Original Research Article

Lipid derangement and cardiovascular risk in female patients with major depressive disorder

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Abstract: Lipid disorder is well recognized risk factor for cardiovascular disease. The association of lipid derangement with depressive disorder has been a recent focus of research specially in female. The objective of this study was to investigate the serum lipids in female major depressive disorder patients(MDD). This case control study was done in the department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka during 2014. This study included 60 female MDD patients, diagnosed by psychiatrist according to the criteria of diagnostic and statistical manual (DSM IV) and 30 healthy females as control. Fasting blood glucose and Triglyceride (TG) Total cholesterol(TC) and High density lipoprotein cholesterol (HDL) was estimated by commercial diagnostic kit and auto analyser. Low density lipoprotein (LDL), TC/HDL and LDL/HDL was determined by calculation. For statistical analysis, independent sample t test and chi-square test was applied. Odds ratio and confidence interval for atherogenic risk was calculated by SPSS 16 version. Serum level of TG(P<0.001), TC, (P<0.01) HDL(P<0.05), LDL(P<0.05), TC/HDL(P<0.05) and fasting glucose (P<0.001)was significantly higher in MDD compared to control. Elevated fasting glucose, hypertriglyceridemia, hypercholesterolemia, elevated LDL were noted in, 45%, 27%, 20% and 6.7% patients respectively. Elevated level of TC/HDL was found in 34% depressed patients which was significantly higher in MDD. The odds ratio for atherogenic risk I ((increased HDL/LDL) and risk II (LDL/HDL) showed significant association (P<0.05) with MDD patients. This study concluded that lipid and lipoprotein abnormality along with some component of metabolic syndrome is highly prevalent in female MDD patients which identify them as high risk group for CHD or CVD.

Keywords: Lipids, lipoprotein ,Major depressive disorder. TC, TG, HDL, LDL.

INTRODUCTION

Depression is the most common chronic medical condition and out of ten, one patient is suffering from major depression visiting psychiatric department [1]. Depression has been found associated with increased risk for cardiovascular disease. Five percent of female with Major Depressive Disorder(MDD) had elevated triglyceride[2]. Depressed patients with elevated levels of cholesterol appears to be treatment resistant. Earlier study on Taiwanese population reported significant inverse correlation between HDL-C and depression and several other psychological condition and suggested link between lipid disorder and psychological symptoms[3].

Previous studies on lipids in MDD and its several subtypes and in other psychiatric illness reported conflicting results. Both lower and higher values TG, TC, HDL, LDL and Lipoprotein ratios in MDD patients than healthy control has been reported [3-8]. Lower TC, HDL, LDL,TC/HDL and LDL/HDL in MDD patients were found by some authors [4-6]but others found higher level[5-8]. Hashem et al. found high cholesterol in 36.5%, High TG in 22.5%, high LDL in 42.5%, Low HDL in 32.5%, high TC/HDL in 25% and moderate risk LDL/HDL in50% of elderly depressed patients[9].

During recent years, the relationship between metabolic syndrome and depression has been a subject of research. Multiple cross sectional and prospective studies found varying results. [10] According to National cholesterol education program(NCEP) and Adult treatment plan III(ATP III), Metabolic syndrome is a condition of multiple interrelated metabolic risk factors characterized by abdominal obesity, atherogenic

dyslipidemia, hypertension, insulin resistance, pro-thrombic, pro-inlammatory state[11]. It has been endorsed in the National Cholesterol NCEP & ATP III as an important emerging risk factor for CHD [11- 12]. Recently, the association between metabolic syndrome and depression has been reported by some[13-14] while others did not find it.[2,10]. The relationship still remains controversial. Being the marker for CHD risk, any component of metabolic syndrome in MDD patients remains an important area of investigation[13].

Several previous studies investigated and found association between lipid abnormalities and depression symptoms. [3,6-9,15-16]. Further, they suggested dyslipidemia as marker to differentiate the subtypes of depression [4,5]. Most of these earlier studies focused association of lipid abnormality to the development of depression and other psychiatric illness such as anxiety, different sub types of depression, schizophrenia, bipolare disorder[3-9,18-20].

But very few reports on relationship between CVD risk and dyslipidemia in depression particularly in patients with major depressive disorder has been published. Fava & colleagues anticipated that increased risk for coronary heart disease is more likely with co morbidity of anxiety and depression than depression alone[21]. Moreover, only few researchers highlighted atherogenic lipid and lipoprotein as risk for CHD in some other psychiatric illness [7] and there is lack of information about the role of dyslipidemia for the coronary heart disease and cardiovascular disease risk particularly in the major depressive disorder female patients.

In view of the above, this study aimed to investigate lipids and fasting blood glucose in female patients of MDD to examine the propensity of coronary heart disease(CHD) and cardiovascular risk (CVD) in MDD patients.

METHODS

This Case control study was done by department of Physiology Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, Bangladesh during 2014.The protocol of this study was approved by the Institutional Review Board (IRB) of BSMMU. This study included 60 recently diagnosed female patients of MDD according to DSM IV criteria with age range 29 to 44 years visiting out patient department of the department of Psychiatry of BSMMU. MDD patients were not suffering any physical illness and were free from any systemic disease and other co morbid psychiatric condition. Age BMI and sociodemographic match 30 apparently healthy females without any physical or mental illness were included as control and

selected among the relatives of patients and hospital staff. Diagnosis of patients were made by a Psychiatrist with questionnaire following criteria of DSM IV. Patients were examined and under aseptic precaution 5 ml of fasting blood samples were collected from the antecubital vein before starting treatment with anti depressive or other medication. Before collection of blood samples, the aim and purpose of this study was explained to all subjects and a written informed consent was taken. A detail medical, personal and dietary history of all subjects was taken. A thorough clinical examination was done height, weight was measured following standard procedure and BMI was calculated and all information were recorded in a data schedule. All lipid parameters including Triglyceride (TG), Total cholesterol (TC),HDL,LDL and fasting blood glucose was determined by a commercial reagent kit and autoanalyzer.TC/HDL and LDL/HDL were calculated. Data were expressed as mean ± SE and in percentage. For statistical analysis, independent sample t test and chi-square test were done as applicable. SPSS 16 version was used for calculation of odds ratio and confidence interval of data. $P<0.05$ was considered significant.

RESULTS

No significant differences were found in age, socioeconomic status, dietary habits between cases and control subjects but BMI, Blood pressure were found significantly ($P<0.01$) in patients than that of control (Table 1)

In this study, mean fasting serum glucose, TG,TC,LDL,HDL and TC/HDL level were found significantly ($p<0.001$)higher in MDD patients but mean value of and LDL/HDL did not differ significantly from that of control. (Table 2) Again, obesity, hypertension, elevated fasting glucose, hyper triglyceridemia, hypercholesterolemia, elevated LDL were noted in 66%,27%,45%, 27%, 20% and 6.7% of MDD patients respectively. In control group ,10% subjects were obese and only 3.33% subjects were found with hypertension and high fasting glucose level whereas no control subjects were affected with these hyperlipidemia except hypercholesterolemia in only 1 subject. The differences of frequency % of all these abnormal metabolic parameters between patients and control were statistically significant. (Table 3) One of the atherogenic risk index, elevated TC/HDL was found in 34% depressed patients which was significantly ($P<0.001$)higher in MDD than control. On further analysis, the odds ratio for atherogenic risk I ((increased HDL/LDL) and risk II (LDL/HDL) showed significant association ($P<0.05$) with MDD patients.(Table 4).

Table 1: Age, BMI and BP in different groups (n=90)

parameters	Control (n=30)	MDD Patients (n=59)	P value
Age(Years)	37.23±2.1	33.96±1.1	>0.05
BMI(Kg/m^2)	23.73±0.54	27.09±0.39	<0.01
SBP(mmHg)	107.25±3.3	120.42±1.33	<0.01
DBP(mmHg)	71.5±2.21	79.15±1.20	<0.01

Data were expressed as mean ±SE. For statistical analysis independent sample t test was used,

Table 2: Lipid and lipoprotein levels in both groups(n=90)

parameters	Control (n=30)	Depressed patient (n=59)	P value
Fasting Glucose(mmol/dl)	4.75±0.22	5.71±0.09	<0.001
TG(mg/dl)	119.16±7.18	184±3.45	<0.001
TC(mg/dl)	166.30±6.2	195.41±7.74	<0.01
LDL(mg/dl)	102.73±8.5	129.76±2.8	<0.05
HDL(mg/dl)	38.95±	47.03±0.8	<0.05
TC /HDL	3.85 ±0.24	4.34±0.09	<0.05
LDL /HDL	2.20±0.23	2.57±0.07	>0.05

Data were expressed as mean ±SE. For statistical analysis independent sample t test was used

Table-3: Frequency of increased BMI, BP, fasting plasma glucose, hyperlipidemia and lipoproteinomia in both group

Para meters	Control (n=30)	MDD (n=59)	P value
BMI >25	3(10%)	39(66%)	<0.001
BP >130/85 mmHg	1(3.33%)	16(27%)	<0.01
Fasting glucose >6.1mmol	1(3.33%)	27(45.7%)	<0.001
elevated Triglyceride	0(0%)	16(27%)	<0.001
Elevated cholesterol	1(3%)	12(20%)	<0.01
Elevated LDL	0(0)%)	04(6.7%)	<0.05

Data were expressed as no and percentage. For statistical analysis chi square test was used. Cut off value for TG 200 mg; for TC 220mg ; for LDL 160mg [11]

Table-4: Frequency percent of average atherogenic risk in both groups[23]

Atherogenix index	Control (n=30)	Patient (n=59)	P value	Odds ratio	CI	P value
TC /HDL>4.5	4(13%)	20(34%)	<0.001	3.33	10.69-1.03	<0.05
LDL /HDL>3.2	4(13%)	11(18%)	>0.05	1.49	5.05-2.29	<0.05

Data were expressed as no and percentage. For statistical analysis chi square test was used.

DISCUSSION

The propensity of CVD to various Psychiatric illness is a subject of research interest since many days. Previous studies investigated various risk factors including lipid disorder in different Psychiatric disorders. Some studies reported higher lipid levels in anxiety disorder, posttraumatic stress, schizophrenia, major depression and other depressive disease[5].

The purpose of the present study was to explore the lipid derangement and some metabolic disorder with Major depressive disorder and to investigate their risk profile for cardiovascular diseases. This study investigated lipid and lipoprotein and fasting glucose status in MDD patients to find out the status of lipid and lipoprotein disorder as a potential risk to develop atherosclerosis and also obesity, hypertension, fasting hyperglycemia as high risk for developing cardiovascular disease in this psychiatric illness. The key results showed that MDD patients had significantly higher levels of fasting Triglyceride, Total cholesterol, LDL, fasting serum glucose compared to healthy control. Similar results were observed in several studies [5-9,18]. Our results are opposite to Roohafza et al. who reported lower TC, HDL, LDL but TG was not different in MDD compared to control[4]. Our results also did not agree to Huang and Chen. They investigated lipid and lipoprotein in Major depressive patients with melancholic and atypical feature and found TC, TG, LDL, TC/HDL and LDL/HDL was lower than healthy

control but the observed higher HDL in these patients is similar to our findings[5]. Similarly, to explore the relationship between serum cholesterol and depression, in a study Olusi and Fido reported lower cholesterol and higher HDL in MDD than healthy control. In addition, in their study they observed clinical improvement of MDD was accompanied by increase in cholesterol and thereby suggesting relationship between low serum cholesterol and depression[6]. Previous studies also reported lower TG and TC in MDD patients only but higher TG and TC in case of comorbid anxiety with depression disorder[4]. In our study, the results of the higher TG and TC in MDD than normal control are in line with Gupta et al. but they did not clearly mention the clinical type of Psychiatric patients[7]. In majority studies, lower cholesterol was explained by the fact of reduced cholesterol synthesis and impaired reverse cholesterol transport observed in MDD[22]. But no significant relationship was observed between poor cholesterol level and depression.

In the present study HDL was found higher in MDD when compared to control. This result is consistent to the result of Olusi and Fido [6] and Huang and chen [5] but most of the studies presented lower HDL in MDD patients[3,4,7,18]. HDL showed significant inverse correlation with depression score in a Taiwanese population study[3].

In this study, LDL was significantly higher as well as significant percentage of MDD patients had abnormally elevated levels of both TC and LDL. In contrast to the results of this study, significantly lower LDL and no change in TG were found in MDD patients compared to control[4].

There is strong evidence that LDL is a powerful atherogenic lipoprotein. LDL>160 has been proposed as high risk for significant acceleration of atherogenesity & CHD [11]. LDL has been identified as primary target for drug therapy by ATP I in 1988 then subsequently by ATP II &III to prevent CHD recognizing it a major cause of CHD based on the reports of Laboratory animal experiment, clinical trials and epidemiological survey. ATP III had proposed to include diabetes as CHD risk equivalent list[12]. The result of this study also suggest a similar proposal to identify MDD as CHD risk equivalent but it needs support of epidemiological and clinical trial data.

TC/HDL &LDL/HDL Ratios are used as atherogenic index to estimate the probability of atherogenosity and indicators of vascular risk[23].It is claimed that these ratios have greater predictive value than isolated lipid parameters. These ratios may act as more effective mirror of metabolic and clinical interactions between lipid components[23]. Both lower and higher values of these ratios are noted in MDD patients when compared to normal subjects especially in women [8]. Research results suggested these indices as

marker for likely association between lipid and depression[5,7,8]. Gupta et al. investigated the relationship of psychiatric disorder and lipid derangements. They reported significantly higher level of these atherogenic index in newly diagnosed Psychiatric patients though they did not delineate clearly the type of psychiatric illness[7]. Though emphasis is given to LDL level as prime index for cardiovascular disease risk and made it principal target for lipid lowering therapy[11,12], TC/HDL & LDL/HDL are also used as atherogenic risk indicators with greater predictive capacity than any isolated parameters principally LDL in clinical practice.[23] The result of significantly higher level of TC/HDL in our MDD patients support the evidence based anticipation of previous studies about the increased risk of atherogenecity and ultimately increased threat to develop cardiovascular morbidity and mortality in patients with major depressive disorder if not given appropriate and timely intervention in these group of Psychiatric patients.

The frequency of dyslipidemia including hyper triglycedemia, hyper cholesterolemia and hyper lipoproteinemia in MDD patients showed their significantly higher prevalence of lipid derangement in this category of depressive illness. It is important to note 6.7% MDD patients in this study presented LDL level to fall into high risk categories for CHD according to guideline of NCEP[12]. Moreover, the profile of atherogenic risk index TC/HDL & LDL/HDL ratio in MDD and their significant results of odds ratio further intensify their predisposition to high risk of CHD.

In addition to presence of hyper triglyceridemia and hypercholesterolemia, higher SBP, DBP, BMI, physical inactivity strongly support their trends as risk factors of metabolic syndrome[12].

Previous studies addressed the problem of metabolic syndrome in depressed and other psychiatric illness. They highlighted prevalence of metabolic syndrome in patients with depressive disorder including MDD[14].

The area of metabolic syndrome was taken under serious concern in the 3rd report of NCEP & ATP III for risk evaluation of CHD[12]. Metabolic syndrome comprised clusters of metabolic risk factors closely associated with insulin resistance which is characterized by obesity, high TG, low HDL, high BP, impaired fasting glucose and hyper coagulability. Presence of any three or more features is suggestive of metabolic syndrome[11,24].

The results of high risk LDL along with features of metabolic syndrome in substantial percent of MDD patients in our study greatly increase their risk to develop CHD.

The pathogenesis of the features of lipid and lipoprotein disorder in these MDD patients are not known. Several previous studies indicated involvement of serotonergic receptor defects, abnormal transport of lipoproteins. Elevation of threshold for 5HT receptor or poor activity 5HT transporter in MDD may be the result of direct binding of cholesterol to membrane receptor or transporter and thereby changing the fluid status of neuronal membrane due to high cholesterol level[17].The significant increased frequency of lipid disorders in the present result suggest that there is a high prevalence of lipid and glucose metabolic abnormalities in MDD patients.

Though few previous reports indicated relationship between lipid abnormality and depressive symptoms [3, 6,13] but the etiology for lipid derangement in depressive patients is not yet clearly known. This warrants further investigation.

CONCLUSION

The results of this study confirms the high prevalence of lipid and lipoprotein abnormality along with metabolic syndrome which spot the MDD patients belong to high risk group for cardiovascular disorder. According to our results evaluation of lipid profile is essential in female MDD patients to identify the risk profile for cardiovascular disorder.

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