ISSN: 2395-6429

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170049

RESEARCH ARTICLE

ALTERED LEVEL OF LIPID PROFILE IN DEPRESSION -A CASE CONTROL STUDY

Supriya.,[1]* Swapna Bondade[2]., Mangala Sirsikar[3]., Parineetha P B[1]., Iyshwarya U[1] and Jayaprakash M DS[1]

[1]Department of Biochemistry, the Oxford Medical College Hospital and Research centre Yadavanahalli, Attibele Hobli, AnekalTaluk, Bengaluru, Karnataka,India

[2]Department of Psychiatry,The Oxford Medical College Hospital and Research centre Yadavanahalli, AttibeleHobli, Anekal Taluk, Bengaluru, Karnataka, India

[3]Department of Biochemistry, VydehiInstitute of Medical Sciences and Research Centre, #82, EPIP Area,White Field, Bangalore, Karnataka, India

ARTICLE INFO

Article History:

Received 8th January, 2017
Received in revised form 25th February, 2017
Accepted 10th March, 2017
Published online 28th April, 2017

Key words:

Depression, Lipid Profile, Dyslipidemia in Depression

ABSTRACT

Association between dyslipidemia with major depressive disorder is complex and isdebatable. Lower levels of circulating lipid fractions and cholesterol are risk factors for impulsivity and depressive disorder.Thus aim of this study was to investigate the levels of serum lipids (cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol LH ratio) and BMI in patients with major depression. Assess the severity, correlation and whether lipid components differ between depressed and non-depressed people. The study included 65 patients affected by depression. Diagnosis of major depressive disorder was made according to the criteria by applying HAMD and HAMA questionnaire.65 Age and sex matched healthy controls. Serum concentrations of cholesterol, triglycerides LDL-cholesterol and HDL-cholesterol were determined by enzymatic method. VLDL-cholesterol and LDL/HDL -cholesterol ratio were determined by calculation methods. The correlation was calculated using Pearson correlation coefficient. The P values were two tailed and probability level for significant difference was set at $P < 0.05$. In our result we found that Depressive symptoms were significantly associated with low total cholesterol, low triglycerides, low high-density lipoprotein cholesterol (HDL-C), low low-density lipoprotein cholesterol (LDL-C) and VLDL and also found associations of serum lipids with depressive symptoms were statistically significant. To conclude Elevated depressive symptoms are associated with low concentration of each component of lipid profile, showing inverse relationship associated with measures of depression and anxiety.

INTRODUCTION

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide. Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported having an episode of depression in the previous year Depressive disorders often start at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is the leading cause of disability worldwide in terms of total years lost due to disability. The demand for curbing depression and other mental health conditions is on the rise globally. A recent World Health Assembly called on the World Health Organization and its member states to take action in this direction (WHO, 2012)Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. For every person who completes a suicide, 20 or more may attempt to end his or her life (WHO, 2012).[1] While depression is the leading cause of disability for both males and females, the burden of depression is 50% higher for females than males (WHO, 2008). In fact, depression is the leading cause of disease burden for women in both high-income and low- and middle-income countries (WHO, 2008)[2]Many factors may play a role in depression, including genetics, brain biology and chemistry, and life events such as trauma, loss of a loved one, a difficult relationship, an early

childhood experience, or any stressful situation. Depression can co-occur with other serious medical illnesses such as diabetes, cancer, heart disease, and Parkinson's disease. Depression can make these conditions worse and vice versa. Sometimes medications taken for these illnesses may cause side effects that contribute to depression. Depressive disorders, also known as mood disorders, include three main types: major depression, persistent depressive disorder, and bipolar disorder. Depressive disorders can affect people of any age, including children, teenagers, adults, and older adults.

Cholesterol is synthesized ubiquitously in the human body as an essential component of cell membranes and lipoproteins and is a precursor of steroid hormones and bile acids. Hypercholesterolemia is associated with an increased risk of atherosclerosis and coronary heart disease. Dietary or therapeutic lowering of cholesterol is able to reduce the number of deaths due to coronary disease [3], but in several studies, a significant increase in mortality due to suicide or violence was observed [4,5].

Serum cholesterol has been associated with late-life depression. However, some research has showed rather inconsistent results, ranging from positive and negative association to no association between total cholesterol and depression.[6,7]this may reflect the complexity of the relationship between cholesterol and depressive symptoms. In addition, other components of serum lipids, such as triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) may also play a role in the development of depression. However, very few population-based studies have so far examined the associations between a broad range of lipid profile and depressive symptoms among older people.[8] There is a clear evidence indicates that disturbances of fatty acids and phospholipids metabolism can play a part in a wide range of psychiatric, neurological and developmental disorders in adultsMcLoughlin *et al*.[9] speculated that lipids and some elemental micronutrients constitute major parts of the human brain.

Therefore, the factors affecting cerebral lipids could have profound effects on normal brain functioning.[10] The possible mechanism for low cholesterol as follows, the cholesterol-serotonin hypothesis was initially proposed to explain the link between low cholesterol levels and depression. This hypothesis states that reduction of serum TC may decrease brain cell membrane cholesterol and thereby lowering micro viscosity of the cell membrane and subsequently decreasing the exposure of protein serotonin receptor on the membrane surface resulting in poorer uptake of serotonin from blood and less serotonin into brain cells leading to depression.[11]Another possible mechanism may be that interleukin-2 lowers cholesterol and increases triglycerides and also suppresses melatonin secretion, thus causing depression and suicidal tendencies.[12]

MATERIAL AND METHODS

The present study was carried out in Department of Biochemistry "oxford Medical college and Research Centre Bangalore". Age and sex matched 130 patients were selected for this study and divided in two groups as follows: Group I - Control (Normal Healthy Subjects) age and sex matched healthy control subjects were selected from non-blood relatives of patients.. (n=65) and Group II - Newly Diagnosed psychiatric patients (n =65). Informed consent was obtained prior to inclusion on the study and the subjects were explained in detail about the nature and purpose of the study. The controls were of either sex, aged between 18 and 60 years, had no current psychiatric diagnosis, scored less than 2 on General Health Questionnaire (GHQ), receiving no psychotropic medication and had no alcohol or substance dependence disorder, other than nicotine. Exclusion criteria for control and patients include the presence of organic diseases such as hypertension, diabetes, cardiovascular, hepatic and thyroid disorder documented by physical and clinical examination. Pregnant and menopausal women were also excluded from the study group. Current history of substance abuse (except nicotine), borderline personality disorder, psychosis or eating disorder, Persons with known history of dyslipidemia, Persons who are under any treatment or diet or having illness known to interfere with lipid metabolism.

After explanation of the study, informed consent was obtained from all participants before the study. About 5 milliliter of blood was collected under aseptic precaution in a sterile bulb from selected subjects. All the subjects and controls underwent estimation of their serum cholesterol, LDL and HDL cholesterol, serum TG levels. A fasting blood sample was taken in plain tube without anticoagulant for measurement of TC, HDL and TG by standard enzymatic method. The samples were stored at −70°C until analysis. Serum cholesterol was estimated by cholesterol oxidase method, TG by enzymatic hydrolysis and HDL cholesterol by phosphotungstate-magnesium chloride precipitation method. LDL cholesterol was calculated using Friedwald formula, i.e., LDL cholesterol = Serum TC − (TG/5 − HDL cholesterol).Cut off values to define dyslipedemia were as follows: Total Cholesterol > 200mg%, HDL <40 mg%, LDL > 130mg%, VLDL >35mg% & TG >160 mg%. [13]

Hamilton Rating Scale for Depression (HRSD)[14]Rating Scale (HDRS), abbreviated HAM-D, is a multiple item questionnaire used to provide an indication of depression, and as a guide to evaluate recovery. The HAM-D is designed to rate the severity of depression in patients. Although it contains 21 areas, calculate the patient's score on the first 17 answers.

Scoring

Total Items 1 To 17

0 - 7 = Normal,8 - 13 = Mild Depression, 14-18 = Moderate Depression, 19 - 22 = Severe Depression, > 23 = Very Severe Depression

The HAM-A was one of the first rating scales developed to measure the severity of anxiety symptoms, and is still widely used today in both clinical and research settings. The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety.

Scoring

Each item is scored on a scale of 0 (not present) to 4(severe), with a total score range of 0-56, where <17 indicates mild severity, 18-24 mild to moderate severity and25-30 moderate to severe.[15]

RESULT

The mean age of the subjects of study group in years is 36.81±9.79 and in the control group, it is 32.43±2.13. Total

number of depression symptoms found more between age group 30-40(68%) then compared to 18-29 and 41-60.The number of males and females in the study group were 17 and 48 respectively, in the control group were 18 and 47, respectively. More female subjects (72.3%) in study and control group then male 27.7%. Nearly 83.1% individuals of the sample were married and there was no difference in marital status between study group and control group. (58.5%) of the study samples were unemployed whereas all the controls were employed. Nearly (84%) subjects had no family history and only (20%) subjects had family history of depression. (27.69%) subjects in study group had past history. Nearly (53%) subjects had suicidal tendencies. There was significant difference in employment status between two groups (**P** = 0.02). The mean BMI in 65 subjects of patient group was 23.11 ± 1.87 kg/m^2, while it was 21.85 ± 1.9 kg/m^2 in control group. The difference in BMI between two groups was significant (P = 0.006).

Table1 Distribution of lipid parameter in cases and control

Lipid parameters	Cases	Controls
Cholesterol mg/dl	203.5±34.64	213.3428571±47.36
Triglycerides mg/dl	112±18.38	219.3571±90.00
HDL mg/dl	48.5±2.12	46.11429±5.96
LDL mg/dl	147.5±57.27	122.2114±34.53
VLDL mg/dl	21.5±4.94	44.08571±18.03

Table 2 Pearson correlation between HMA-A/HMA-D and lipid profile parameter

Lipid Parameters	HMA-A (r) Value	Correlation	P Value	HMA-D (r)value	Correlation	P -Value	significance
Cholesterol mg/dl	-0.067	Negative	0.59	-0.38	Negative	0.001	<0.01
Triglycerides mg/dl	-0.168	Negative	0.18	-0.28	Negative	0.02	<0.05
HDL mg/dl	-0.112	Negative	0.37	-0.36	Negative	0.003	<0.01
LDL mg/dl	-0.128	Negative	0.30	-0.29	Negative	0.01	<0.05
VLDL mg/dl	-0.164	Negative	0.20	-0.26	Negative	0.05	<0.10
BMI	-0.180	Negative	0.15	-0.40	Negative	0.01	<0.01

Serum lipid profiles

The mean Total cholesterol of 65 patients in study group was203.5±34.64mg/dl while it was 213.34±47.36mg/dl in 65 control subjects of group. The mean LDL cholesterol of 65 patients in study group was147.5±57.27 mg/dl while it was 122.21±34.53mg/dl in 65 control subjects of group. The mean HDL cholesterol of 65 subjects in study group was 48.5±2.12mg/dl while it was 46.11±5.96 mg/dl for 65 subjects of control group. The mean TC of 65 subjects in study group was 112±18.38mg/dl while it was 219.3571 ± 90.00mg/dl for 65 subjects of control group.

Thus TC, HDL and TG levels were significantly low in the study group than the control group. The duration of illness in patient group ranged from 20 days to 2 years with a mean of 4.97 ± 4.67 months. Out of 65 subjects with depression based on HAMA/HAMD Score showed mild severity 49.2%, mild to moderate severity of 29.2%, moderate to severe 21.55% The cutoff score on the HAMD that maximized the sum of sensitivity and specificity was 17 for the comparison of mild vs. moderate depression and 24 for the comparison of moderate vs. severe depression. Thus in our study we found more patient in moderate to severe depression).

DISCUSSION

Our study we found no significant association between the low levels of serum lipid profile and psychiatric diseases since the results aren't strongly suggestive of link between low cholesterol and psychiatric disorders. Our findings are consistent with very few studies since majority of studies strongly support the association between the low lipid profiles and psychiatric diseases. Fiedorowicz JG *et al*., studied association between low serum cholesterol levels and suicide attempts in patients with major affective disorders and reported that there was no link between the two[16]. Huang *et al*[17] reported the role of TG, VLDL as the possible biological markers for depressive syndromes[17]

Our study found that the TC levels were significantly low in patients suffering from depression as compared to healthy individuals. According to Sheikh N *et al* this may be due to changes in the cholesterol content of the synaptosomal membrane and a decrease in the number of serotonin receptors due to a decrease in cholesterol concentration [18]. According Weverling-Rijnsburger AW *et al* [19] in his recent study, men who have relatively low levels of cholesterol (< 160 mg/dl) are four to seven times more likely to report symptoms of severe depression than men with high cholesterol levels.

Fowkes et a l[20] and Ancelin ML, *et al* [21]. Showed in his study is that there was a significant increase in plasma triglyceride in depression, irrespective of the severity of disease, mood (suicide tendency or not) or level of plasma total cholesterol.

It was also noted that the change was more pronounced in female patients when compared with their male counterparts [21]

Results were similar to our study. In our study also found female preponderance. Fifty percent of middle aged women experience a dramatic change in their emotion as well as change in physical states because of alteration in their hormone levels. Bromberger *et al*.[22] concluded that the menopausal transition and postmenopausal years are accompanied by health problems, inadequate social support, marital / sexual issues and other stressful events (e.g. disease, death of a spouse, children leaving home) could increase the risk for depression. The possible role of triglyceride metabolism in the aetiology of depression is largely unknown but Fowkes *et al* in an earlier study also indicated a positive relationship between serum circulating triglyceride concentration and personality trait in depression.

Association between low cholesterol levels and depressive symptoms was observed in the higher age categories and not in the younger age categories as recently reported by Brown *et al*. [23] similar results obtained by our study more subjects found between the ages of 30-60 ages would play a crucial role for explaining the results of our study.

Papakostas *et al.*[24] have proposed that both elevated and low cholesterol levels may be associated with serotonergic dysfunction. The positive correlation between depression and

coronary artery disease is well-established. There is evidence of hypothalamo-pituitary-adrenal axis hyperactivity in depression, which can cause hypercortisolemia, which further can induce hypercholesterolemia and hypertension and thereby increasing the risk for coronary heart disease.[25] So as per result of our study, i.e. low cholesterol is associated with depression, it would be difficult to interpret the relation between depression and coronary heart disease. However, studies have also shown that subjects having high cholesterol were having depressive symptoms. Papakostas *et al***.** also showed that Low serum cholesterol in depression could be a consequence of depression because of their poor health and decreased food intake.

Maes *et al*.[26] reported that changes in serum lipid comparison may be related to suicide, major depression and immune inflammatory responses. Their findings suggest that major depression is accompanied by reduced formation of cholesterylesters and perhaps by impairment of reverse cholesterol transport. The latter is reportedly accompanied by lower serum high density lipoprotein cholesterol (HDL - C). They concluded major depression is accompanied by lower serum HDL-C or by abnormal levels of serum total cholesterol, triglycerides, low density lipoprotein C Not only the depression but also the suicidality is associated with the lipid levels. Lalovic *et al* [27] reported higher suicidal rates among biological relatives of subjects with partial deficiency of 7-dehydro- cholesterol reductase enzyme. According to Rabe-Jablonska *et al* [28], low cholesterol & low LDL may be helpful in determining the suicidality among depressed. Kim *et al* [29] reported higher incidence of suicide among patients with low serum cholesterol.

Horstenetal.[30] investigated associations between cholesterol and other psychosocial factors (social support, vital exhaustion, and stressful life events), which are known to be related to depression in middle-aged women.

CONCLUSIONS

This work is conducted to show the correlation between serum cholesterol and depressive disorder to find out risk factors for impulsivity and depressive disorder.

These results do not suggest that serum lipid profiles can be used as biological markers to distinguish depressive or anxiety disorders. Given the inconsistencies in the data, it appears that only some individuals with low serum cholesterol levels evidence depressive symptoms, mood disorders, suicidal ideation, and/or suicide attempts. However, this area of investigation appears potentially fertile. Indeed, future investigations need to examine whether some individuals have a predisposition to depressive symptoms/mood disorders and suicidal ideation/suicide attempts that is presaged by low serum cholesterol levels; whether cholesterol assessment, in conjunction with the measurement of other metabolic or neurohormonal parameters, might suffice as a biological marker in some susceptible individuals; and whether in affected individuals, cholesterol elevation with treatment signifies a consistently good response to medications. Only further investigation will clarify these intriguing cholesterol quandaries.

Reference

1. World Health Statistics 2012. Available from: http://www.who.int/gho/indicator registry. [Last accessed on 2017 April 23].
2. Bebbington P, Dunn G, Jenkins R, *et al*. The influence of age and sex on the prevalence of depressive conditions: report from the National Survey of Psychiatric Morbidity. *Int Rev Psychiatry* 2003; 15:74-83.
3. Treasure CB, Klein JL, Weintraub WS, Talley JD, Stillabower ME, Kosinski AS, *et al*. Beneficial effects of cholesterol-lowering therapy on the coronary endothelium in patients with coronary artery disease. *N Engl J Med*1995; 332:481-7.
4. Muldoon MF, Manuck SB, Mathews KM. Lowering cholesterol concentrations and mortality. A quantitative review of primary prevention trials. *Br Med J* 1990; 301:309-14.
5. Davey Smith G, Pekkanen J. Should there be a moratorium on the use of cholesterol lowering drugs? *Br Med J* 1992; 304:341-8.
6. Huang TL, Wu SC, Chiang YS, Chen JF. Correlation between serum lipid, lipoprotein concentrations and anxious state, depressive state or major depressive disorder. *Psychiatry Res* 2003; 118:147-53.
7. Aijanseppa S, Kivinen P, Helkala EL, Kivela SL, Tuomilehto J, Nissinen A. Serum cholesterol and depressive symptoms in elderly Finnish men. *Int J GeriatrPsychiatr.* 2002; 17:629-34.
8. Kamezaki F, Sonoda S, Nakata S, Okazaki M, Tamura M, Abe H, *et al*. Elevated depressive symptoms are associated with hypertriglyceridemia in Japanese male workers. *Intern Med* 2011; 50:2485-90.
9. John W. Metabolic syndrome and mental illness. A M J Manaq Care.2007; 13(7):170-177.
10. McLoughlin I, Clarke P. Lipid lowering drugs. *Br. J Psychiatry* 1989; 154:275-276.
11. Engelberg H. Low serum cholesterol and suicide. *Lancet* 1992; 339:727-9.
12. Penttinen J. Hypothesis: low serum cholesterol, suicide and interleukin-2. *Am J Epidemiol*. 1995;141(8): 716-718.
13. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA2001; 285(19):2486-2497. doi: 10. 1001 / jama. 285.19.2486.
14. Hedlund JL, Viewig BW. The Hamilton rating scale for depression: A comprehensive review. *Journal of Operational Psychiatr*y 1979; 10:149-165.
15. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol* 1959; 32:50-55.
16. Fiedorowicz JG, Coryell WH. Cholesterol and suicide attempts: a prospective study of depressed inpatients. *Psychiatry Res* 2007; 152(1):11-20.
17. Huang TL, Chen JF. Lipid and lipoprotein levels in depressive disorders with melancholic feature or atypical feature and dysthymia. *Psychiatry ClinNeurosci* 2004; 58:295-9.

18. Sheikh N, FarhadiNasab, Araghchian M and Mani KashaniKh. The relationship of cholesterol and triglyceride with depression. *ActaMedicaIranica* 2004;42(3):185-87.
19. Weverling-Rijnsburger AW. Total cholesterol and risk of mortality in the oldest old. *Lancet* 1997; 350(9085):1119-23.
20. Fowkes, FG, Leng GC, Donnan PT, DearyIJ, Riemersma RA, HouselyE. Serum cholesterol, triglyceride and aggression in the general population. *Lancet* 1992; 340 (8826): 995-998.
21. Ryan J, Carriere I, Scali J, Ritchie K, Ancelin ML. Lifetime hormonal factors may predict late-life depression in women. *International psychogeriatrics IPA* 2008; 20(6):1203-1218.
22. Bromberger JT, Matthes KA, Schott LL. Depressive symptoms during the menopausal transition: the study of women's health across the nation (SWAN). J *Affect Disord* 2007; 103: 267-72.
23. Brown SL, Salive ME, Harris TB, Simonsick EM, GuralnikJM, Kohout FJ. Low cholesterol concentrations and severe depressive symptoms in elderly people. *B M J* 1994; 308(6940): 1328-1332.
24. Papakostas GI, Ongür D, Iosifescu DV, Mischoulon D, Fava M. Cholesterol in mood and anxiety disorders: Review of the literature and new hypotheses. *EurNeuropsychopharmacol* 2004; 14:135-42.
25. Raadsheer FC, Hoogendijk WJ, Stam FC, Tilders FJ, Swaab DF. Increased numbers of corticotropin-releasing hormone expressing neurons in the hypothalamic paraventricular nucleus of depressed patients. *Neuroendocrinology* 1994; 60:436-44.
26. Maes M, Smith R, Christophe A, Vandoolarghe E, Vangastle A, Neels H, *et al*. Lower serum high density lipoprotein cholesterol(HDL-C) in major depression and in depressed men with serious suicidal *IJSAR* 2014;1(2):33-40.
27. LalovicA, Merkens L, Russell L, Arsenault-Lapierre G, Nowaczyk MJ, Porter FD, *et al*. Cholesterol metabolism and suicidality in Smith-Lemli-Opitz syndrome carriers. *Am J Psychiatry* 2004; 161:2123-6.
28. Rabe-Jablonska J, Poprawska I. Levels of serum total cholesterol and LDL-cholesterol in patients with major depression in acute period and remission. *Med SciMonit* 2000; 6:539-47.
29. Kim YK, Myint AM. Clinical application of low serum cholesterol as an indicator for suicide risk in major depression. *J Affect Disord* 2004; 81:161-6.
30. Horsten M, Wamala SP, Vingerhoets A, Orth-Gomer K. Depressive symptoms, social support, and lipid profile in healthy middle-aged women. *Psychosom Med* 1997; 59:521-8.

****