

Status of Interlukin-6 and lipid profile in depression disorder

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Abstract

Introduction: Present study was conducted to evaluate the role of interleukin-6 and lipid profile in patients of depression.

Materials and Methods: A case-control study consisted of 100 patients and 50 controls, who were attending psychiatric O.P.D in Geetanjali medical college & hospital, Udaipur Rajasthan. Inclusion criteria-depressive subjects those attending psychiatric O.P.D of Geetanjali hospital (20-60yrs). Exclusion criteria- patients undergoing treatment of any other hypertension, diabetes, cardiovascular disorders documented by physical & clinical examination. Level of IL-6 and lipid profile was measured in serum. Analysis was done using SPSS version 16.0 at significant level of 95% confidence level and p-value ≤ 0.005 .

Results: The mean total cholesterol level in depression patients was 136.08 ± 24.08 , mean HDL-c was 41.97 ± 16.50 , mean LDL-c was 109.33 ± 21.06 , mean triglycerides level was 134.28 ± 16.02 and mean interleukin-6 level was 4.19 ± 1.33 . The mean total cholesterol level in controls was 182.3 ± 35.76 , mean HDL-c was 51.3 ± 13.08 , mean LDL-c was 121.9 ± 25.69 , mean triglycerides level was 154.7 ± 24.45 and mean interleukin-6 level was 2.02 ± 0.43 . We found that there is a significant negative correlation between interleukin-6, total cholesterol (-0.730) and triglycerides (-0.896). There is significant positive correlation between interleukin-6 and LDL-c (0.977).

Conclusion: Depression is undoubtedly a multidimensional disorder. IL-6 exerts a multilayered effect on determinants of behavior, and understanding the role of IL-6 in the pathophysiology of depression may facilitate the elucidation of its effect on alterations in lipid metabolism.

Keywords: Cholesterol, Depression, HDL, Interlukin-6, LDL, Triglycerides.

Introduction

Depression is a mood disease that does persistent feelings of unhappiness, low mood & enjoyment, loss of concern and reduced energy. It is one of the most widespread disease across the world and a major factor in problems of mental health.¹ Interlukin-6 is a cytokine not only involved in inflammation and infection response but also in the regulation of metabolic regenerative and neural process.²

In depressive orders IL-6 is one of most important biochemical marker involved. IL-6 is a protein plays a pro-inflammatory cytokine. Along with immune cells of the peripheral blood but also by activated & microglia cells in CNS synthesized & released IL-6.³

In coronary artery diseases IL-6 levels is a strong independent inflammatory marker for increased mortality. Several studies have described that depression is a risk factor for occurrence of sub clinical carotid atherosclerosis and coronary artery disease, whereas other studies did not find a significant indication for a correlation between depression and coronary artery calcification.⁴ Especially, IL-6 was shown to be associatory with the diagnosis of CHD in really pooped patients. The relationship between depression and lipid profile & IL-6 serum concentration is less evaluated. But raised plasma levels of IL-6 anti-inflammatory cytokine predict contrary clinical consequence in chronic heart patients with depressive indications.

Neurons secrete serotonin and noradrenalin in response to IL-6. Noradrenalin can cause astrocytes to secrete IL-6. Selective serotonin reuptake inhibitors are generally considered first line treatment for the depression. It suggests

that higher plasma IL-6 activity was associated with the refractoriness of depression and high level of it might be a predictor for the reaction to selective serotonin reuptake inhibitors.⁵ Even we do not know whether raised IL-6 level in depressive patients are of immune origin because glutamate and nor epinephrine in CNS might contribute to increased IL-6 synthesis via microglia or astrocyte. So that IL-6 could serve as an immunological marker in mood disorder pathogenesis as well.⁶

The connection between the depressed mood and serum level of IL-6 has notably stronger in men than women. Cytokine are involved in the regulation of mood, sleep-wake cycle and food consumption. It is shown that IL-6 can also be raised in stress in humans.

An abnormal lipid metabolism is closely associated with psychiatric disorders. Levels of serum lipid are typically altered in patients of psychiatric illness linked with higher risk of coronary heart disease (CHD). Psychiatric patients have raised triglycerides and LDL-c level along with reduced HDL-c levels in comparison with non-psychiatric and this is associated with higher risk of CHD in them. High levels of HDL-c can lower an individual's risk of developing heart diseases. If HDL-c accounts for 20% of individual total cholesterol then the risk of arising heart disease is less than average. HDL-c fraction is importantly lower in many patients with major depressive disorder than in non-depressed individuals, and that clinical betterment following anti-depressant therapy is often associated with a significant increase in serum total cholesterol elevated HDL- c concentration are protective against coronary heart

disease, while reduced HDL-c concentration, particularly in conjunction with elevated TG, increase the cardiovascular risk.

Depression occurs about 2 times more frequently in women than in men. Psychiatric disorders and their relationship with dyslipidemia have been subjects for research since long but their correlation is not very clear.⁷

The survey of literature also revealed that very few studies have been carried out so far and that too, no study has ever been taken in Rajasthan and in the Udaipur, therefore the present study was undertaken to study the relationship of IL-6 and the lipid profile patients having depression and depressive disorder.

Materials and Method

A case-control study consisted of 100 patients and 50 controls selected from both genders ranging in age between 20-60 years, who were attending psychiatric O.P.D in geetanjali medical college & hospital, Udaipur Rajasthan.

Inclusion Criteria

Depressive subjects those attending psychiatric O.P.D of Geetanjali hospital (20-60yrs).

Exclusion Criteria

Patients undergoing treatment of any other hypertension, diabetes, cardiovascular disorders documented by physical & clinical examination. Level of IL-6 and lipid profile was measured in serum. Serum IL-6 was measured by solid phase sandwich ELISA method.⁸ Cholesterol measured by CHOD/POD, HDL by PEG-cholesterol esterase method, Triglycerides measured by GPO method and calculated LDL-c was measured by fridwald formula and called as calculated LDL-c. Analysis was done using SPSS version 16.0 at significant level of 95% confidence level and p-value ≤ 0.005 . Level of IL-6 was measured by Elisa method and lipid profile was measured on fully auto analyzer.

Results

This study included 150 patients of depression, who attended Psychiatric unit of Geetanjali medical college and hospital.

In present study, total 100 depression patients and 50 controls were taken and their lipid profile and interlukin-6 level was evaluated. The mean total cholesterol level in depression patients was 136.08 ± 24.08 , mean HDL-c was 41.97 ± 16.50 , mean LDL-c was 109.33 ± 21.06 , mean triglycerides level was 134.28 ± 16.02 and mean interlukin-6

level was 4.19 ± 1.33 . The mean total cholesterol level in controls was 182.3 ± 35.76 , mean HDL-c was 51.3 ± 13.08 , mean LDL-c was 121.9 ± 25.69 , mean triglycerides level was 154.7 ± 24.45 and mean interlukin-6 level was 2.02 ± 0.43 . This difference of lipid profile in patients and controls was highly significant with a p-value less than 0.05 (Table 1).

Table: 2 show the Pearson correlation between different parameters in patients

	Total Cholesterol	Triglycerides	LDL-c
Interlukin-6 (r)	-0.730	-0.896	0.977
Covariance	-23.417	-19.121	27.410
p-value=0.0001; Degrees of freedom:98			
Correlation is significant at the 0.05 level (2-tailed).			

Here, we calculate the Pearson correlation between interlukin-6 and lipid profile. We found that there is a significant negative correlation between interlukin-6, total cholesterol (-0.730) and triglycerides (-0.896). There is significant positive correlation between interlukin-6 and LDL-c (0.977). We also calculated covariance, which is measure how changes in one variable are associated with changes in a second variable. Specifically, covariance measures the degree to which two variables are linearly associated (Table 2). we also calculate correlation graph between interlukin-6 and different lipid profile parameters (Fig. 1; Fig. 2 and Fig. 3).

Discussion

Most persisting result address to affirm that higher concentration of IL-6 in the exacerbation psychiatric illness and its reduction during remission,⁹ including raised IL-6 to be a state marker of exacerbation.¹⁰ The association between the depressed state of mind and serum level of IL-6 has already have been depicted as significantly stronger in men than in women.¹¹

Raised level of IL-6 plasma levels at the time of acute depression and schizophrenia are in good agreement with recent reports.¹² That IL-6 levels of schizophrenic patients correlate with duration of illness. In our study we concluded that serum concentration of IL-6 (pg/ml) was significantly higher in cases as compared to healthy control ($p=0.0001$). The mean $\pm$ SD of IL-6 in depression disorder patients was 4.27 ± 1.38 , while in control group it was 1.95 ± 0.36 .

Table 1: Evaluation of clinical parameters of depression patients

Parameters	Cases (n=100)		Controls (n=50)		P-value
	Mean	SD	Mean	SD	
Total Cholesterol (mg/dl)	136.08	24.08	182.3	35.76	0.0001
HDL-c (mg/dl)	41.97	16.50	51.3	13.08	0.0006
LDL-c (mg/dl)	109.33	21.06	121.9	25.69	0.0016
Triglycerides (mg/dl)	134.28	16.02	154.7	24.45	0.0001
Interlukin-6	4.19	1.33	2.02	0.43	0.0001

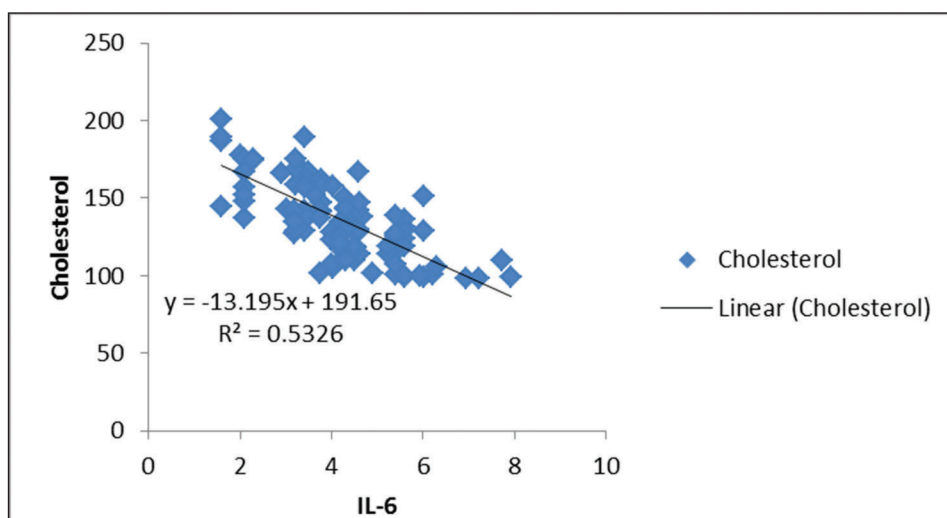


Fig. 1: Showing a negative linear Pearson correlation ($r = -0.730$; $R^2 = 0.532$) between cholesterol and Interlukin-6 in depression patients

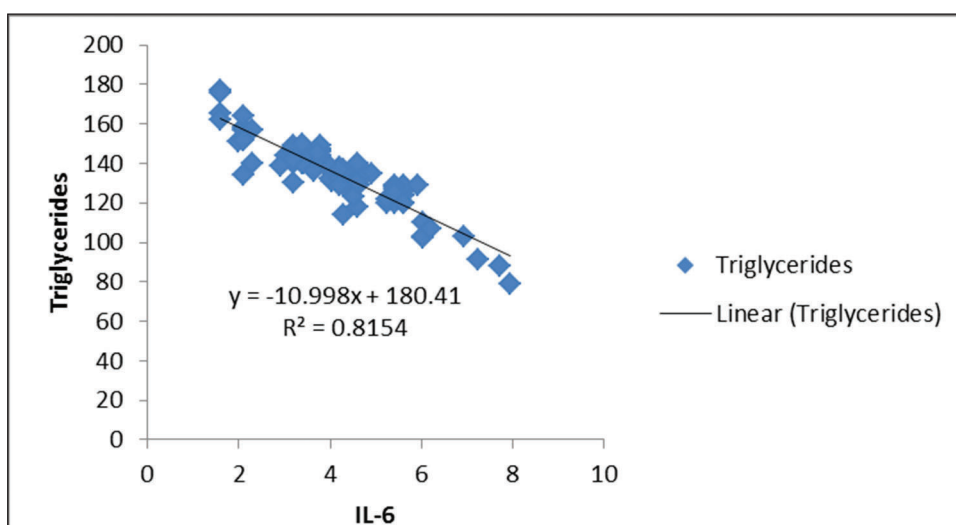


Fig. 2: Showing a negative linear Pearson correlation ($r = -0.896$; $R^2 = 0.815$) between Triglycerides and Interlukin-6 in depression patients

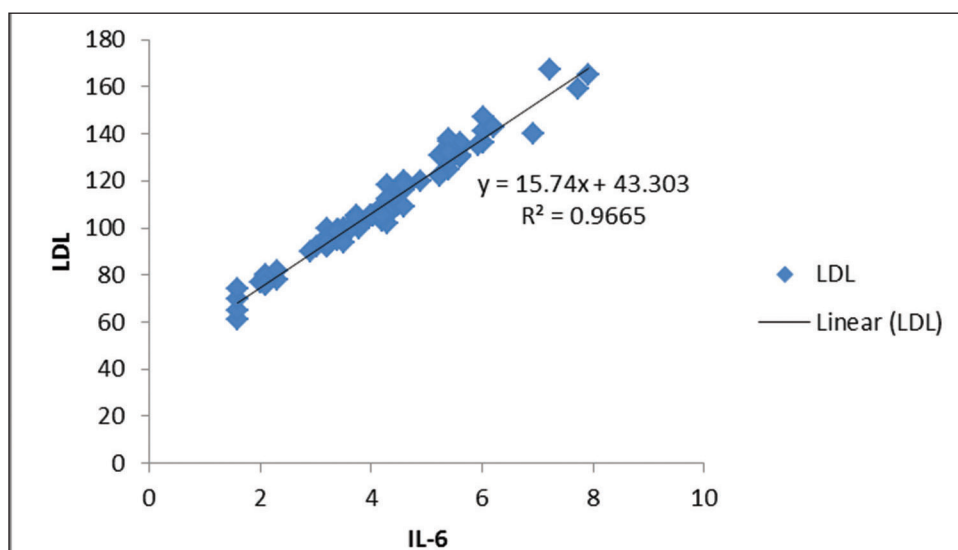


Fig. 3: Showing a Positive linear Pearson correlation ($r = 0.977$; $R^2 = 0.966$) between Triglycerides and Interlukin-6 in depression patients

The mean $\pm$ SD of subjects in cases of cholesterol (mg/dl) came to be 200.2 $\pm$ 51.41 and that of control group was 185.3 $\pm$ 37.32 which is statically significant ($p=0.005$). Present study suggested that plasma total cholesterol was associated with depression.

Similarly, the changes in mean LDL-c and triglyceride concentration were significantly altered when compared to the respective values in the control group. But they are at similarly with other who showed that the mean total cholesterol was either reduced¹³ or elevated¹⁴ in depression. The most striking change in lipid profile in this study is the significant increase in plasma triglyceride in depression, irrespective of the severity of disease, mood (suicide tendency or not) or level of plasma LDL-c (mg/dl) was higher in depression disorder patients and found the value of LDL-c was 128.3 $\pm$ 40.38 is compared to 118 $\pm$ 29.65 in control group. Therefore the rise LDL-c level was again statistically significant. ($p=0.0007$)

Serum HDL-c (mg/dl) level was decrease in depression disorder patients and values of HDL-c 42.2 $\pm$ 16.45 as compared to 50.8 $\pm$ 15.38 in control group. Therefore the difference among cases and control was not statistical significant ($p=0.160$).

The possible role of triglyceride metabolism in the etiology of depression is largely unknown but¹⁵ in an earlier study indicated a positive relationship between serum circulating triglyceride concentration and personality trait in depression. Similarly a previous study¹⁶ had reported that hypertriglyceridemia is associated with dementia.

In our study serum il-6 (pg/ml), serum LDL-c, cholesterol & TG level are increase in depression disorder as compared with control group. The difference among three groups was statistically significant whereas serum HDL-c level decrease in depression disorder as compared with control group.

Conclusion

Depression is undoubtedly a multidimensional disorder. In addition to stress as the most important cause of depression, other disease processes are increasingly being implicated in the depression pathophysiology. Age-associated accumulation of inflammatory insults may support the role of disease processes in behavioral alterations. IL-6 exerts a multilayered effect on determinants of behavior, and understanding the role of IL-6 in the pathophysiology of depression may facilitate the elucidation of its effect on alterations in lipid metabolism.

Conflict of Interest: None.

References

1. Sarokhani D, Delpisheh A, Veisani Y, Sarokhani MT, Manesh RE, Sayehmiri K, et al. Prevalence of Depression among University Students: A Systematic Review and Meta-Analysis Study. *Depress Res Treat* 2013;2013:373857. DOI: 10.1155/2013/373857. Epub 2013 Sep 25.

2. Scheller J, Chalaris A, Schmidt-Arras D, Rose-John S. The pro- and anti-inflammatory properties of the cytokine interleukin-6. *Biochim Biophys Acta* 2011;1813(5):878-88.
3. Dunn AJ. Endotoxin-induced activation of cerebral catecholamine and serotonin metabolism: comparison with interleukin-1. *J Pharmacol Exp Ther* 1992;261(3):964-9.
4. Rugulies R. Depression as a predictor for coronary heart disease. a review and meta-analysis. *Am J Prev Med* 2002;23(1):51-61.
5. Yoshimura R, Hori H, Ikenouchi-Sugita A, Umene-Nakano W, Ueda N, Nakamura J. Higher plasma interleukin-6 (IL-6) level is associated with SSRI- or SNRI-refractory depression. *Prog Neuropsychopharmacol Biol Psychiatry* 2009;33(4):722-6.
6. Miranda, HC, Sandraodebrecht VN, Edna Maria VR, Julie Massayo M., Maria Angrlica EW, et al. Higher than normal plasma il-6 concentration in Brazilian patients with mood disorders. *Braz Arch Biol Technol* 2011;54:717-22.
7. Cohn T, Prud'homme D, Streiner D, Kameh H, Remington G. Characterizing coronary heart disease risk in chronic schizophrenia: high prevalence of the metabolic syndrome. *Can J Psychiatry* 2004;49(11):753-60.
8. Bowcock AM, Kidd JR, Lathrop GM, Daneshvar L, May LT, Ray A, et al. The human "interferon-beta 2/hepatocyte stimulating factor/interleukin-6" gene: DNA polymorphism studies and localization to chromosome 7p21. *Genomics* 1988;3(1):8-16.
9. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB, et al. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97(18):1837-47.
10. Chen CC, Huang TL. Association of serum lipid profiles with depressive and anxiety disorders in menopausal women. *Chang Gung Med J* 2006;29(3):325-30.
11. Penninx BW, Kritchewsky SB, Yaffe K, Newman AB, Simonsick EM, Rubin S, et al. Inflammatory markers and depressed mood in older persons: results from the Health, Aging and Body Composition study. *Biol Psychiatry* 2003;54(5):566-72.
12. Maes M, Bosmans E, Meltzer HY, Scharpé S, Suy E. Interleukin-1 beta: a putative mediator of HPA axis hyperactivity in major depression? *Am J Psychiatry* 1993;150(8):1189-93.
13. Chen CC, Lu FH, Wu JS, Chang CJ. Correlation between serum lipid concentrations and psychological distress. *Psychiatry Res* 2001;102(2):153-62.
14. Shizuka K, Yambe T. Relationship between depression and lipid metabolism in the elderly with hypertension. *Nihon Ronen Igakkai Zasshi* 2001;38(6):785-90.
15. Fowkes FG, Leng GC, Donnan PT, Deary IJ, Riemersma RA, Housley E, et al. Serum cholesterol, triglycerides, and aggression in the general population. *Lancet* 1992;340(8826):995-8.
16. Rogers RL, Meyer JS, McClintic K, Mortel KF. Reducing hypertriglyceridemia in elderly patients with cerebrovascular disease stabilizes or improves cognition and cerebral perfusion. *Angiology* 1989;40(4 Pt 1):260-9.

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