects. Examples of Typical antipsychotics are Chlorpromazine, Levomepromazine, Mesoridazine, Promazine, Thioridazine, Loxapine, Droperidol, Flupentixol, Haloperidol. [8] Atypical antipsychotics abbreviated as AAP, also known as second generation antipsychotics (SGAs). In general, these drugs are also termed as major tranquilizers. These drugs are also widely used to treat various psychiatric conditions. The definition for atypicality depends on absence of extra pyramidal side effects, but certain evidences states that, atypical antipsychotics can induce extra pyramidal side effects (lesser degree than typical antipsychotics). Atypical antipsychotics are safer when compared to typical antipsychotics; but severe side effects have been noted such as tardive dyskinesia, diabetes, cardiac death. Significant weight gain may occur. Examples of atypical antipsychotics include Risperidone, Quetiapine, Olanzapine, Ziprasidone, Palperidone, Aripiprazole, Clozapine. [9]

Risperidone is a second generation antipsychotic that has affinity for D2, 5-HT2A, alpha 1, alpha 2 and H1 receptor. It improves negative symptoms of psychosis and reduce incidence of EPS. [10] It has high affinity for serotonin type 2 (5HT2) receptors; binds to dopamine D2 receptors with 20 times lower affinity than that for 5HT2 receptors, antagonizes alpha 1-adrenergic, and histaminergic receptors; has moderate affinity for serotonin type (5HT1C, 5HT1D, 5HT1A) receptors; has weak affinity for dopamine D1 receptors; has no affinity for muscarinic, beta 1- adrenergic, and beta2- adrenergic receptors. Quetiapine is a second-generation atypical antipsychotic drug that is used to treat schizophrenia, depression, and other bipolar disorders. Quetiapine is associated with increased therapeutic efficacy and decreased risk of adverse effects on prolong usage. It is tolerated and choice of drug for patients having more sensitivity to certain drugs. Quetiapine has affinity for D2, 5-HT2A, H1, alpha 1 and 5- HT1A receptors. However, its mechanism is unknown, but according to the dopamine theory of schizophrenia, antipsychotic effects exhibited by quetiapine is due to reduced dopaminergic neurotransmission in the mesolimbic pathway in neurons. [11] Metabolic syndromes are a leading cause of morbidity and mortality in psychiatric patients having a prevalence rate double that of non-psychiatric populations. Many research studies recommend that psychiatric patients receiving long-term usage of Atypical Antipsychotics should undergo regular monitoring of weight, symptoms of hyperglycemia, triglycerides and cholesterol levels. Evaluated parameters include Abdominal obesity: weight circumference >102 cm in men, >88cm in women, Triglycerides: LDL > 150mg/dl, HDL <40mg/dl, Fasting glucose: >110 mg/dl, Blood pressure: >130/85mmHg. [12] However, first generation antipsychotic

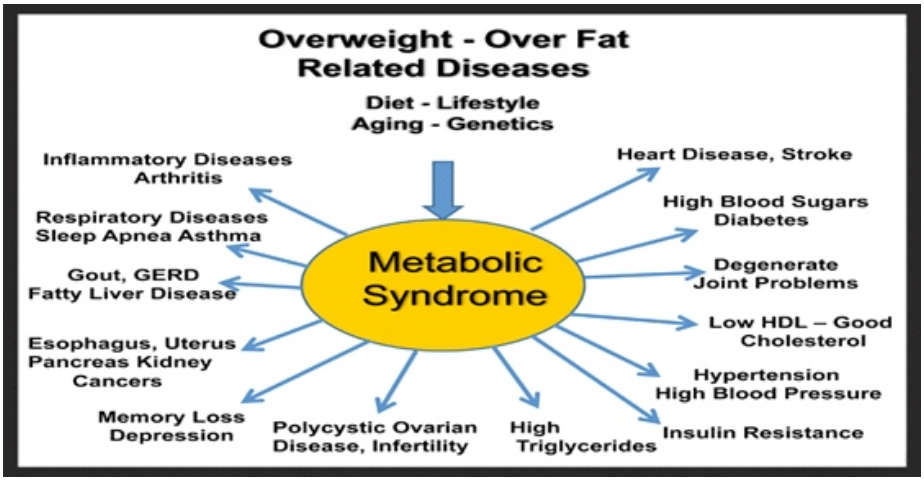


**Fig. 2 :** Patients suffering from metabolic disorders

drugs usage leads to alterations in weight, glucose metabolism, but independent of adiposity as glucose metabolism abnormalities occur with or without weight gain. Furthermore, weight gain is observed within first few months of treatment and is increased gradually as treatment is prolonged. Individual with low body mass index (BMI) are more vulnerable to these effects, manifested as intra-abdominal obesity (i.e., increased waist circumference), play a significant role in development of metabolic syndrome and affects overall quality of life of patient with psychiatric disorders. All antipsychotics especially, A typical antipsychotics associate with several adverse effects and leads to long term consequences in terms of life expectancy i.e., increased risk of hyperlipidemia and effect on glucose metabolism. [13]

## METHODOLOGY

A hospital based prospective observational study was carried out in psychiatry department patients at Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa for a period of 6 months i.e., from May 2018 to November 2019. RIMS Hospital is a 750 bedded multi-disciplinary tertiary care teaching hospital. A total of 50 patients were recruited for this study. Patient who were willing to participate, both male and female patients who were diagnosed as psychiatry disorder and prescribed with either Resperidone or Quetiapine were included in our study. Patients who were not willing to participate in the study, neonates, pediatrics, patients receiving both Risperidone and Quetiapine at the same time, patients suffering from metabolic disorders were excluded. Ethical approval was taken from respective ethical committee. After taking consent from the patient, a self-designed patient data collection form was used to collect data such as demographic details, provisional diagnosis, confirmatory diagnosis, radiographic data, social habitats, daily prognosis of patient was recorded and regular follow-ups of patients after discharge to monitor the therapy outcomes. Periodical measurements of lipid level, blood glucose level, and weight for every 4 weeks was done to a greater extent. Complete information was collected, analyzed and documented. Patients were also provided with patient information leaflets at the time of discharge.

## STATISTICAL ANALYSIS

Results were represented as frequencies, percentages, mean and medians. Percentage method was used for analyzing the data. Graph pad prism software was applied to analyze the data. In some cases, inferential statistics like analysis of variance (ANOVA) followed by student t-test, (at 95% confidence interval and $p<0.05$ considered as significant) using SPSS 21.0 software. In addition, we also utilized the facilities for regular follow ups of prescriptions for undergoing a smooth and sophisticated research work.

## RESULTS

Mental disorders can affect both the genders at different rates. Depression, schizophrenia and anxiety are more common in women when compared to men. The reasons for this is doesn't known so far. It can be due to social factors, biological factors and hormone changes during puberty. According to age group, people between 36-50 years are more prone to mental illness because these age group peoples may experience life stressors that are more common in later life because of events such as bereavement or reduced socioeconomic status after retirement. All these stressors lead to isolation, loneliness or psychological disorders in geriatric age group peoples. On the basis of clinical diagnosis, people with schizophrenia are prone to violation of human rights in mental health institutions and also in community surroundings. Stigma of schizophrenia is too high. This contributes to discrimination which can in turn limit access to general health care, education, housing & employment. Patients suffering from co-morbid medical conditions contribute to the higher mortality rate among individuals in schizophrenia patients.

### *Patients distribution based on gender:*

Out of 50 patients being recruited, it was found that 35 (70%) were females and 15 (30%) were males.

### *Patients distribution based on age groups:*

Out of 50 patients; 8 (15%) patients were found to be in 21-35 years, 17 (35%) were found to be in 36-50 years, 15 (30%) were found to be in 51-65 years, 10 (20%) were found to be in 66-80 years.

### *Patients distribution based on clinical diagnosis:*

Out of 50 patients being recruited, 20 (40%) were diagnosed as schizophrenia, 18 (35%) patients suffering from depression, 10 (20%) patients had mania symptoms, 2 (5%) patients had complaints of mental retardation.

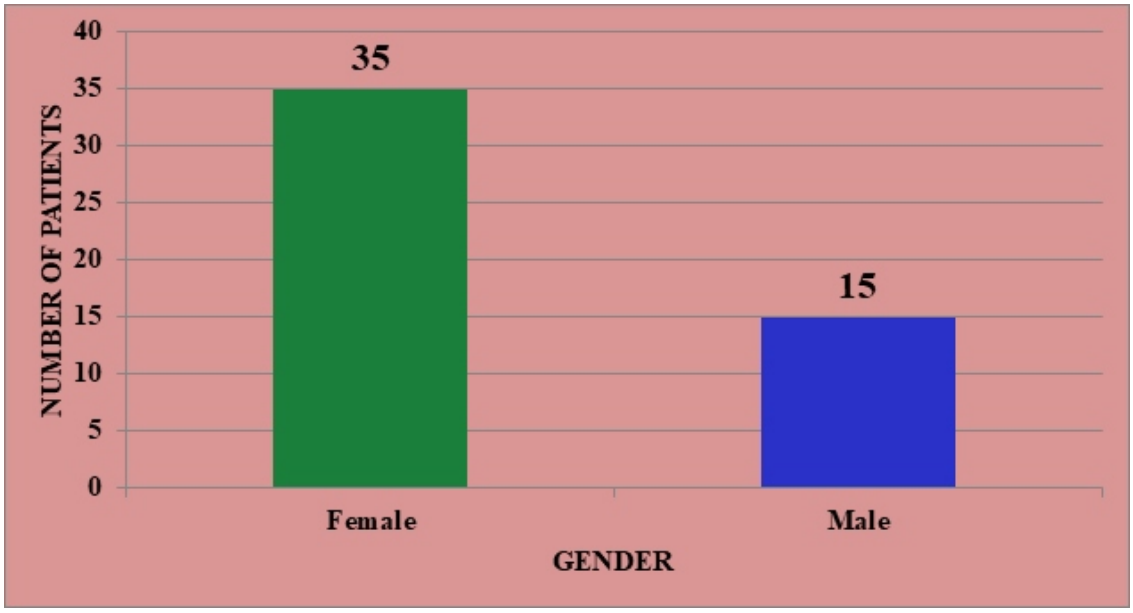


**Fig. 3 :** Graphical Representation of Female Patients & Male Patients

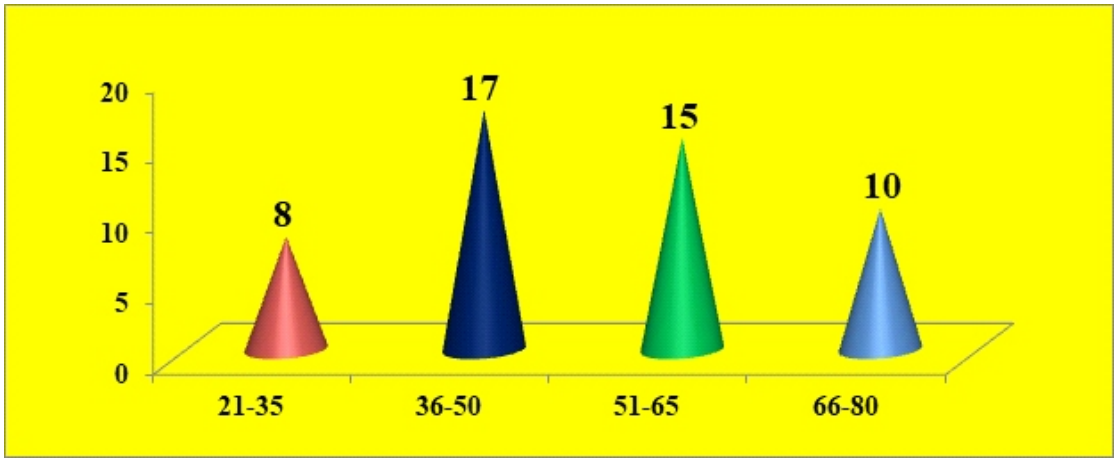


**Fig. 4 :** Graphical representation of different age groups patients

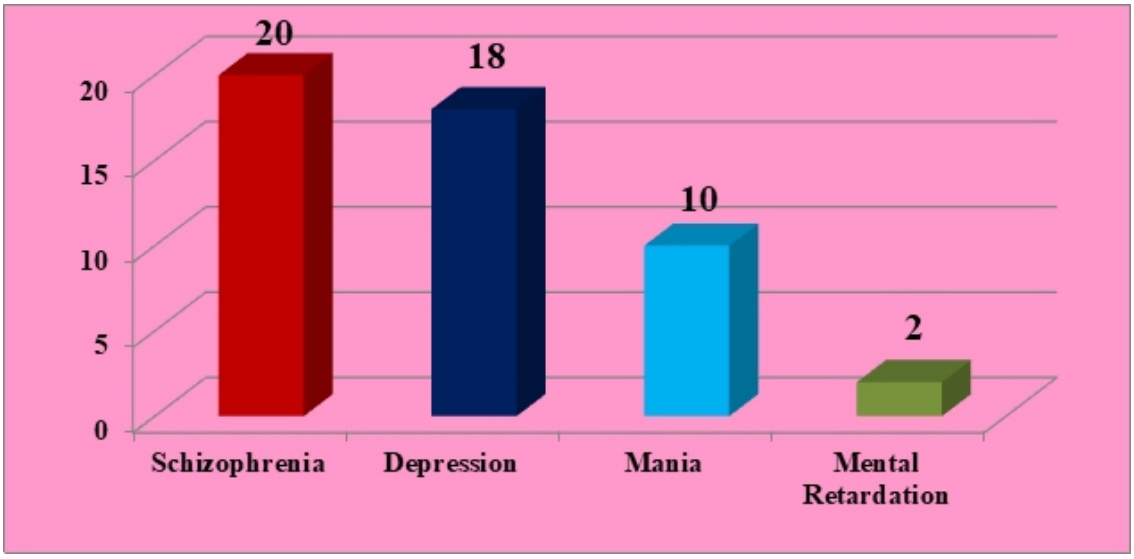


**Fig. 5 :** Graphical representation of patients based on diseases

***Assessment of Body Mass Index (BMI) levels:***

**Table No. 1:** Average value of Patients based on changes in Body Mass Index

| Name of the drug | Baseline | 1st Follow up | 2nd Follow up | 3rd Follow up |
|---|---|---|---|---|
| Risperidone | 20.64 | 21.58 | 21.73 | 22.01 |
| Quetiapine | 21.17 | 22.50 | 23.67 | 23.46 |

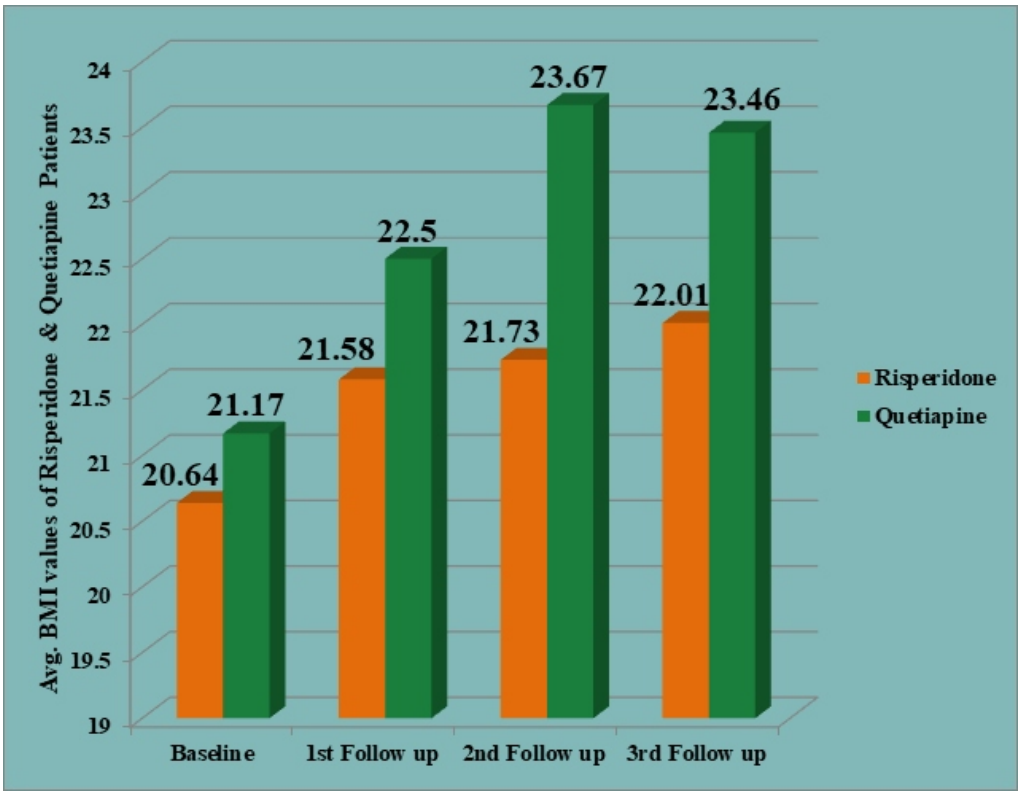


**Fig. 6 :** Average graphical representation based on changes in Body Mass Index

***Assessment of Fasting Blood Sugar (FBS) levels:***

**Table No. 1:** Average value of Patients based on changes in Fasting Blood Sugar

| Name of the drug | Baseline | 1st Follow up | 2nd Follow up | 3rd Follow up |
|---|---|---|---|---|
| Risperidone | 77.56 | 81.36 | 86.2 | 90.52 |
| Quetiapine | 89.84 | 92.0 | 92.36 | 89.4 |

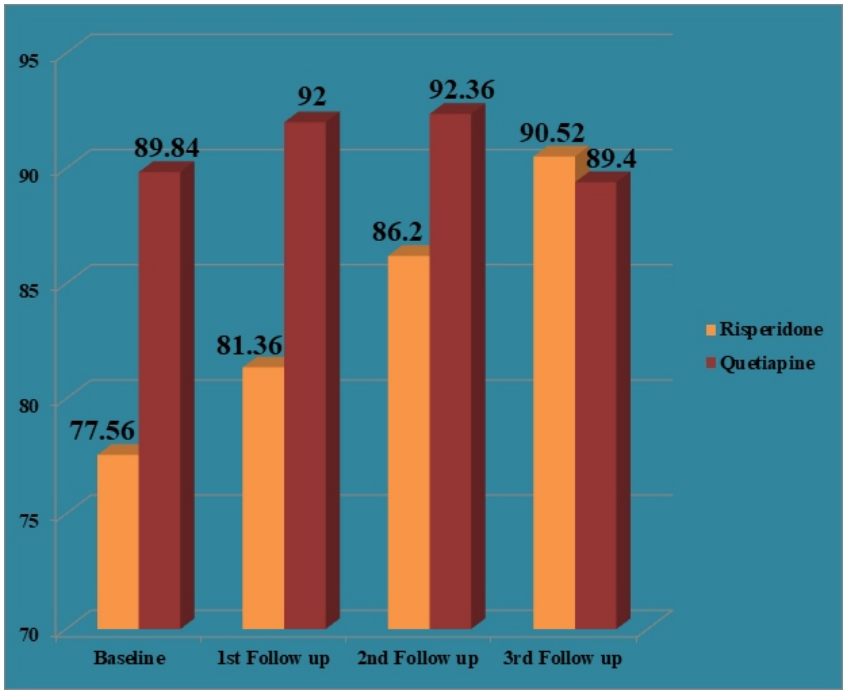


**Fig. 7 :** Average graphical representation based on changes in Fasting Blood Sugar

***Assessment of Total Cholesterol (TC) levels:***

**Table No. 3:** Average value of Patients based on changes in Total Cholesterol

| Name of the Drug | Baseline | 1st Follow up | 2nd Follow up | 3rd Follow up |
|---|---|---|---|---|
| Risperidone | 115.44 | 128.2 | 153.52 | 157.04 |
| Quetiapine | 117.24 | 140.44 | 161.08 | 150.32 |

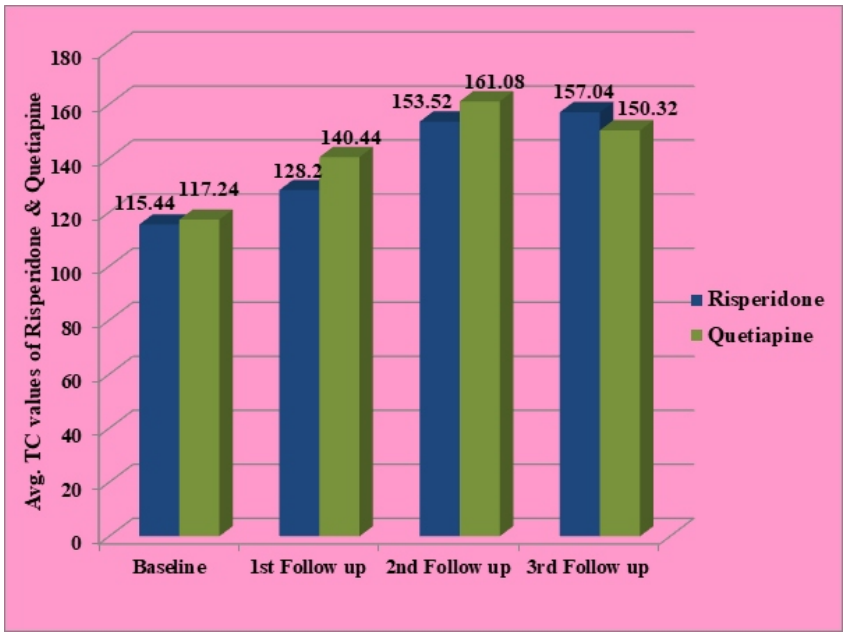


**Fig. 8 :** Average graphical representation based on changes in Total Cholesterol

***Assessment of Tri Glyceride (TG) levels:***

**Table No. 4:** Average value of Patients based on changes in Triglycerides

| Name of the Drug | Baseline | 1st Follow up | 2nd Follow up | 3rd Follow up |
|---|---|---|---|---|
| Risperidone | 100.56 | 108.96 | 116.52 | 123.72 |
| Quetiapine | 108.72 | 118.12 | 122.96 | 118.76 |

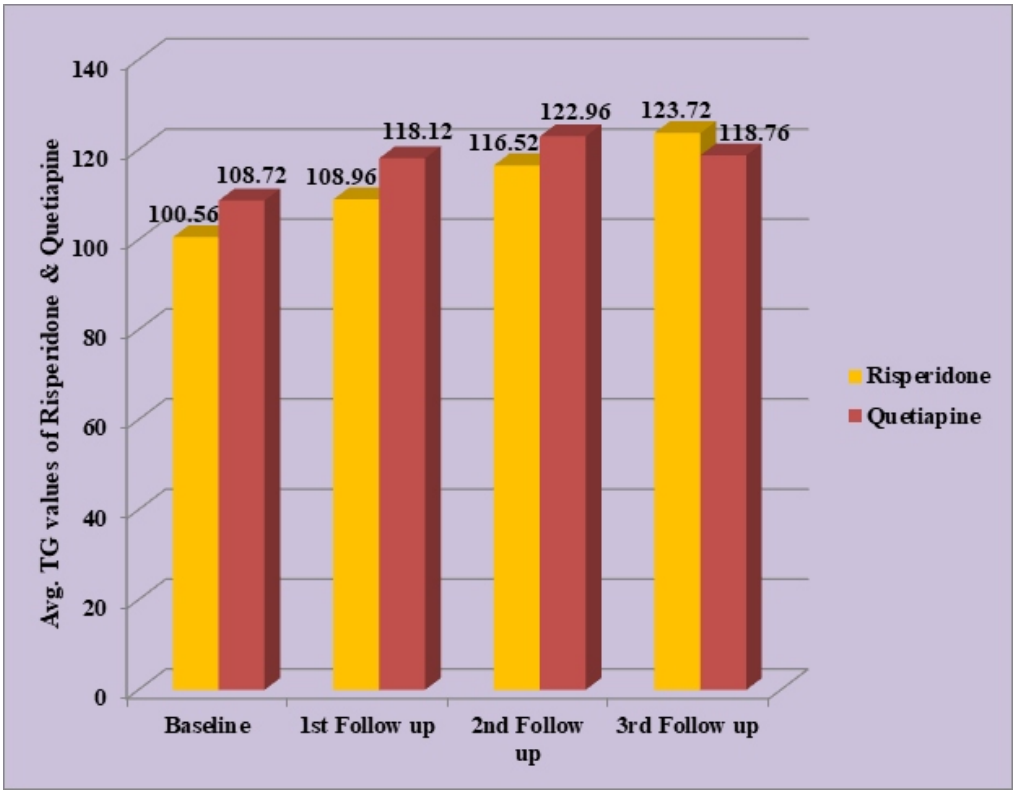


**Fig. 9 :** Average graphical representation based on changes in Triglycerides

## DISCUSSION

Within the last 20 years, there has been striking increase in the incidence of metabolic disease in psychiatric population. Along with obesity, many reports give a basic information that patients are also effecting with significant increase in blood sugar levels. Biomarkers and predictors of cardiovascular disease are consistently altered in patients experiencing low HDL, high TG and elevated free fatty acids. The increase in obesity and metabolic disease appear to coincide with the development of a new class of drugs designed to treat psychiatric disorders (schizophrenia, BPAD, depression etc.) termed the second generation anti-psychotics or atypical anti-psychotics. Our aim was to explore the SGAAP'S associated with risk of elevated BMI, blood glucose and lipid levels of patients in the psychiatric department of tertiary teaching government general hospital (RIMS), Kadapa. Performed research proposal was supported by Karen et al., "Atypical anti-psychotics and the neural regulation of food intake and peripheral metabolic disorder is more in psychiatric patients on atypical anti-Psychotics therapy."

In a total of 50 patients, 70% accounted as female and 30% were male was found during our study of 6 months. This present research study was supported by "Steven et al., (2006) conducted a study on "A double-blind comparison of risperidone, quetiapine and placebo in patients with schizophrenia experiencing an acute exacerbation requiring hospitalization". Out of 50 patients 8 (15%) patients belong to the age group of 21-35 years, 17 (35%) patients belong to the age group of 36-50 years, 15 (30%) patients belong to the age group of 51-65 years, 10 (20%) patients belong to the age group of 66-80 years and maximum number of patients were suffering from schizophrenia disorder i.e., 20 (40%) patients were having schizophrenia, 18 (35%) patients were having depression, 10 (20%) patients were having mania, 2 (5%) patients were having mental retardation. Our study was correlated with Linden et al., "Changes in glucose and cholesterol levels in patients with schizophrenia with typical or atypical antipsychotics" (2003) assessed changes in total cholesterol and

blood glucose.

Out of 50 patients it was found that there is significant increase (total cholesterol) are observed during Base line, 1st follow up, 2nd follow up & 3rd follow up. Risperidone receiving patient has increased total cholesterol and blood glucose levels compared to quetiapine. Our study was supported by Mackin et al., "Metabolic disease and cardiovascular risk in people treated with antipsychotics in the community" (2007) assessed increased in lipid profile. Out of 50 patients it was found there is significant increase in lipid profile (total cholesterol, triglycerides) both the parameters were seeming to be increased during atypical Anti-psychotic therapy resulting cardiovascular risk. Risperidone shows higher increase in lipid profile when compared with quetiapine based on averages obtaining during the baseline,1st follow up, 2nd follow up and 3rd follow up. Research hypothesis was also compared with Saifi et al, Quetiapine safety in older adults (2016). Quetiapine is an antipsychotic drug belonging to second generation, commonly prescribed psychiatry diseases in older adults. However, little information about its safety and efficacy is known in this population.

By this, quetiapine was safe and causes lesser metabolic syndromes when compared with other second generation atypical anti-psychotics. This was correlated with our study that risperidone has more risk of developing metabolic syndromes when compared quetiapine. So while instituting antipsychotic therapy a careful monitoring of at-risk patients aids in the prevention of metabolic syndrome as well as the management of any potential symptoms should they occur, suitable life style modifications are also needed to decrease problems such as increased weight (obesity). Electroconvulsive therapy can also be named as electroshock therapy in olden days. It is one of the psychiatric treatment in which seizures are electrically induced to patients so that mental relief can be adopted to psychiatric patients through sedation mechanism. ECT works better when other treatments do not give expected results after the completion of full course of treatment. [14] ECT will be a suitable option to treat severe cases of depression, treatment-resistant depression, mania, catatonia and agitation. [15]

## CONCLUSION

This research work clearly highlights the study of second generation atypical antipsychotics that increase the risk of metabolic diseases. AAPS induced weight gain is the most serious adverse effect. On long term usage of antipsychotics, majority of patients suffer from metabolic disorders like obesity, type 2 diabetes mellitus, hypertension, hyperlipidemia, atherosclerosis, ischemic stroke. From the assessment of 50 patients, it was clearly witnessed that second generation antipsychotics are emerging as treatments with valid efficacy and approved by FDA for the treatment of all phases of psychiatric disorders. It was observed that females have increased risk of developing metabolic disorders than males. It was found that majority of patients suffering from various psychiatry diseases belong to 36-50 years' age group. It was noticed that majority of psychiatry patients had schizophrenia as their clinical diagnosis. With respect to base line and three follow-up values, on assessing body mass index, fasting blood sugar, total cholesterol and triglycerides, patients treated with Risperidone has increased risk of developing metabolic disorders when compared to Quetiapine. More over the management of psychiatric disorders should be multidisciplinary including family involvement, diabetologist and non-psychiatrists to provide comprehensive care. Treatment should include anti-diabetics, anti-psychotics and psychotherapeutic interventions so that patients exhibit better life.

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## AUTHORS' CONTRIBUTIONS

1) Dr. R. Venkata Ramudu; designed the study,

2) Dr. Shaik. Kareemulla; interpreted the data and wrote the first draft of the manuscript.

3) Chaitanya Bharathi, Tejaswini, Yaseen Vamaliya, Yasmeen; wrote the protocol, collected data, managed the literature searches and performed the statistical analysis.

This manuscript has been read and approved by all the authors, and the requirements for authorship have been met, and we believe that this manuscript represents honest work.

## CONFLICTS OF INTEREST

No any conflicts of interest to disclose.

## AUTHORS FUNDING

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