Original Research Article

HDL and blood glucose levels in schizophrenia: A comparative study among untreated, treated and their first degree relatives

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Abstract

Objective: to compare any differences in the hdl levels and blood glucose levels among untreated schizophrenia patients, treated schizophrenia patients and their first degree relatives. **Methodology:** the study is conducted among untreated schizophrenia patients, treated schizophrenia patients and their first degree relatives who came to Mamata general hospital, khammam. Total study sample consists of 90 out of which there are 30 treated schizophrenic patients, 30 untreated schizophrenic patients and 30 first degree relatives of either group who were randomly selected. estimation of hdl levels by peg precipitation method, estimation of blood glucose by glucose oxidase/peroxidase method **Results:** In present study we observed that mean fbs was significantly higher in treated schizophrenics compared to untreated schizophrenics and fdr. There was significantly higher rate of impaired fasting glucose in patients treated with anti-psychotics when compared to drug naive and first degree relatives. in present study we observed mean hdl was significantly lower in treated schizophrenics compared to untreated schizophrenics and fdr. mean hdl was significantly lower in untreated schizophrenics compared to fdr. There was significantly higher rate of low hdl in patients treated with anti-psychotics when compared to drug naive and first degree relatives. **Conclusion:** use of second generation anti-psychotics in schizophrenia patients significantly affects lipid profile and glucose metabolism.

Key Words: anti-psychotics, schizophrenia, lipid profile in schizophrenia, hdl in schizophrenia, blood glucose levels in schizophrenia.

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INTRODUCTION

Schizophrenia is a clinical syndrome of variable, but profoundly disruptive, psychopathology that involves cognition, emotion, perception, and other aspects of behavior. The expression of these manifestations varies across patients and over time. But the effect of the illness is always severe and is usually long lasting. It probably causes more suffering and distress and blights more lives than any other cancer and certainly represents a major burden for care-givers, health services and society as a whole.[1] Antipsychotic medications are the mainstay of treatment for psychotic illnesses and are also widely used in many other psychiatric conditions. Introduced about 50 years ago, these medications have helped millions of people manage their symptoms. For people who respond well, antipsychotics can mean the difference between leading an engaged, fulfilling community life and being severely disabled.[2] The first-generation antipsychotics (FGAs) are still widely available and are effective at treating positive symptoms of psychosis, such as hallucinations and delusions. FGAs do not however, adequately alleviate many other common and important aspects of psychotic illness, such as negative symptoms (e.g., withdrawal, apathy, poverty of speech), cognitive

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impairment and affective symptoms.[2] The introduction of second-generation antipsychotics (SGAs) or "atypical "antipsychotic drugs promised enhanced efficacy and safety. The newer agents appear more efficacious than conventional drugs in reducing negative symptoms (e.g. lack of emotion, interest, and expression). The safety advantages of the atypical drugs have been questioned because of their propensity to induce weight gain and alter glucose and lipid metabolism.[3] Patients with schizophrenia treated with phenothiazines and other drugs for long periods (average 9 yr) had decreased HDL-C levels[4], but it is still not clear whether phenothiazine administration caused this low HDL-C level. Abnormal lipid biology may play a significant role in the pathophysiology of schizophrenia. Most studies show that patients with schizophrenia have higher levels of serum lipids (cholesterol and triglyceride) than a healthy population.[5,6] This dyslipidemia has been regarded as a result of antipsychotic medication and lifestyle factors[7], but dyslipidemia has also been demonstrated in unmedicated schizophrenia patients.[8,9,10,11] Patients with schizophrenia also appear to have higher rates of impaired glucose tolerance, insulin resistance, and type II diabetes mellitus than the general population.[12] Most of the evidence indicating that type II diabetes mellitus occurs more commonly in schizophrenia has come from studies in which patients were either receiving neuroleptics or had been exposed to neuroleptics in the past.[13,14,15] It is difficult to determine whether schizophrenia per se has an independent role in the development of abnormal glucose metabolism, as both conventional and atypical neuroleptics have been implicated in the pathogenesis of type II diabetes mellitus and impaired glucose tolerance.[16,17,18] The aims of the current study are to determine if there are differences in HDL and blood glucose levels of untreated schizophrenia patients, treated schizophrenia patients and their first degree relatives.

MATERIALS AND METHODS

Present cross sectional study was conducted at Mamata General Hospital, Khammam from January 2014 to December 2014. A total of 90 study sample were included in the study.

Inclusion Criteria

1. Patients of either sex aged between 18 and 65 years suffering from schizophrenia and receiving a single second generation antipsychotic agent for 3 months or more.
2. Patients of either sex aged between 18 and 65 years suffering from schizophrenia and who were never been on any antipsychotic drugs.
3. First degree relatives of patients suffering from schizophrenia and who are mentally healthy.

Exclusion Criteria

1. Patients receiving more than one antipsychotic medication.
2. Patients with a known diagnosis of type 1 or type 2 diabetes mellitus.
3. Patients suffering from anorexia nervosa, bulimia nervosa or neoplastic disease..
4. Patient on treatment for any major medical or surgical illness.
5. Pregnant and lactating women.
6. Non complying patients.

Materials: A semi-structured demographic Proforma with age, gender, marriage status used.

Estimation of HDL levels by: PEG precipitation method,

Estimation of blood glucose by: Glucose Oxidase/Peroxidase method

The study was approved by the research ethics committee. Subjects were briefed in detail about the nature and purpose of the study. Confidentiality was assured and informed consent was taken.

Statistical Analysis: The data was analyzed using SPSS software version 17.0. Descriptive results are expressed as mean and SD of various parameters in different groups. Multiple comparisons ANOVA was used to assess the significance of difference of mean values of different parameters in between groups. F value was used to calculate the significance in between groups. Significance < 0.05 was considered as significant and level > 0.05 was considered as non significant. Chi-square test was done for comparison of distribution between the groups. Significance < 0.05 was considered as significant and level > 0.05 was considered as non significant.

RESULTS

Table 1: Distribution of sample based on age

Age group in years	Treated		Untreated		First Degree Relatives	
	No.	%	No.	%	No.	%
15-24	3	10	12	40	7	23.3
25-34	9	30	11	36.7	7	23.4
35-44	11	36.7	5	16.6	10	33.3
>45	7	23.3	2	6.7	6	20
Total	**30**	**100**	**30**	**100**	**30**	**100**
Mean±SD	**34.2±8.38**		**31.6±9.91**		**32.7±9.21**	

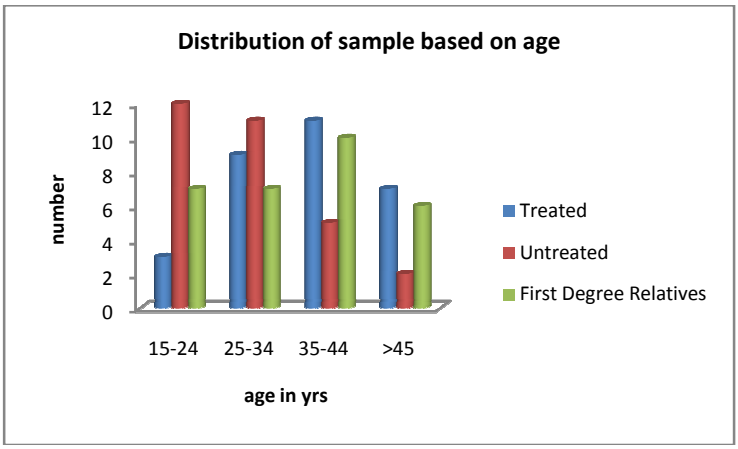

Figure 1:

Table no-1 and Figure-1 depicts that majority of patients in treated group were in the age group of 35-44 yrs. majority of patients in the untreated group were in the age group of 15- 24yrs and majority of subjects in FDR group were in the age group of 35-44 yrs. There was no significant difference in the mean ages between treated, untreated and FDR group (p>0.05). There was no significant difference in the distribution of sample between the three groups based on age groups.

Table 2: Distribution of sample based on gender

Gender	Treated		Untreated		First Degree Relatives	
	No.	%	No.	%	No.	%
Male	15	50	17	56.7	16	53.3
Female	15	50	13	43.3	14	46.7
Total	**30**	**100**	**30**	**100**	**30**	**100**

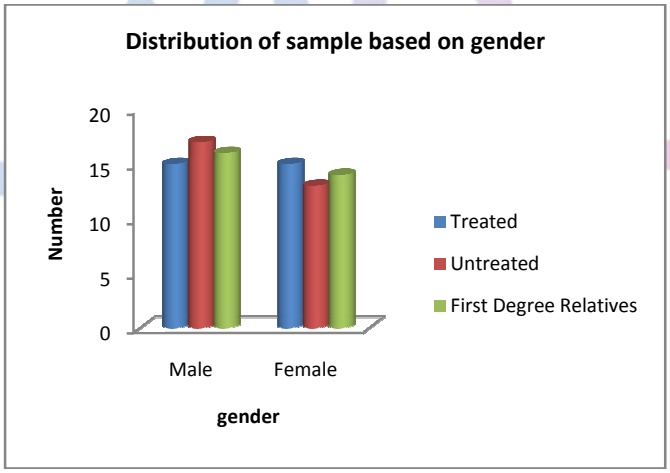

Figure 2: Distribution of sample based on gender

Table no-2 and Figure no-2 depicts that treated group comprised 50 % males and 50% females, untreated group comprised 56.7 % males and 43.3 % females and FDR group comprised of 53.3% males and 46.7 % females. There was no significant difference in gender distribution in either of the groups (chi square = 0.268, p=0.87).

Table 3: Distribution of HDL levels in the sample

HDL Levels in mg/dl	Treated		Untreated		First Degree Relatives	
	No.	%	No.	%	No.	%
Male< 40mg/dl Female< 50mg/dl	19	63.3	12	40	7	23.3
Male≥ 40mg/dl Female≥ 50mg/dl	11	36.6	18	60	23	76.6
Total	**30**	**100**	**30**	**100**	**30**	**100**
x^2	9.92					
p value	<0.01					

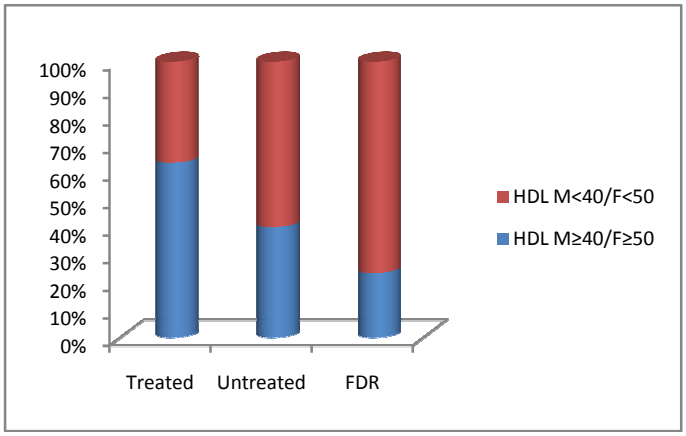

Figure 3:

Table 4: Mean±SD Values of HDL- C in controls and cases

Parameter	Treated		Untreated		First Degree Relatives		f value (p value)
	Mean	SD	Mean	SD	Mean	SD	
HDL - C	40.6	5.4	44.8	6.9	47.9	5.8	10.8 (<0.001)

Table 5: ANOVA multiple comparison of significance for HDL-C

Parameter	First Degree Relatives with Treated patients	First Degree Relatives with Untreated patients	Treated patients with Untreated patients
Significance	<0.001	0.049	0.01

Table 7: Distribution of FBS levels in the sample

FBS levels mg/dl	Treated		Untreated		First Degree Relatives	
	No.	%	No.	%	No.	%
≥100 mg/dl	12	40	6	20	3	10
<100 mg/dl	18	60	24	80	27	90
Total	**30**	**100**	**30**	**100**	**30**	**100**
x^2				**7.83**		
p value				**0.02**		

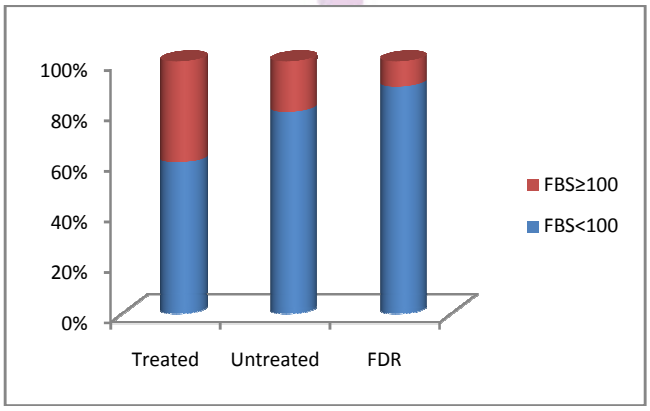

Figure 4:

Table 8: Mean±SD Values of FBS in controls and cases

Parameter	Treated		Untreated		First Degree Relatives		f value (p value)
	Mean	SD	Mean	SD	Mean	SD	5.7
FBS	102.2	12.5	94.97	12	92.7	9.3	(0.005)

Table 10: ANOVA multiple comparison of significance for FBS

Parameter	First Degree Relatives with Treated patients	First Degree Relatives with Untreated patients	Treated patients with Untreated patients
Significance	0.002	0.44	0.015

DISCUSSION

In present study we observed that Mean FBS was significantly higher in treated schizophrenics compared to untreated schizophrenics and FDR. There was no significant mean difference in FBS between untreated schizophrenics and FDR. The distribution of impaired fasting glucose in the present study it was observed that 40% of AAP treated schizophrenic patients had impaired fasting glucose (fbs≥100) when compared to 20% in drug naive schizophrenic patients and 10% in first degree relatives who were taken as controls. There was significantly higher rate of impaired fasting glucose in patients treated with anti-psychotics when compared to drug naive and first degree relatives. This finding of impaired fasting glucose in 20% of drug naive patients is similar to the studies in which Drug naive patients are reported to have significantly higher fasting plasma glucose levels, impaired fasting glucose tolerance, elevated insulin and cortisol levels, and insulin resistance in various studies.[10,11,19,20,21] Impaired glucose tolerance has also been reported in first degree relatives of drug naive schizophrenia patients, suggesting a possible genetic association between diabetes and schizophrenia reported impaired glucose tolerance in 18.2% of first degree relatives compared to 10.5% in general population which is higher than findings of this study. Findings in this study are similar to that of, Arranz and co-workers[22] who compared plasma glucose drug naive patients with drug treated schizophrenia patients and healthy controls. Drug naive subjects showed no significant changes in any parameters. Whereas patients previously exposed to antipsychotics had significantly increased plasma glucose. According to them drug naive patients may not have pre-existing impairment of glucose metabolism, use of antipsychotics may have lasting effects even long after discontinuation. In contrary to findings of this study two studies have found an increased risk for diabetes in first-degree relatives of patients with schizophrenia.[23] Rates of impaired glucose in this study are higher than a meta-analysis which revealed that 1 in 5 schizophrenic patients appear to have significant hyperglycaemia and 2.2% to 12.7% of un-medicated patients and 23% to 32.9% of medicated patients met criteria for hyperglycaemia (>100 mg/dl).[24] In present study we observed Mean HDL was significantly lower in treated schizophrenics compared to untreated schizophrenics and FDR. Mean HDL was significantly lower in untreated schizophrenics compared to FDR. In the present study it was observed that 63.3% of AAP treated schizophrenic patients had low HDL levels (HDL m<40, f<50) when compared to 40% in drug naive schizophrenic patients and 23.3% in first degree relatives who were taken as controls. There was significantly higher rate of low HDL in patients treated with anti-psychotics when compared to drug naive and first degree relatives. Mean HDL levels were significantly lower in untreated schizophrenics when compared to FDR but there were no significant differences between the two groups when low HDL rate was compared according to ATP Ill a criteria. This finding is similar to that of following studies, The population of schizophrenic patients is at greater risk for developing obesity, type-2 diabetes, dyslipidemia and hypertension than in the general population.[25] The relationship between weight gain caused by antipsychotic drugs and the occurrence of dyslipidemia is not yet entirely clear. Some studies suggest that weight gain and metabolic syndrome are certainly associated with the treatment with antipsychotics, but the occurrence of dyslipidemia was significantly associated with antipsychotic treatment.[26] The HDL-C level decreased shortly after initiation of phenothiazine therapy in new patients. Thus, the low HDL-C levels observed in chronic and new schizophrenic patients seemed to correlate with phenothiazine administration. The mechanism of HDL-C lowering by phenothiazine administration in patients with schizophrenia is not known. Since we found a negative correlation between TG and HDL-C levels in chronic schizophrenics receiving phenothiazines, low HDL-C levels could, in part, reflect the high TG levels. Neuroleptic drugs, including phenothiazines, are known to reduce blood estrogen levels, and this has been attributed to hypothalamic depression.[27,28] Therefore, the low HDL-C levels might result from low estrogen levels that have been previously correlated with low HDL-C levels. The role of a low HDL-C level, with regard to atherogenicity in schizophrenic patients treated with phenothiazines remains unknown.[29] One study which compared 38 drug naive schizophrenia patients with 44 matched healthy controls found no differences in HDL, or triglycerides.[30] Sengupta *et al*[31] in a Study on first episode psychosis (FEP) patients also did not find any lipid derangements except a slight trend of lower HDL levels. One meta-analysis reported on low HDL cholesterol levels, The prevalence rate was 37.5in schizophrenia patients. Medicated multi episode patients had significantly higher rate of low HDL levels when

compared with drug naive patients and general multi-episode patients had a significantly higher risk for low HDL cholesterol levels.[32] Findings of lipid derangements in this study are higher ‘than a meta-analysis which reported, the rate of hypertriglyceridemia in undedicated patients was 16.9% and the proportion of those with low HDL was 20.4% compared to medicated patients in whom it was 41.1% and 44.7%.[24,32]

CONCLUSION

There was significantly higher rate of impaired fasting glucose in patients treated with anti-psychotics when compared to drug naive and first degree relatives. There was significantly higher rate of low HDL in patients treated with anti-psychotics when compared to drug naive and first degree relatives. Use of second generation anti-psychotics in schizophrenia patients significantly affects lipid profile (low HDL levels) and glucose metabolism (hyperglycemia)

LIMITATIONS

Study sample was collected from only one tertiary care hospital, which was the major limitation of the study and further research can be conducted, so results cannot be generalised to the population.

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