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ORIGINAL ARTICLE

Assessment of Serum High Density Lipoprotein, Low Density Lipoprotein, and Very Low Density Lipoprotein in Bipolar Disorder Subjects

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ABSTRACT

Background: Bipolar disorder (BD) is a psychiatric condition and is defined as mood swings that alternate between mania, hypomania, and depression. Studies have been conducted globally to assess lipid profile (High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), and Very Low Density Lipoprotein (VLDL)) for BD with varying results. No such studies have been conducted in Pakistan. Therefore, current study was designed to assess lipid profile (HDL, LDL, VLDL) in clinically diagnosed bipolar BD.

Materials and Methods: One hundred and twelve blood samples were collected of diagnosed BD patients visiting Sheikh Zayd Hospital (SZH) and Punjab Institute of Mental Health (PIMH) Lahore. HDL, LDL and VLDL were estimated using standard biochemical methods.

Results: Results obtained were statistically analyzed using SPSS. A total of 112 BD patients, 48 (58.5%) were manic, 26 (31.7%) were depressive, 8 (9.8%) were euthymic. The mean HDL (41.26±12.57 mg/dl), LDL level (115.15±38.26 mg/dl) in bipolar group (manic, depressive and euthymic) as compared to control group were statistically significant with p-value 0.026. The mean VLDL level (33.17±18.43 mg/dl) level in bipolar and control groups was statistically insignificant with p-value 0.609.

Conclusions: The present study suggests that HDL level is decreased in manic BD patients. The raised value of LDL-C is found in depressive and euthymic patients. VLDL level was same in BD and control groups.

Keywords: Bipolar Disorder, Lipid Profile, High Density Lipoprotein, Low Density Lipoprotein, Very Low Density Lipoprotein

INTRODUCTION

BD is a mental pathology, a term that comes from the Greek "μανια," which means "madness" or "frenzy"[1].It is characterized by periods of depression and abnormally hyper (elevated mania/ hypomania) behavior. Individuals with BD exhibit emotional characteristics i.e. depression and madness. More recently,[2] BD ranks as the 17th leading source of disability in the worldwide. Mirza & Jenkins,[3] indicated that Pakistan has a relatively high (45.5%) prevalence of depression among women, and it has been linked to social position, poverty, illiteracy, and relationship issues.

Mania symptoms include feeling incredibly irritable, being readily distracted, having racing thoughts, speaking quickly, and changing topics mid-sentence, restlessness, boundless energy, insomnia, not feeling tired, inflated self-esteem, increased agitation, poor decision making, detachment from reality, also including considerable weight loss or increase, sleeping excessively or experiencing other sleep issues like insomnia, restlessness or sluggish behavior, suicidal ideas, plans, or attempts, feelings of guilt and worthlessness, difficulty focusing, lack of energy, exhaustion, loss of interest in activities and anxiety.

HDL is associated with cholesterol removal. High levels of HDL are referred to be "good" cholesterol since they lower the risk of heart disease and stroke. Many population studies have shown that HDL is a strong, negative independent predictor of CHD incidence and mortality in men and women[4]. LDL is referred described as "bad" cholesterol because it can cause artery plaque accumulation, heart disease, and stroke when levels are high. According to the American Heart Association (2012)[5], LDL levels are classified as optimal, (≤100 mg/dl), borderline risk, (130 to 159 mg/dl), high risk (160 to 189 mg/d) and very high risk (≥190 mg/dl). VLDL is one of the three significant gatherings of lipoproteins (Chylomicrons, LDL, IDL) that grant fats and cholesterol to move inside the water-based arrangement of the circulation system. VLDL is converted in the bloodstream to LDL[6]. They are synthesized from Chylomicron remnants by the liver and comprise mainly of triacylglycerol [7].

Many studies[8] have been shown that there is some relation between lipid profile (HDL, LDL and VLDL) and bipolar disorder. Wysokiński et al., 2015 described that the prevalence of lipid is high in unipolar and bipolar patients from Poland.[9] More recently, Su et al., 2019 [10] documented that LDL and VLDL were significantly different between unipolar and BD in China population.

Multiple studies have been conducted globally to assess lipid profile for BD with varying results[11]. No such studies have been conducted in Pakistan. There is need for conducting research study to asses' lipid profile (HDL, LDL and VLDL) in local Lahori population with BD.

MATERIALS AND METHODS

The subjects of BD for the present study were selected after clinical psychiatric diagnosis from Sheikh Zayed Hospital Lahore (SZH) and Punjab Institute of Mental Health Lahore (PIMH). The age of the participants was between 20-70 years. There were 76 (67.85%) males and 36(32.14%) female subjects participated in this study Fasting samples were collected and histories were recorded on a separate proforma. Among 112 samples 82 were with BD and 30 samples were belonging to normal healthy controls.

Venpuncture was used to collect 3-5 ml of venous blood samples from the individuals between 7 and 9 a.m., using aseptic procedure. Selections of the sample were made on the inclusion and exclusion criteria. Inclusion criteria include number of depressive or manic episodes, presence or absence of suicidal behavior and presence of psychotic behavior. On the other hand patients were excluded on the following diabetes mellitus, cardiovascular disease, chronic inflammatory disease, hypertension, and other mental illnesses.

Serum was separated after centrifugation at 4000 rpm for a total of 5 minutes. The serum thus separated was kept at -20°C in eppendorf tubes until it was time to analyze it.

HDL in the sample was separated into a supernatant for HDL tests using a precipitant. The supernatant was then aliquot and stored until it was needed.

Estimation of HDL-Cholesterol

HDL in sample was estimated calorimetrically. The estimation of HDL was evaluated through chemical precipitation method by using the spectrophotometer and taken the absorbance at 500 nm (Kit method)[12]

LDL was estimated based on the Friedewald equation.[13]

VLDL was calculated as the concentration of Triglycerides/5.

Data was interpreted by using standard Statistical Package for the Social Sciences (SPSS) software version-20 (SPSS Inc, Chicago). The continuous variable's mean and Standard Deviation (SD) were calculated. Significance of study was determined using a Student t-test (two-tailed, independent). P values considered significant at 0.05

RESULTS

By considering their family history 28 cases had BD, 41 cases showed the psychotic behavior, 17 cases showed suicidal behavior and 50 cases underwent stressful life events. This data revealed the age of onset of disease from 6 months to 50 years and the total duration was prolonged from 1 month to 58 years of suffering.

Table1: Demographic Characteristics of the Study Participants:

VARIABLES	CHARACTERISTICS
Gender	Male (76) and Female (36)
Age (Years)	20-70
Family history of Bipolar (cases)	Yes (28)
Duration of disease	1 month to 58 Years
Age of onset of disease	6 month to 50 Years

Table 2: Biochemical Evaluation of Study Participants:

Variables	Control group	BD Group	F	P-VALUE
N	30	82		
HDL-C	44.57±11.68	41.26±12.57	0.953	0.015*
LDL-C	107.93±36.30	115.15±38.26	2.614	0.031*
VLDL-C	31.02±15.15	33.17±18.43	0.483	0.854

HDL-C: NORMAL (>55 mg/dl), STANDARD RISK LEVEL: (35-55mg/dl), RISK INDICATOR (<35mg/dl).
LDL-C: NORMAL (150mg/dl), HIGH (190 mg/dl).
VLDL-C: NORMAL (2-30mg/dl), HIGH (> 30 mg/dl).

Questionnaire scoring among the BD subjects indicated 48 manic, 26 depressive and 8 euthymic subjects with the prevalence of 58.5%, 31.7% and 9.8% respectively. Among the BD subjects, depressive subjects are 3x prevalent than the euthymic subjects and manic subjects have 6x more prevalence in comparison to euthymic subjects. In the present study, the overall prevalence is 34% (112/240).

Biochemical evaluation HDL, LDL, and VLDL of the study subjects is presented in Table 2 and graphical data is depicted in fig 1.

In BD groups HDLwas found to be 41.26±12.57 as compared to control 44.57±11.68. It was discovered to be statistically significant (p-value 0.015). In BD groups LDL was found to be and 115.15±38.26 as compared to control 107.93±36.30. It was found to be statistically significant (p-value 0.031).

When independent t test performed on stages of BD it has been found that the all the parameter of lipid profile (HDL-C, LDL-C and VLDL-C show statistically insignificant (p-value>0.05).

Table 3: Biochemical Evaluation of Stages of BD:

Stages of BD	Variables	Male	Female	P-value
Manic	No of cases	39	11	
	HDL-C	37.05±12.67	43.82±12.86	0.126
	LDL-C	110.82±33.89	113.05±50.73	0.864
	VLDL	34.09±19.85	39.06±24.84	0.491
Depressive	No of cases	14	11	
	HDL-C	42.86±12.02	42.73±10.23	0.977
	LDL-C	119.64±32.20	148.18±39.45	0.058
	VLDL	31.65±12.02	29.96±19.14	0.790
Euthymic	No of cases	5	2	
	HDL-C	34.20±10.99	58.00±21.21	0.092
	LDL-C	127.00±29.27	72.00±57.98	0.134
	VLDL	31.44±4.47	32.30±12.87	0.889
Control	No of cases	17	13	
	HDL-C	45.71±13.23	43.07±9.60	0.551
	LDL-C	120.17±33.77	91.92±34.25	0.032*
	VLDL	31.01±9.71	31.02±20.70	0.998

INDEPENDENT SAMPLE T TEST, P-VALUE SIGNIFICANT AT 0.05
HDL-C: NORMAL (>55mg/dl), STANDARD RISK LEVEL: (35-55mg/dl), RISK INDICATOR (< 35mg/dl)
LDL-C: NORMAL (150mg/dl), HIGH (190 mg/dl)
VLDL-C: NORMAL (2-30mg/dl), HIGH (> 30 mg/dl)

This bar chart gives the graphical representation of the BD patients vs. controls as well as comparison of values
of lipid profile in both groups. It shows highest value of HDL for euthymic and LDL for depressive group.

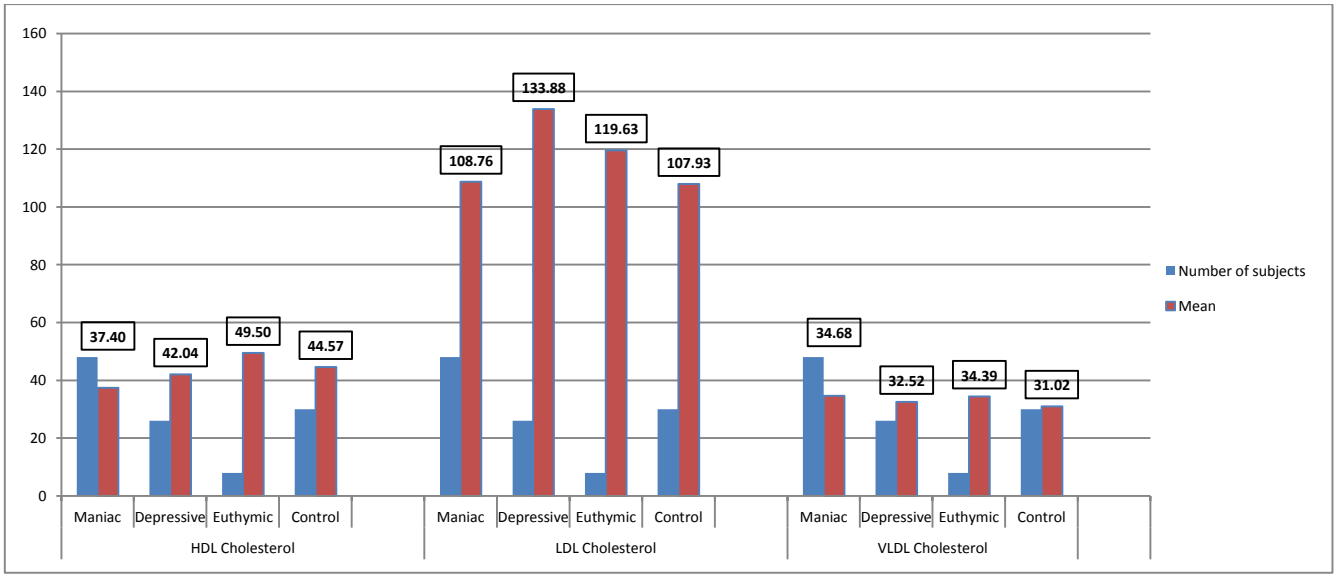

Fig 1: Bar Chart to Explain Lipid Profile in BD and Control subjects

DISCUSSION

The present work was conducted to assess lipid profile (HDL, LDL and VLDL in bipolar subjects. The study population consisted of 112 subjects (82 bipolar patients and 30 control subjects). There were 76 (67.85%) males and 36 (32.14%) were females in both groups. Among bipolar subjects, there 50 (44.6%) patients were manic, 25 (22.3%) were depressive and only 07 (6.25%) were euthymic.

Overall prevalence in the current study was 34% (112/240) in bipolar subjects. Individual group stages prevalence was 48 (58.5%) in manic, 26 (31.7%) in depressive and 8 (9.8%) in euthymic subjects.More recently, Smith et al., 2013conducted a meta study with over 500,000 participants and reported the prevalence rates and single lifetime episode of major depression (6.4%), likely intermittent significant depression (moderate) (12.2%), likely repetitive significant major depression (serious) (7.2%) and probable BD (1.3%).[14] They used this study to research hereditary and non hereditary risk factors for an extensive variety of unfavorable health results. Similarly Shumaila et al., 2014 found the prevalence around 14.3% for bipolar spectrum disorder among students of Pakistan. No significant difference in prevalence of BD was observed in either gender**.** [15]

No statistically significant association (p>0.05) was found as regard lipid profile (HDL, LDL, and VLDL) values between males and females in BD subjects. In addition to this no gender differences among male and female patients among lipid profile as regard to BD stages- manic, depressive and euthymic. Similar results were obtained by Huang 2017[16], among Chinese BD patients. However, Shiny 2014[17], showed significant association with respect to HDL value (p<0.01).

Significant association was observed between lipid profile (Lower HDL-C and High LDL-C) with BD as compared to controls (p<0.05). BulBul et al., 2014 [18] reported that increase LDL-C levels was not significant in Turkeys female patients p=.056.

In the current review, statistically contrast was found in serum HDL and LDL level between patients with BD and healthy controls (F = 0.953, P = 0.015) (F = 2.614, P = 0.031) respectively. No difference was found by Hui et al., 2019[19] in serum HDL levels between patients with BD and healthy controls (F = 0.04, df = 73, P = 0.85).

The level of VLDL-C was high in bipolar group 33.17±18.43mg/dl as compared to control 31.02±15.15mg/dl but statistically insignificant association was found among bipolar subjects and controls (F-value 0.489) and (F-value 0.483, P-value 0.854) respectively. There was no statistically significant association found in VLDL-C among the bipolar subjects and healthy controls. Chung et al., 2007[20] conducted study on state of mind (mood) and side effects and serum lipids in acute phase of BD in Taiwanese bipolar patients. Contrasted and past examinations on Western population, contrasts might exist in lipids profiles of BD patients during acute mood episodes.

The presented study revealed that components of lipid profile such as HDL, and LDL can be used as tentative diagnostic criteria in BD. Further studies are needed to verify this observation.

Huang et al., 2018[21] did a research work on alterations of lipid profiles in patients with BD. They compared Low Density Lipoprotein, and HDL of manic or depressed patients in the acute phase and normal controls. The low level of dyslipidemia, HDLwas also observed in acute mania.

John, 2014[22] conducted a descriptive study to investigate the relationship between lipid profile and psychiatric disorders. They also compare the lipid profile values in males and females showing some statistically significant association (p<0.01) concerning HDL values, but in normal range. Further when lipid profiles were analyzed between psychosis and neurosis, there was no measurably significant association as p<0.05. At the end of their study they concluded no statistical significance in different psychiatric diseases as regards to lipid profile.

Su et al., 2019[23] in their research on the differences in the serum levels of lipid among unipolar and bipolar depressed population of China, found that the bipolar group had lipid levels (LDL, and VLDL) significantly lower as compared with the unipolar group. At the end of their study they concluded that, LDL and VLDL levels were significantly different in bipolar depressed patients when compared to unipolar, which can possibly be the differential markers for diagnosis.

Vemuri et al., 2011[24]did research work on gender specific lipid profiles in BD patients. This study assessed gender effects of dyslipidemia in outpatients with BD. When they compared men with women, they show significantly higher mean High Density Lipoprotein (60.17 ±17.56 vs. 46.07 ±11.91 mg/dl, p < 0.001), lower mean LDL (109.84 ±33.47 vs. 123.79 ± 35.96 mg/dl, p = 0.004). At the end they concluded that males and females had lower prevalence of LDL, and HDL. No huge contrasts were found among people with respect to Body Mass Index (BMI), smoking propensities, bipolar sickness type, disease seriousness, age of patient or duration.

Sagud et al., 2009[25] have done research work on role of serum lipids which include HDL and LDL. They observed that the Serum HDL levels were significantly (F=22.575, P<0.000) different in controls and patients with BD. The degree of LDL did not contrast altogether between controls and patients with BD. At the end they concluded that all patients had altogether lower HDL values than control subjects. The results revealed no differences in LDL levels and Weight Index, yet huge contrasts in the proportions of LDL-C/HDL-C among groups.

CONCLUSION

In conclusion the present on BD indicated marked decrease in HDLlevel in Mania patient. The raised value of LDL is observed in depressive and euthymic patients. The values of VLDLare in normal range when contrasted with the control group.

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