



## A Study of Total Cholesterol Level in Depressive Females in Tertiary Care Hospital of Aligarh

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### Abstract

**Background:** Depression is a common illness worldwide, with more than 264 million people affected. It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. Close to 800 000 people die due to suicide every year. Suicide is the second leading cause of death in 15-29-year-olds. Cohort and case control studies have found that lower serum total cholesterol is associated with depression. **Methods:** A total of 25 depressed patients and matched non-depressed controls were included in the study. The patients were diagnosed according to the DSM-IV criteria in the OPD by the consulting psychiatrist. Severity of depression was graded by 17-point Hamilton rating scale for depression. **Results:** Out of the 25 patients with depression, 7 patients were studied in the first episode of major depression, 18 patients met DSM-IV criteria for recurrent unipolar depression. The results for total serum lipids are shown in table. The total serum lipid for group A is 158.39+-22.05 and for group B is 170+-38.26. The level of total serum cholesterol is lower in group A but the difference is not significant by independent sample "t" test. **Discussion:** A decrease in total cholesterol levels was observed in depressive patients, and this decrease was not significant (p>0.05). This decrease is in accordance with Shiny SY and Giltay EJ. Shiny SY also recommended that lipid levels of depressive patients should be monitored as it has been reported that the risk of suicide is higher in patients with major depression with low total cholesterol levels.

**Keywords:** Total Cholesterol Level, Depression, Suicide

### INTRODUCTION

Depression is a common illness worldwide, with more than 264 million people

affected.<sup>[1]</sup> Depression is different from usual mood fluctuations and short-lived emotional responses to challenges in everyday life. Especially when long-lasting and with moderate or severe intensity, depression may

become a serious health condition. It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. Close to 800 000 people die due to suicide every year. Suicide is the second leading cause of death in 15-29-year-olds.

Cohort and case control studies have found that lower serum total cholesterol is associated with depression.<sup>[2]</sup> Studies amount patients suffering from major depression show an association between low cholesterol and major depression. Besides, some trials showed that clinical recovery may be associated with a significant increase of total cholesterol.<sup>[3]</sup>

Colin A et al (2003) in his review stated that several cohort studies (on non-depressed subjects) have assessed the relationship between plasma cholesterol and depressive symptoms with contradictory results. Though some results found a significant relationship between a decrease of total cholesterol and high scores of depression, some others did not. Studies among patients suffering from major depression signaled more constantly an association between low cholesterol and major depression. Besides, some trials showed that clinical recovery may be associated with a significant increase of total cholesterol.<sup>[3]</sup>

Giltay EJ et al (2008) in their study on elderly men found that Serum total cholesterol was inversely associated with the Zung Self Rating Depression Scale (-0.61 points per 1 mol/L increase in cholesterol; 95% CI: -1.05 to -0.17;  $p < 0.05$ ), after adjustment for country, age, body mass index, smoking and alcohol intake. There was a modes inverse relationship between depression scores and serum total cholesterol in elderly men, but no associations with lipoprotein fractions or with the APOE genotype.<sup>[2]</sup> It can be thus concluded from their study that this decrease

in cholesterol was dietary in nature and the levels of cholesterol are decreased in depressive patients.

Shin JY et al (2008) in their meta-analysis of two cardiac risk factors found that higher total cholesterol was associated with lower levels of depression,  $d = -0.29$ ; this association was substantially larger among medication free samples ( $d = -0.51$ ). An inverse, non-significant association was observed between LDL and depression ( $d = -0.17$ ). High HDL was related to higher levels of depression, especially among women ( $d = 0.20$ ). Therefore they concluded that total cholesterol and depression were inversely related, with the strongest associations in medically naive samples, which is noteworthy because such samples should involve fewer confounds. One clinical implication is that the lipids of patients treated for depression should be monitored.<sup>[4]</sup>

## MATERIALS AND METHODS

The study was carried out in the department of physiology on 25 cases of mood disorders attending the Psychiatric OPD on their first visit to a psychiatrist of the department of psychiatry, Jawaharlal Nehru Medical College & Hospital, Aligarh Muslim University.

A total of 25 depressed patients and matched non-depressed controls were included in the study. The patients were diagnosed according to the DSM-IV criteria in the OPD by the consulting psychiatrist. Severity of depression was graded by 17-point Hamilton rating scale for depression. The control group consisted of premenopausal woman and were recruited from the Obstetrics & Gynecology department. The controls were having no current or past psychiatric illness.

All subjects signed an informed consent. Ethical clearance was obtained from institutional ethical committee.

Exclusion criteria: All subjects were medically healthy and were not treated for the current episode of depression. The patients and controls with the following conditions were excluded from the study.

1. Patients taking oral contraceptive pills.
2. Patients on psychotropic medications or other medications with the exception of aspirin or acetaminophen for more than 3 months prior to the study.
3. Pregnant or breast feeding subjects.

This was a case control study.

Collection of samples:

Blood samples were collected from female patients who were diagnosed as suffering

from mood disorders. The day of the menstrual cycle on which the sample was collected was calculated from the day of the last menstrual period. Each control woman was age matched with the depressed patient as blood sample was collected on the same day of her cycle as that of the corresponding depressed patient.

Intracubital venous blood (4 ml) was collected from the subjects. The blood was allowed to coagulate for 60 minutes in incubator at 37 C. Serum was separated after centrifuging at 3000 rpm for 10 minutes and was stored at -20 C till the estimation of total cholesterol was done. Estimation of LH, FSH, Total cholesterol was analyzed by ZAK method.

Statistical analysis was done by SPSS 11th ed.

## RESULTS

A total of 50 cases and control were taken and they were divided into two groups:

Group A: Consisted of 25 cases.

Group B: Consisted of 25 controls.

Both groups were further divided into follicular phase and luteal phase according to the phase of the menstrual cycle, during which the blood samples were obtained.

Patient Particulars	Phase of Menstruation	No of Samples (N)	Mean age (yrs)
Group A	Follicular	12	31.17±7.63
	Luteal	13	29.15±7.24
Group B	Follicular	12	34.17±5.22
	Luteal	13	29.23±7.97

The difference in age in the two groups was not significant ( $P>0.05$ ) on applying independent sample t test.

Hamilton Score	Hamilton Score	No Depression	Mild Depression	Moderate Depression	Severe Depression
Group A	20±4.73	0	0	9 (36%)	16 (64%)
Group B	2.12±1.76	25 (100%)	0	0	0

Out of the 25 patients with depression, 7 patients were studied in the first episode of major depression, 18 patients met DSM-IV criteria for recurrent unipolar depression. In 9 subjects, dysthymia preceded the onset of the current episode of depression. 6 patients met DSM-IV criteria for endogenous depression for the current episode, 12 for probable endogenous depression, and 7 for non-endogenous depression. 14 of 25 subjects met criteria for at least 1 anxiety disorder; 11 with generalized anxiety, 3 with panic disorder.

23 of 25 depressed patients suffered from sleep disorders. Of these 16 suffered sleep difficulty in all the three phases, 5 had difficulty in initial and middle phases only, and 2 had difficulty in middle and late phase.

	Total Serum Cholesterol (mg%)
Group A	158.39±22.05
Group B	170.02±38.26

T=1.85, p>0.05

The results for total serum lipids are shown in table. The total serum lipid for group A is 158.39±22.05 and for group B is 170±38.26. The level of total serum cholesterol is lower in group A but the difference is not significant by independent sample “t” test.

## DISCUSSION

Only female patients were recruited in the study because it has been found consistently that females have a higher incidence of depression.<sup>[5]</sup> The difference is almost two times more in females than in male and is associated with anxiety.<sup>[6,7]</sup> On Hamilton scoring, it was found that majority of depressive females were having higher scores. About 14 (56%) of the patients were suffering from some kind of anxiety. 11 of these patients were suffering with

generalized anxiety disorder and 3 were suffering from panic disorder which was severely hampering their functioning. These findings are consistent with Myers JK, Kessler RC, and Weissman M who found that the anxiety component is more predominant in female suffering from mood disorders.<sup>[7,8,9]</sup> A decrease in total cholesterol levels was observed in depressive patients, and this decrease was not significant (p>0.05). This decrease is in accordance with Shiny SY and Giltay EJ.<sup>[7,8]</sup> Shiny SY also recommended that lipid levels of depressive patients should be monitored as it has been reported that the risk of suicide is higher in patients with major depression with low total cholesterol levels.

Depression is associated with dietary factors and epigenetics. Serum cholesterol, which is prone to dietary influences, has been linked to symptoms of depression. This relationship may be (in part) due to altered epigenetic regulation of Methylene tetrahydrofolate Reductase (MTHFR). MTHFR codes for the MTHFR enzyme, which has diverse metabolic functions, and has recently been linked individually with diet, serum cholesterol levels and depressive symptoms. In 514 mother-child pairs, they examined prospective relationships between maternal (pregnancy) and child (7 years) serum cholesterol, MTHFR DNA methylation (DNAm; birth, 7 years), and development of depression symptoms from 8-15 years. After adjusting for potential confounding, we had three main findings. First, higher prenatal cholesterol associated (at a small effect size) with higher MTHFR DNAm at birth. Second, there was small effect size continuity for MTHFR DNAm between birth and age 7. Third, higher age 7 MTHFR DNAm associated with higher initial symptoms of depression symptoms at age 8, again at a small effect size. Overall, our findings

provide preliminary evidence for a relationship between prenatal cholesterol, MTHFR DNAm, and symptoms of depression in children.<sup>[10]</sup>

Jing DU, Ming Zhu, et al, in their review have hypothesized that chronic stress and sleep deprivation increase cortisol levels, which in turn leads to oxidative stress and high homocysteine levels and, subsequently, to mitochondrial damage and lipid degradation in neuronal circuits. The lipid raft region is composed of cholesterol, polyunsaturated fatty acids (including EPA, DHA), and sphingolipids and mediates neurotransmitter signaling through G-protein coupled receptors and ion channels. It has been shown that depletion of cholesterol, or EPA and DHA caused a decrease in numbers of lipid raft on the neuronal membrane, which may lead to the aberrant G-protein coupled receptor signaling. Lower serum cholesterol and DHA levels are associated with suicide attempts. It has been suggested that mitochondrial dysfunction and reduced formation of lipid raft may be involved in the etiology of depression and suicidal behavior.<sup>[11]</sup>

Engelberg suggested that, starting from the consideration that cholesterol, in biological membranes, is distributed in the phospholipid layer and can freely exchange with serum cholesterol. Thus, a reduction in serum cholesterol might decrease brain-cell membrane cholesterol and lower the lipid micro-viscosity. This could decrease the exposure of protein serotonin receptors on the membrane surface, leading to a reduced uptake of serotonin from the blood and reduced serotonin entry into brain cells. This lowering of serotonin entry leads to depression and suicidal tendencies.<sup>[12]</sup>

Cepeda and Kern, et al in their cross-sectional study using the National Health and Nutrition Examination Survey (NHANES) found no association of low cholesterol or any other lower type of cholesterol levels with increased risk of depression. They included subjects aged  $\geq 18$  years who responded to NHANES surveys from 2009 to 2015. Subjects were classified as having major depression if the Patient Health Questionnaire scores were  $\geq 10$ . Exposures were total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride levels. They considered the age, body mass index, gender, smoking, alcohol use, health status, and exposure to statins and antipsychotics as potential confounders. A total of 19,527 subjects were analyzed, and 8% had depression. Subjects with depression were more likely to be women and smokers, and to have higher body mass index, poor health, higher levels of total cholesterol and triglycerides and lower levels of high-density lipoprotein cholesterol than subjects with no depression. After adjustment, low levels of total cholesterol ( $< 129$  mg/dL) were associated with decreased risk of depression compared with higher levels, OR = 0.64 and 95% CI (0.42-0.98).<sup>[13]</sup>

Limitations of the study: The sample size of the study was very small. Due to this the results of the study cannot be generalized to the whole population.

Implications of the study: The study could not resolve the debate about the relationship of cholesterol levels and risk of suicide in depressive patients. Nevertheless, a decrease in cholesterol levels were seen in depressive patients. So, patients who are on statins and are being treated for depression should have their cholesterol levels monitored as well to

rule out the possibility of low levels of cholesterol hampering the efficacy of psychiatric treatment.

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