VOLUME - 9, ISSUE - 7, JULY - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Psychiatry

ASSESSMENT OF LIPID PROFILE IN PATIENTS OF DEPRESSION – A CASE CONTROL STUDY

Sheetal Tripathi	Junior Resident,dept Of Psychiatry, Era's Lucknow Medical College & Hospital, Lucknow, Uttar Pradesh .
Priyanka Sharma*	Assitant Professor,dept Of Psychiatry,gr Medical College & Jah,gwalior,mp.*corresponding Author
A Q Jilani,	Associate Professor, Dept Of Psychiatry,era's Lucknow Medical College & Hospital,lucknow,Uttar Pradesh.
Nitin Sharma	Senior Resident, Dept Of Psychiatry,ihbas,Delhi.
Shantanu Bharti	Senior Resident, Dept Of Psychiatry,ihbas,Delhi.
Ruchita Sharma	Associate Professor Dept Of Psychiatry,era's Lucknow Medical College & Hospital,lucknow,Uttar Pradesh

ABSTRACT **Background:** Major depressive disorder (MDD) has a prevalence of around 4.4 % worldwide and would be a leading cause of disability by 2020 but etiological causations relating to MDD remains unclear. Lipids have a role in neuronal functioning and may have potential to be used as biomarkers in depression. The role of lipids in MDD is controversial. Majority of the studies have shown consistent relationships and few have shown no relationship. The assessment of lipid profile in patients of depression could be delineated by the results of present study which may add to the existing evidence.**Material and methods:** A total of 60 cases of MDD diagnosed as per ICD-10 criteria and 60 age and sex matched control were taken up. In both the groups we have measured lipid profile which includes serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), and very low-density lipoprotein cholesterol (VLDL). **Results:** The MDD subjects have lower levels of TC and LDL-cholesterol compared with healthy controls. **Conclusion:** Depression is associated with low serum cholesterol levels.

KEYWORDS : Assessment ,Depression, Lipid profile, Neuronal functioning.

INTRODUCTION

Depression is a multifactorial disorder and both genetic and environmental factors are thought to play an important role in its etiology and treatment. An early diagnosis of depression and implementation of proper treatment provide a good chance of suicide prevention. Despite various advances in the pharmacotherapy of depression, treatment of depression is still challenging. Indeed, not all patients respond to the treatment and considerable individual variability to existing treatments has been observed. Taking these issues into consideration, there is a need to better understand the various factors that contribute to the development of this disease, including genetic and lifestyle factors, to identify biomarkers and develop alternative pharmacotherapies. According to WHO, depressive disorders currently rank fourth among the foremost causes of disease burden, and they are even projected to rank second in the world and first in high income countries by the year 2030 (1).

Many researchers have pointed out that among metabolic factors lipid profiles play one of the contributors (2). A well-known explanation of the role of cholesterol by tedders et al, presented its crucial role in the maintenance of neuronal membrane and henceforth significant role in neurotransmission and in the second messenger system (3). Likewise, changes in the blood lipid levels such as reduced cholesterol results in neuronal dysregulation and membrane instability, which may lead to depression and suicidal behavior (4). It has been hypothesized that changes in the cholesterolcontent of the synaptosomal membrane leads to reduction in the number of serotonin receptors due to decrease in cholesterol concentration leading to depression (5).

The neurobiology of depression hence is a topic of interest for researchers as a large number of people are on lipid lowering therapies and lipid levels are very commonly measured in clinical practice. Similar to the health risks of high lipid levels, the effects of low lipid levels produce certain consequences. A number of earlier studies had proposed that lowered or low cholesterol (especially high-density lipoprotein – cholesterol (HDL-C)), which is a beneficial cholesterol had impact on psychological health, and among middle aged men whose levels of serum HDL-C are persistently low, the prevalence of depression increase (2)(6). An adequate level of cholesterol is essential to preserve a healthy mind and body balance, and very low cholesterol produces alarming signals in the form of depression. The lower the level, the deeper is the depression. In contrast to this, a study by Ledochowski M, et al. showed an association between increased serum cholesterol and signs of depressive mood (7). As per two large population-based studies from Finland, had concluded that subjects having high cholesterol were having depressive symptoms (8)(9). Whereas in a study done on depressed patients in inpatient units, no correlation was found between serum cholesterol levels and depression (10). This implies that the link between cholesterol and depression is complicated.

Hence further researches are required to fill this lacuna. In view of such contradictory findings, the present study aims to study the association between lipid profile and depression.

METHODOLOGY:

A case control study carried over a period of 1 year in the department of psychiatry Era's Lucknow medical college and hospital, Lucknow with a group consisting of 60 drug naïve patients diagnosed as case of depression with symptoms present more than 2 weeks based on International classification of diseases, tenth revision, diagnostic criteria for research (ICD-10-DCR) criteria(11) for diagnosis of depression and 60 healthy controls in the age group of 18-60 years age and sex matched non blood related normal individuals without depressive symptoms and any other

psychiatric illnesses, screened by Mini International Neuropsychiatric Interview (M.I.N.I). After taking informed consent, both cases and controls were interviewed to obtain relevant data. The subjects excluded with any organic brain lesions, other major illnesses like cardiovascular diseases, hypothyroidism, liver disorder, diabetes mellitus and malignancy, on cholesterol lowering drugs, Pregnancy, lactation, use of OCPs, Substance abuse except nicotine, History of recent significant weight loss, known history of dyslipidemia, with severe depression with psychosis. The nature and purpose of study explained to the subjects. Clearance from the institute ethics committee was taken.

ASSESSMENT TOOLS:

Diagnosis was based on ICD-10 DCR and controls were screened by using Mini International Neuropsychiatric Interview (M.I.N.I) [12]. Severity of depression was rated on 21 item beck's depression inventory II (BDI II) [13]. Each item is scored with a value between 0 and 3, yielding a total score between 0 and 63, according to which depression was graded as normal (0-13), mild (14-19), moderate (20-28), and severe (29-63).

The body mass index (BMI) was calculated using the formula:BMI = weight/height^2 (kg/m^2)

Based on cut-offs for Asian Indian, proposed by the World Health organisation (14), underweight below 18.5, normal weight 18.5-24.9, pre obesity 25.0-29.9, obesity ≥30 kg/m^2.

LABORATORY INVESTIGATION:

After informed consent 3-5 ml of blood taken in a plain tube without anticoagulant from antecubital vein under aseptic precautions, and were stored at – 70 c until analysis. The serum was separated by centrifugation and used for analysis of total cholesterol (TC) by cholesterol oxidase method, triglycerides (TG) by glycerol phosphate oxidase peroxidase (GPO-POD) method, LDL cholesterol (LDL-C) by direct assay method and HDL cholesterol (HDL-C) by phosphotungstic acid method [15].

STATISTICAL ANALYSIS:

All recorded parameters were expressed in mean ± standard error of the mean. The two groups are compared by Student's independent t-test. Relationship between parameters was assessed by Pearson's correlation coefficient using SPSS (Statistical package for social sciences) software version and MS-excel. p-value of less than 0.05 was considered statistically significant.

RESULTS:

Results are expressed as mean ± SD. Table 1 shows the socio-demographic distribution of subjects. The mean age of patients was 39.58 ± 11.94 years while it was 40.20 ± 11.31 years for the control group. However, as study included age and sex matched individuals, so no difference was observed. Majority of subjects were married in both groups (90% cases & 28% control) with Majority belonging to nuclear families. Among the clinical profile in Table 2, the majority of the cases (65%) were having moderate depressive episodes. 66% of patients have the first episode of depression and 56% have onset of illness in the age group of 21-40 years. Family history found positive in 28% cases. The estimated result in Table 3 showed the significant low lipid profile in the study group. The mean values of serum TC levels, LDL-C, & HDL-C was significantly decreased in cases as compared to controls (p<0.001). whereas there was no signific160t difference found in serum HDL-C levels in cases as compared to controls.

Table 1: Comparison of Demographic and General Profile of cases and controls

S.N	Characteristic	Cases (n=60)		Controls (n=60)		
		No.	%	No.	%	'p'
1.	Mean Age±SD	39.58±11.94		40.20±11.31		
2.	Sex					
	Male	31	51.7	31	51.7	1
	Female	29	48.3	29	48.3	
3.	Domicile					
	Rural	31	51.7	31	51.7	1
	Urban	29	48.3	29	48.3	
4.	Marital status					
	Married	54	90.0	17	28.3	<0.001
	Unmarried	5	8.3	43	71.7	
	Widowed	1	1.7	0	0	
5.	Monthly family income (Rs)					
	<Rs 5,000	19	31.7	18	30.0	0.750
	5,000-10,000	23	38.3	26	43.3	
	10,000-20,000	15	25.0	15	25.0	
	>20,000	3	5.0	1	1.7	
6.	Family type					
	Joint	14	23.3	15	25.0	0.831
	Nuclear	46	76.7	45	75.0	
7.	Education					
	Illiterate	13	21.7	13	21.7	1
	Primary	13	21.7	13	21.7	
	Junior	8	13.3	8	13.3	
	High School/Secondary	18	30.0	18	30.0	
	Graduation or above	8	13.3	8	13.3	

Table 2: clinical profile of cases

variables	No.	%
Type of depression		
• Mild	7	11.7
• Moderate	39	65.0
• severe	14	23.3
Age at onset		
• ≤20 years	7	11.7
• 21-40 years	34	56.7
• >40 years	19	31.7
Number of depressive episodes		
• 1	40	66.7
• ≥2	20	33.3
Family history	17	28.4
Duration of illness		
• ≤1 month	39	65.0
• >1 month	21	35.0

Table 3: Comparison of lipid levels between cases and controls

SN	Characteristic	Cases (n=60)		Controls (n=60)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	Total cholesterol (mg/dl)	116.10	13.64	148.47	9.17	-15.254	<0.001
2.	LDL cholesterol (mg/dl)	46.65	10.65	81.66	8.81	-19.619	<0.001
3.	HDL cholesterol (mg/dl)	49.82	5.24	50.37	5.26	-0.571	0.569
4.	Triglycerides (mg/dl)	98.11	18.03	82.17	19.58	4.639	<0.001

DISCUSSION:

Our main findings in the present study was that lipid profile

(TC, LDL & TG) were significantly lower in depressive patients as compared to normal healthy controls. The results are consistent with our hypothesis. Further we observed that with increasing severity of depression, there is a significant decline in cholesterol levels. The exact pathophysiology underpinning the association is poorly understood. This may be due to changes in the cholesterol content of the synaptosomal membrane and results in decrease in the number of serotonin receptors. Few studies have provided an explanation for a relationship between serum cholesterol and low mood. A primary decrease in cholesterol levels may directly lead to decreased brain serotonergic activity through a variety of mechanisms. Ranging from an alteration in serotonin levels, to serotonin receptor concentration and serotonin transporter activity. Being a major component in the myelin, cholesterol plays a central role in synaptogenesis. Beasley et al have reported evidence of myelin pathology in depressed subjects that can be attributed to reduced levels, together with synapse reduction (16). Similar findings were explained by papakostas et al; that reduced cholesterol lead to serotonin dysfunction (17).

Another mechanism that supports this hypothesis is nutritional imbalance and chronic illnesses. It postulates that reduced intake of food i.e. reduced appetite and weight loss results in a decrease in serum fatty acids. Hence low cholesterol in the body is also reflected in different cellular systems resulting in reduced serotonin density (18) (19). Also, the cholesterol particularly in the prefrontal cortex of our brain is sensitive to serotonin changes. As explained by Sun et al. who exposed rats to chronic mild stress (CMS) for 28 days and found significantly reduced total cholesterol level in the medial prefrontal cortex (mPFC), and reversed this behaviour by chronic dietary supplementation, furthermore an injection of a serotonin (5-HT1A) antagonist into the mPFC blocks the effects produced by dietary supplementation. This suggests serotonin receptors play a role in the pathology and treatment of depression (20).

Our study is supported by some previous studies which explains that lipid profile abnormalities occurs in drug naïve first episode (kuwano et al; 2018) and remitted major depressive disorder (MDD) patients (wagner et al; 2019) (21)(22). The similar study by BN patra, et al reported an association between low serum cholesterol concentration and depressive episodes (23). Besides this a meta analysis was done to find out the role of total, low- and high-density cholesterol with depression, and concluded that total cholesterol is inversely related to depression except HDL-C levels which was directly proportional (24). The patients with suicidal tendencies found to have low HDL-C, as explained by gambit, et al. among 37 adult outpatients (OPD). Alternatively, there are some studies that do not claims the similar findings, showing a lack of associations while some explained mixed results (25)(26)(27).Although our study gives evidence that lipid profile can be used as biomarkers for depression but due to controversial results, it needs further exploration. Besides, the mechanism and pathophysiology explained above is not applicable at all age groups, as it might differ among geriatric age groups. Some areas of interest like immuno-neurobiology, need more attention to clear the doubts related to illness. Other limitations in our study like lower sample size cannot generalise the result. A long term follow up is lacking in our study to see the effects of antidepressants treatment on lipid profile. Also, the changes in the severity scoring with the treatment. A significant change in lipid profile after treatment may enhance knowledge of the facts.

CONCLUSION

This study concludes that the serum lipid levels are significantly associated with depression. The low levels of lipids are the indicators of depression, but due to lack of much evidence it is still questionable whether lipids should be included in the treatment of depression. So further analysis in the future is required to introduce it as a biomarker in depression. It will be helpful for clinicians in early detection and management of depression and hence reducing the morbidity due to illness.

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