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AN ANALYSIS OF TOTAL CHOLESTEROL AND SERUM TRIGLYCERIDE LEVELS IN SCHIZOPHRENIA: DRUG-NAÏVE, AFTER TREATMENT, AND THEIR FIRST-DEGREE RELATIVES

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ABSTRACT

Background: Schizophrenia, a chronic mental disorder, is often associated with metabolic abnormalities, including dyslipidemia. Antipsychotic medications, particularly second-generation antipsychotics (SGAs), which are commonly used to treat schizophrenia symptoms, have been linked to worsening these metabolic abnormalities. These drugs can cause considerable weight gain and unfavorable lipid profile alterations, thereby increasing the risk of cardiovascular disease. **Aim:** To investigate the potential variations in total cholesterol and serum triglyceride levels among drug naive, after treatment of schizophrenia patients and their first degree relatives. **Methods:** A cross sectional study of 60 participants, including drug-naïve schizophrenia patients (n=30), same patients after 2 months of treatment, and their first-degree relatives (n=30), were recruited. Lipid profiles, including total cholesterol and serum triglycerides, were measured using standardized biochemical assays. Statistical analysis was performed using ANOVA to compare the groups. **Results:** The study found significantly higher levels of total cholesterol and serum triglycerides in schizophrenia patients after-treatment compared to drug-naïve patients and their first-degree relatives. The mean ± SD values of total cholesterol were 195.9 ± 33.1 mg/dL for after-treatment patients, 171.4 ± 34.4 mg/dL for drug-naïve patients, and 161.9 ± 18.8 mg/dL for first-degree relatives. Similarly, serum triglyceride levels were 127.7 ± 34.3 mg/dL for after-treatment patients, 96.1 ± 33.0 mg/dL for drug-naïve patients, and 99.6 ± 29.3 mg/dL for first-degree relatives. **Conclusion:** The findings suggest that antipsychotic treatment in schizophrenia patients is associated with significant increases in total cholesterol and serum triglyceride levels. These metabolic alterations may contribute to the higher cardiovascular risk observed in schizophrenia patients.

KEYWORDS: Schizophrenia, Antipsychotic Medication, Total Cholesterol, Serum Triglyceride.

INTRODUCTION

Schizophrenia, a substantial mental illness affecting approximately 1% of the global population, heightens the vulnerability to mortality among that diagnosed.[1] In schizophrenia patients, cognitive and behavioural problem serves as a fundamental characteristic, correlating with reduced adherence to treatment protocols, suboptimal dietary patterns, and compromised independent daily functioning.[2]

The illness is always severe and usually lasts a long time. It likely causes more suffering and distress than any other cancer. It greatly affects many lives and is a major burden for caregivers, health services, and society as a whole.[3]

Antipsychotic medications are the main treatment for psychotic illnesses and are also used for many other psychiatric conditions. Introduced about 50 years ago, these drugs have helped millions manage their symptoms. For those who respond well, antipsychotics can make the difference between living a fulfilling life from being severely disabled.[10]

First-generation antipsychotics (FGAs) are still widely used and effective in treating positive symptoms of psychosis like hallucinations and delusions. However, they don't effectively address other important aspects of psychotic illness, such as negative symptoms (e.g., withdrawal, apathy), cognitive impairment, and affective symptoms. FGAs can also cause significant side effects, including dystonic reactions, drug-induced

Parkinsonism, akathisia, and tardive dyskinesia, which can make treatment intolerable for some people.[4]

Second-generation antipsychotics (SGAs), or atypical antipsychotics, were introduced with the promise of better efficacy and safety. These newer drugs are more effective at reducing negative symptoms (e.g., lack of emotion and interest). However, their safety has been questioned due to their tendency to cause weight gain and affect glucose and lipid metabolism.[5]

The lipids are heterogeneous group of compounds, including fats, oils, steroids, waxes, and related compounds. They may be defined as compounds which are relatively insoluble in water, but freely soluble in non-polar organic solvents like benzene, chloroform, ether, hot alcohol, acetone, etc., actually or potentially related to fatty acid, which are utilized by living cells. Lipids are classified as Simple, Complex and Derived. They play various roles in an organism's body, serving as essential elements in cell membranes, a reservoir for metabolic fuel, and significant signalling agents in cellular functions.[6] Lipids also play an important role in development of neurons and proper functioning of the brain. The major lipids in human serum composed of various components such as cholesterol, phospholipids, triglycerides, and free fatty acids, with lipoproteins including chylomicrons, very low-density lipoproteins (VLDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL).[7]

Triglycerides are the esters of glycerol with fatty acids, which are major form of lipids found in the bloodstream, play a vital role in managing energy levels, insulation, transport of fat-soluble vitamins and encouraging the function of cholesterol-associated transfer proteins.[8] High serum triglycerides usually do not cause any symptoms, but if not treated for long term it can increase risk of serious complications like coronary heart disease and stroke.

However, cholesterol isn't just a bystander in our bodies; it's a key player in shaping cell membranes, transmitting signals, also they are the precursor for synthesis of all other steroids, vitamin D and bile acids. It pulls off a balancing act, managing very important tasks like soaking up nutrients, handling glucose, influencing reproduction, and even reacting to stress.[9] Dysregulation of Cholesterol Metabolism can lead to Cardiovascular Disease and Atherosclerosis.

Abnormal lipid biology may play a significant role in the pathophysiology of schizophrenia. The majority of research indicates that individuals diagnosed with schizophrenia exhibit elevated serum triglyceride as well as total cholesterol levels compared to healthy individuals.[10,11,12] This lipid imbalance is commonly attributed to both antipsychotic medication and lifestyle factors. However, it has also been observed in schizophrenia patients who are not receiving medication.[13,14,15]

Given the importance of lipid metabolism in the context of schizophrenia this current study seeks to investigate the potential variations in total cholesterol and serum triglyceride levels among drug naive, after treatment of schizophrenia patients and their first degree relatives.

METHODOLOGY

Study Design and Participants: This cross-sectional study included 60 participants divided into three groups: drug-naïve schizophrenia patients (n=30), same patients after 2 months of treatment, and their first-degree relatives (n=30). The study period was from March 2024 to June 2024. Participants were recruited from out patient department of Lokopriya Gopinath Bordoloi Regional Institute of Mental Health, Tezpur, Assam. Inclusion criteria for patients included a diagnosis of schizophrenia based on DSM-5 criteria, while first-degree relatives were selected based on their familial relationship with the patients.

Inclusion Criteria for Patient with Schizophrenia and First degree relatives

1. The patient between the ages 18 to 59 was included in the study irrespective of Sex who was newly diagnosed as schizophrenia and without any antipsychotic drugs.
2. Same patient after receiving a single second generation antipsychotic agent for 2 months or more.
3. First degree relatives of patients with schizophrenia with age group of 18-59 years.
4. The patient's guardian/person who were willing to sign the consent form.

Exclusion Criteria for Patient with Schizophrenia

1. The patient's guardian refuses to give informed consent.
2. Patients receiving more than one antipsychotic medication.
3. Patients with other psychiatric illness, epilepsy or mental retardation, suffering from endocrinological or cardiovascular diseases
4. Patient on treatment for any major medical or surgical illness.
5. Using alternative medicine
6. Pregnant and lactating women
7. Obesity, body mass index (BMI) ≥ 28.0
8. Hypertension
9. Smoked nicotine use and alcohol harmful use or dependence

Exclusion Criteria for First degree relatives

1. The person refuses to give informed consent.
2. History of psychiatric illness, epilepsy or mental retardation, suffering from endocrinological or cardiovascular diseases
3. History of treatment for any major medical or surgical illness.
4. Pregnant and lactating women

5. Obesity, body mass index (BMI) ≥ 28.0
6. Hypertension
7. Smoked nicotine use and alcohol harmful use or dependence

Sample Analysis: 2 ml of venous blood sample was collected in a Clot Activator vial and analyzed for total cholesterol and serum triglyceride levels in the Biochemistry Laboratory of LGBRIMH by using enzymatic determination in the Beckman Coulter-DxC 700AU Fully Automated Analyzer.

Statistical Analysis: Data were analyzed using SPSS version 29.0. Descriptive statistics were used to summarize the data. One-way ANOVA was employed to compare the mean lipid levels between the three groups. Post-hoc analysis was conducted using the Tukey test to identify specific group differences. p-value of <0.05 was considered statistically significant.

RESULTS

The mean ± SD values of total cholesterol and serum triglycerides across the three groups are presented in Table 1. Schizophrenia patients after-treatment exhibited significantly higher total cholesterol and serum triglyceride levels compared to drug-naïve patients and their first-degree relatives.

Table 1: Mean ± SD Values of Total Cholesterol and Serum Triglyceride Levels.

Parameter	Mean	Std. Deviation
TC level in Drug Naïve Schizophrenia Patients	171.40	34.382
TG level in Drug Naïve Schizophrenia Patients	96.10	32.959
TC level in After Treatment of Schizophrenia Patients	195.90	33.054
TG level in After Treatment of Schizophrenia Patients	127.70	34.259
TC level in First Degree Relatives	161.87	18.765
TG level in First Degree Relatives	99.60	29.291

The results of the ANOVA multiple comparisons for serum triglycerides and total cholesterol indicate that there are significant differences between patients with after treatment schizophrenia and first degree relatives (total cholesterol: p<0.001, serum triglycerides: p=0.003), as well as between patients with after treatment and those without drug exposure (total cholesterol: p=0.005, serum triglycerides: p<0.001). However, there is no significant difference between patients with first degree relatives and those without drug exposure (total cholesterol: p=0.429, serum triglycerides: p=0.907). This demonstrates how treatment affects lipid levels in individuals with schizophrenia.

Table 2: ANOVA multiple comparison of significance for Total Cholesterol and Serum Triglyceride.

Parameter	Significance of TC	Significance of TG
First Degree Relatives with After Treatment Schizophrenia Patients	<0.001	0.003
First Degree Relatives with Drug Naive Schizophrenia Patients	0.429	0.907
After Treatment Schizophrenia Patients with Drug Naive Schizophrenia Patients	0.005	<0.001

Figure 1 depicts the distribution of hypercholesterolemia in the sample, in the present study it was observed that 46.67% of atypical antipsychotics treated schizophrenia patients had (TC≥200) when compared to 26.67% in drug naive schizophrenic patients and 0% in first degree relatives who were taken as controls. There was significantly higher rate of hypercholesterolemia in drug naïve and also patients treated with anti-psychotics when compared to first degree relatives.

Figure 1: Distribution of Total Cholesterol levels in the sample

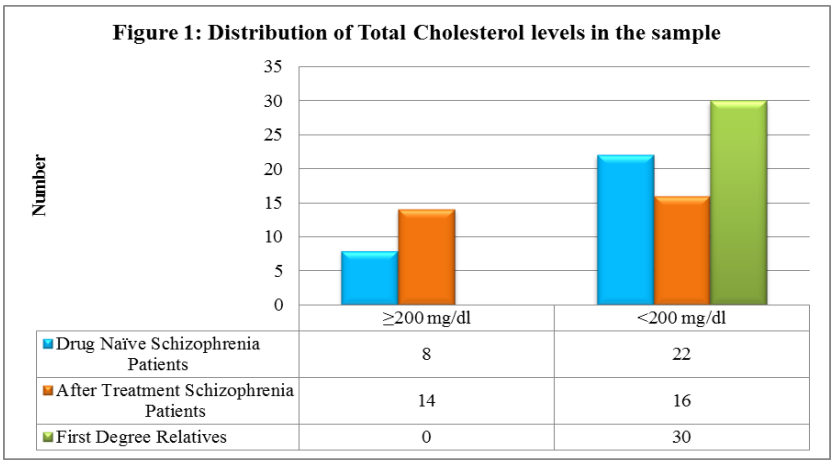
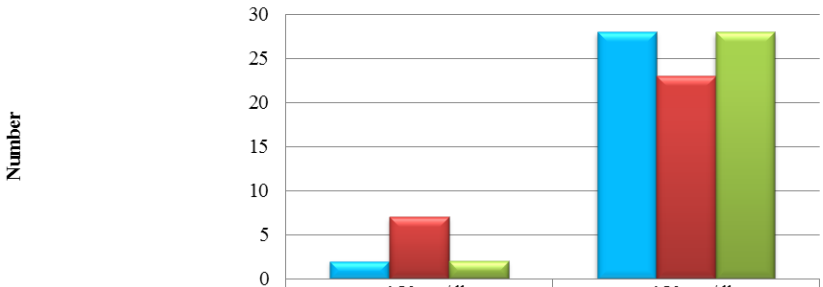


Figure 2 depicts the distribution of hypertriglyceridemia in the sample, in the present study it was observed that 23.33% of atypical antipsychotics treated schizophrenia patients had (TG≥150) when compared to 6.67% in drug naive schizophrenia patients as well as 6.67% in first degree relatives who were taken as controls. There were no significant differences in rate of hypertriglyceridemia among drug naïve, patients after treatment and FDRs.

Figure 2: Distribution of Serum Triglyceride levels in the sample

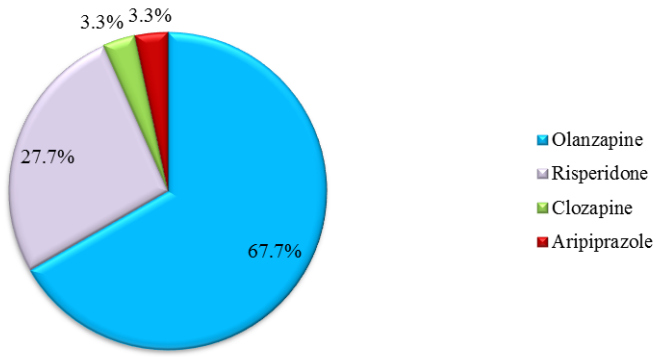


	≥150 mg/dl	<150 mg/dl
Drug Naïve Schizophrenia Patients	2	28
After Treatment Schizophrenia Patients	7	23
First Degree Relatives	2	28

Figure 3 present the distribution of patients with schizophrenia based on the type of antipsychotic medication used. Among the 30 patients: Olanzapine was used by 20 patients, accounting for 66.7% of the sample; Risperidone was used by 8 patients, representing 26.7% of the sample; Clozapine was used by 1 patient, making up 3.3% of the sample & Aripiprazole was used by 1 patient, also making up 3.3% of the sample.

Overall, the most commonly used antipsychotic was Olanzapine, followed by Risperidone, with Clozapine and Aripiprazole being the least used.

Figure 3: Distribution of sample, after treatment based on type of antipsychotic used



DISCUSSION

The study demonstrates a significant increase in total cholesterol and serum triglyceride levels in schizophrenia patients after antipsychotic treatment. This finding aligns with previous research indicating that SGAs are associated with adverse metabolic effects. The elevated lipid levels observed in after-treatment patients suggest a higher risk of cardiovascular diseases, highlighting the need for regular metabolic monitoring and management in schizophrenia patients undergoing antipsychotic therapy.

This study has some limitations. The cross-sectional design limits the ability to establish causality between antipsychotic treatment and lipid alterations. The sample size, although adequate, may not fully represent the diverse schizophrenia population. Longitudinal studies with larger sample sizes are needed to confirm these findings.

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Conflict of Interest
There are no conflicts of interest.

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