A RETROSPECTIVE EVALUATION OF THE INFLAMMATORY MARKER C-REACTIVE PROTEIN (CRP), CHOLESTEROL AND HIGH-DENSITY LIPOPROTEINS IN PATIENTS WITH MAJOR DEPRESSION: PRELIMINARY FINDINGS

F. GAMBI[1], D. DE BERARDIS[1-3], D. CAMPANELLA[1], A. CARANO[1], G. SEPEDE[1], G. SALINI[1], B. SCORRANO[1], S. SPINELLA[1], C.M. CONTI[1], R. LA ROVERE[1], A. VALCHERA[2], E. MANCINI[3-4], D. CEDDIA[3], L. MARCHIONNI[3], E. CALCAGNI[5], C. COTELLESSA[1], R.M. SALERNO[1] and F.M. FERRO[1]

[1]Department of Oncology and Neurosciences, Institute of Psychiatry, University "G. D'Annunzio" of Chieti; [2]ASUR Marche 8; [3]Marinferm, Italian Navy, Ancona; [4]Chinical Psychology, University of Chieti; [5]University of Rome Tor Vergata, Italy

Received February 7, 2005 – Accepted October 4, 2005

The aim of this study was to retrospectively evaluate the role of C-reactive protein, total cholesterol and high-density lipoprotein cholesterol in patients suffering from Major Depression (MD). Data of C-reactive protein, total cholesterol (TC) and high-density lipoprotein cholesterol of 37 adult outpatients (17 men, 20 women) with a DSM-IV diagnosis of MD were analyzed. Depression was measured with the 17-item Hamilton Depression Rating Scale (HAM-D) and with the Beck Depression Inventory (BDI). Suicide risk was evaluated with the Scale of Suicide Ideation (SSI). Patients with a lifetime history of attempted suicide were categorized as having higher suicide risk. Higher suicide risk patients showed higher C-reactive protein levels and lower high-density lipoprotein cholesterol levels than lower suicide risk patients whereas total cholesterol levels were not statistically different. C-reactive protein positively correlated with BDI, HAM-D, SSI scores and with number of previous depressive episodes. High-density lipoprotein cholesterol correlated inversely with BDI, HAM-D and SSI scores, whereas, no significant correlations were found between Total Cholesterol and other variables including C-reactive protein. In linear regression models, C-reactive protein was predictor of more severe depression and increased suicide risk. Lower high-density lipoprotein cholesterol levels were significantly predictive of increased suicide risk.

The role of inflammatory markers in psychiatric disorders such as Major Depression (MD) has been investigated in several studies. More recently, researcher's attention has been focused on interrelationships between high C-reactive protein (CRP) levels and depressive symptoms (1-2). Research suggest that higher CRP levels might be related to an increased risk for coronary heart disease (CHD), peripheral vascular disease and stroke (3-4). In addition, the presence of depressive symptoms is an important predictor of morbidity and mortality in patients with coronary disease, particularly after myocardial infarction, independent of previous cardiac history or CHD severity (5-7). Thus, the relationship of CRP and MD may have a significant clinical relevance.

Key words: major depression, suicide risk, C-reactive protein, total cholesterol, high-density lipoprotein

Mailing address: Francesco Gambi, MD
Department of Oncology and Neurosciences, - Institute of Psychiatry,
University "G. D'Annunzio" Chieti,
Palazzina SE.BI. - Scuole di Specializzazione,
via dei Vestini, 31 - 66013 Chieti (Italy).
Tel:: +3908713556750 - Fax: +3908713556721
Email: f.gambi@unich.it

1721-727X (2005)

Although some reports indicate that changes in serum lipid composition may be related to suicide, major depression and immune-inflammatory responses (8-9, 19), other studies show conflicting results (11-14).

The present study was a retrospective review of adult outpatients diagnosed with MD. Medical records were used to analyze CRP, Total Cholesterol (TC) and High-density lipoprotein cholesterol (HDL) levels, in order to clarify possible connections between inflammatory markers and change in serum lipid levels. Additionally, possible predictive variables associated with MD and suicides were evaluated.

MATERIALS AND METHODS

37 adult outpatient subjects (17 men, 20 women) with a Major Depressive Episode (single episode or recurrent), according to Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) criteria (15), were included in the analysis. Diagnoses were made by clinical assessment, following the Structured Clinical Interview for DSM-IV-Outpatient version (SCID-OP; Italian version) (16). Their average age was 41.3 ± 9.2 years (age range: 27-57 years). Only patients seeking consultation for the first time in our center were considered eligible for the analysis.

Exclusion criteria included: age below 18 years or over 65 years, history of a manic or hypomanic episode, current mania or hypomania, comorbidity with schizophrenia or other psychotic disorders, drug or alcohol dependence, organic mental disorders, pregnant or nursing women, treatment with anti-inflammatory or immunosuppressant drugs. Patients included in the study had no serious medical conditions in their history that required anti-inflammatory treatment for more than one week. Subject with diabetes, other endocrinologic disorders, hypertension, liver dysfunction or other conditions necessitating chronic pharmacotherapy were excluded. Abnormal concentrations of T3, T4, ALT, AST or proteinogram results were exclusion criteria. Patients who received medication for cholesterol dysregulation in the last 6 months and those whose body mass changed substantially within the last 4 weeks prior to screening were also excluded from the analysis.

All participants had to have met criteria for a major depressive episode with a score of at least 15 on the Hamilton Depression Rating Scale, 17-item version (HAM-D) a clinician-administered rating scale (17). Also scores of Beck Depression Inventory (BDI) (18), a 21-item self-report scale that gives a global score on depressive symptoms, were reviewed. To assess suicide risk, the Scale of Suicide Ideation (SSI) scores (19), a 3 point rating scale with statements of suicidal intentions, were evaluated. We used a lifetime history of attempted suicide to identify patients with higher suicide risk from patients without a lifetime history of attempted suicide, who were categorized as lower suicide risk group. Self reported weight and height were used to calculate Body Mass Index (BMI) (kg/m^2).

Serum CRP was measured using a highly sensitive nephelometric assay (BN-II Nephelometer; Dade Behring, Deerfield, IL) (20). This system was able to detect a minimal CRP concentration of 0.22 mg/dl. Total cholesterol was determined by an enzymatic method. High-density lipoprotein cholesterol (HDL) was measured after phosphotungstic acid/$MgCl_2$ precipitation on fresh plasma. Blood samples were taken between 7:30 and 8:30 a.m. after the patients had fasted for at least 10 h.

Statistics

Descriptive statistics (means and standard deviations as appropriate) were computed for the study samples on demographic variables and other parameters. The data were checked for deviations from the Gaussian distribution using the Kolmogorov-Smirnov test. The comparison of data between the groups was performed using the Mann-Whitney U test. The Spearman rank correlation coefficient was used to assess the relationship between the degrees of change on various study measures. Two multiple linear regression analyses were performed to assess predictive factors of depression severity (HAM-D as dependent variable, Model 1) and suicide risk (SSI as dependent variable Model 2) in the study sample. Two-tailed tests were used; P values equal or less than 0.05 were deemed statistically significant. Results are expressed as Mean ± Standard Deviation (SD).

RESULTS

Descriptive statistics of the whole sample are reported in Table I. Gender comparison between all demographic and clinical variables showed no significant differences. Lifetime history of attempted suicide was reported in 14 patients (37.8%). Comparison of CRP indicated that higher suicide risk patients showed higher CRP levels than lower suicide risk patients (respectively 2.6 ± 1.1 vs 1.4 ± 0.6; $p<0.001$) (Fig. 1). Together with higher CRP levels, higher suicide risk patients showed lower HDL levels than lower suicide risk patients

Gender (M/F) (n)	17/20
Age (years)	31.9 ± 8.8
Duration of illness (years)	12.0 ± 7.0
Onset of illness (years)	19.9 ± 5.8
Episodes (number)	2.9 ± 1.5
BMI (Kg/m^2)	23.2 ± 3.2
BDI	26.3 ± 4.9
HAM-D	23.1 ± 5.0
SSI	15.8 ± 7.9
CRP (mg/liter)	1.9 ± 1.0
TC (mg/dl)	188.5 ± 17.4
HDL (mg/dl)	52.9 ± 8.7

Table I. *Demographic and clinical data of whole sample (n=37). Data are expressed as mean ± SD, unless otherwise specified.*

(P=0.04) whereas TC levels were not statistically different (Table II).

Comparison of the clinical data showed that individuals with higher suicide risk had an higher number of previous depressive episodes and higher BDI, HAM-D and SSI scores than patients with lower suicide risk.

In our sample, we found positive correlation between CRP and BDI, HAM-D and SSI scores (Table III). Moreover, CRP positively correlated with number of previous depressive episodes. On the other hand, HDL correlated inversely with BDI, HAM-D and SSI scores whereas no significant correlations were found between TC and other variables including CRP. In linear regression models (Table IV), CRP was predictor of more severe

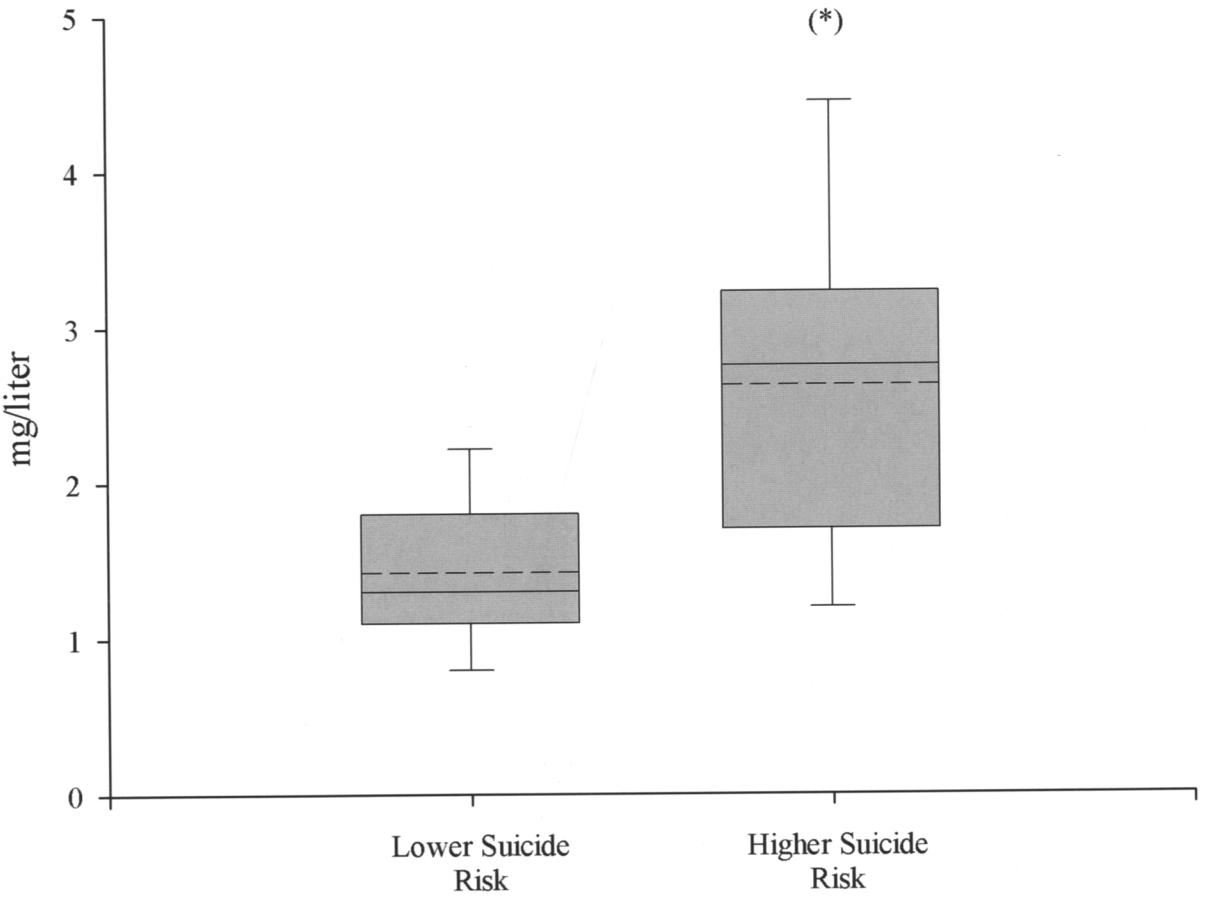

Fig. 1. *Boxplots of CRP levels indicating differences between individuals with higher (patients with a lifetime history of attempted suicide, n=14, 37.8 %) and lower suicide risk (patients without a lifetime history of attempted suicide, n=23, 62.2%). The solid line and short dash line indicate median and mean, respectively. The lower and upper boundary of box indicates 25th and 75th percentile, respectively. The upper and lower error bars define the 10th and 90th percentiles ((*)p<0.001).*

	Lower suicide risk (patients without a lifetime history of attempted suicide) (n=14, 37.8%)	Higher suicide risk (patients with a lifetime history of attempted suicide) (n=23, 62.2%)	P
Age	32.7 ± 9.9	30.7 ± 6.9	NS
Duration	12.5 ± 7.7	13.6 ± 5.3	NS
Onset	20.1 ± 7.1	17.1 ± 2.2	NS
Episodes	2.6 ± 1.5	3.6 ± 1.2	0,02
BMI	23.1 ± 3.1	23.3 ± 3.1	NS
BDI	24.0 ± 4.3	29.9 ± 3.3	<0.001
SSI	10.8 ± 0.7	24.1 ± 1.6	<0.001
HAM-D	20.7 ± 4.5	27.1 ± 2.7	<0.001
TC (mg/dl)	190.7 ± 15.7	184.9 ± 19.8	NS
HDL (mg/dl)	55.8 ± 9.4	48.1 ± 8.0	0.04

Table II. *Comparison of clinical data, cholesterol, and HDL levels among individuals with higher risk (patients with a lifetime history of attempted suicide, n=14, 37.8%) and lower suicide risk (patients without a history of attempted suicide, n=23, 62.2%).*

depression (Model 1) and increased suicide risk (Model 2). Lower HDL levels were significantly predictive of increased suicide risk (Model 2).

DISCUSSION

Two main results come out from our retrospective analysis: 1) CRP was significantly associated with severity of depression and higher suicidal risk; 2) low HDL levels were significantly associated with higher suicidal risk. Our findings on CRP are in line with those of other previous studies. Lanquillon et al. (21) studied 24 inpatients with depression treated with amitriptyline and found that CRP levels were elevated before treatment and decreased slightly with treatment, not predicting responsiveness to treatment. In a case-control study, Sluzewska et al. (22) showed that CRP levels were significantly higher in patients with major depression compared with normal controls. Ford and Erlinger (23) estimated the odds of elevated CRP level associated with depression in 6,914 non-institutionalized men and women from the Third National Health and Nutrition Examination Survey (NHANES III) and found that MD was strongly associated with increased levels of CRP.

Some studies instead pointed out only a weak relationship between CRP and depressive symptoms. Douglas et al. (24) conducted a cross-sectional study of a cohort of 696 consenting, active duty US Army personnel undergoing a periodic physical and found that Depressive symptoms are only weakly correlated with CRP; moreover, after adjusting for BMI, they found no significant relationship between CRP and depression. Kop et al. (25) screened 4,268 elderly subjects for depression while simultaneously measuring CRP levels and found a significantly positive difference between depressed and non-depressed subjects but this relationship disappeared after adjusting for other variables, including weight. Similar results were found by Penninx et al. (26) and Steptoe et al. (27). However, there are several limitations of these studies. First, there were low levels of depressive symptoms among participants that could have led to an underestimation of the size of the relation between depression and inflammation, whereas, in our study the degree of depressive symptoms where much higher. Second, these researchers conducted their analyses on non-clinical samples without a strictly psychiatric assessment that include clinical interviews and administration of clinician compiled rating scales as made in our study. Their approach makes it difficult to discriminate between patients

	BDI	HAMD	SSI	CRP	TC	HDL
Age	0.30	0.22	0.15	-0.05	0.08	0.04
Duration	0.33 (*)	0.34 (*)	0.29 (*)	0.07	0.20	0.03
Onset	0.11	0.05	-0.19	-0.24	0.02	0.07
Episodes	0.43 (**)	0.43 (**)	0.48 (**)	0.36 (*)	-0.13	0.04
BMI	0.13	0.14	0.15	0.22	0.28	0.23
BDI	-	0.80 (***)	0.72 (***)	0.44 (**)	-0.23	-0.40 (*)
HAMD	-	-	0.81 (***)	0.49 (**)	-0.26	-0.45 (**)
SSI	-	-	-	0.53 (**)	-0.19	-0.45 (**)
CRP	-	-	-	-	-0.28	0.02
TC	-	-	-	-	-	0.01

Table III. *Correlations (Spearman coefficient) between demographic, clinical (BDI, HAM-D and SSI scores) and laboratory data (CRP, TC and HDL levels) among whole sample (n=37).*
(***) P<0.001
(**) P<0.01
(*) P<0.05

with "episodic" sadness and subclinical depressive symptoms. The self-rating instruments employed in such large surveys lack specificity when compared to clinical interviews. Third, none of cited studies was conducted on patients with a clinical diagnosis of MD and this may confound results.

In the present study, the results also show that there is no significant difference in total cholesterol levels among patients with lower or higher suicide risk. These findings were consistent with those of others (28-30). Many researchers have explored the relationship between plasma or serum cholesterol and suicide or violence (31-34). Depressive patients with greater suicidal tendency had significantly lower cholesterol concentrations but some failed to find a correlation (9,11). Neaton et al. (35) in a larger sample study, reported that suicide risk increased with serum cholesterol levels lower than 160 mg/dl. Two studies showed depressive states to be inversely related to serum cholesterol (36-37). Muldoon et al. (38) conducted a meta-analysis pointing out that cholesterol-lowering therapy reduced mortality due to CHD, but not total mortality, which increased because of suicide and aggressive behaviours.

However, in our sample, patients with higher suicide risk had lower HDL levels than patients with lower suicide risk and HDL correlated inversely with BDI, HAM-D and SSI. This finding is similar

	Standardized Coefficient	t	*P*
Model 1 (HAM-D Dependent Variable) (*)			
CRP	0.56	4.08	<0.001
Model 2 (SSI Dependent Variable) (**)			
CRP	0.33	3.02	0.005
HDL	-0.44	-2.60	0.015

Table IV. *Two models of linear regression with HAM-D (Model 1) or SSI (Model 2) as dependent variables and CRP, TC and HDL as independent, while controlling for age, gender, duration, number of episodes and BMI (Only statistically significant variables are reported).*

to that of Maes et al. (11) who reported that lower serum HDL levels were a marker for major depression and suicidal behaviour in depressed men. Furthermore, in accordance with Maes et al., we hypothesize that lower serum HDL levels were probably induced by the immune/inflammatory response in depression. In our sample, we found higher levels of CRP which may have been due to an impairment of reverse cholesterol transport from the body tissues to the liver. Also Horsten et al. (39), analyzing data of 300 healthy middle-aged women, found that depressive symptoms showed a significant inverse linear association with HDL. In multivariate models adjusted for smoking, alcohol consumption, exercise habits, body-mass index, waist-hip ratio, menopausal status, age, and educational level, this association remained significant. In addition to lower HDL concentrations, also higher ratios of total cholesterol/high-density lipoprotein (TC/HDL) and low-density lipoprotein/high-density lipoprotein (LDL/HDL) were also reported in patients with major depression (13,40,41).

REFERENCES

1. **Annique S., T. Dorien, L. Richel, K. Gunter, D. Joris, H.J. Crijns, G. Gert, S. Frank, M. Michael and H. Adriaan**. 2005. Inflammatory markers in depressed post-myocardial infarction patients. *J. Psychiatr. Res. 39:137.*
2. **Rothermundt M., V. Arolt, M. Peters, H. Gutbrodt, J. Fenker, A. Kersting and H. Kirchner**. 2001. Inflammatory markers in major depression and melancholia. *J. Affect. Disord. 63:93.*
3. **Bassuk S.S., N. Rifai and P.M. Ridker**. 2004. High-sensitivity C-reactive protein: clinical importance. *Curr. Probl. Cardiol. 29:439.*
4. **Ledue T.B. and N. Rifai**. 2003. Preanalytic and analytic sources of variations in C-reactive protein measurement: implications for cardiovascular disease risk assessment. *Clin. Chem. 49:1258.*
5. **Burg M.M. and D. Abrams**. 2004. Depression in chronic medical illness: The case of coronary heart disease. *J. Clin. Psychol. 57:1323.*
6. **Barth J., M. Schumacher and C. Herrmann-Lingen**. 2004. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom. Med. 66:802.*
7. **Moller-Leimkuhler A.M.** 2003. The gender gap in suicide and premature death or: why are men so vulnerable? *Eur. Arch. Psychiatry Clin. Neurosci. 253:1.*
8. **Ozer O.A., R. Kutanis, M.Y. Agargun, L. Besiroglu, A.C. Bal, Y. Selvi and H. Kara**. 2004. Serum lipid levels, suicidality, and panic disorder. *Compr. Psychiatry 45:95.*
9. **Lee H.J. and Y.K. Kim**. 2003. Serum lipid levels and suicide attempts. *Acta Psychiatr. Scand. 108:215.*
10. **Rabe-Jablonska J. and I. Poprawska**. 2000. Levels of serum total cholesterol and LDL-cholesterol in patients with major depression in acute period and remission. *Med. Sci. Monit. 6:539.*
11. **Deisenhammer E.A., K. Kramer-Reinstadler, D. Liensberger, G. Kemmler, H. Hinterhuber and W. Fleischhacker**. 2004. No evidence for an association between serum cholesterol and the course of depression and suicidality. *Psychiatry Res. 121:253.*
12. **Kim Y.K. and A.M. Myint**. 2004. Clinical application of low serum cholesterol as an indicator for suicide risk in major depression. *J. Affect. Disord. 81:161.*
13. **Maes M., R. Smith, A. Christophe, E. Vandoolaeghe, A. Van Gastel, H. Neels, P. Demedts, A. Wauters and H.Y. Meltzer**. 1997. Lower serum high-density lipoprotein cholesterol (HDL-C) in major depression and in depressed men with serious suicidal attempts: relationship with immune-inflammatory markers. *Acta Psychiatr. Scand. 95:212.*
14. **Tanskanen A., E. Vartiainen, J. Tuomilehto, H. Viinamaki, J. Lehtonen and P. Puska**. 2000. High serum cholesterol and risk of suicide. *Am. J. Psychiatry 157:648.*
15. **American Psychiatric Association**. 1994. In *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. American Psychiatric Association Washington DC, p.1.
16. **Spitzer R.L., J.B.W. Williams, M. Gibbon and M. First**. 1997. In *Structured Interview for DSM-IV (SCID)*, ed. New York State Psychiatric Institute Biometrics Research New York, p.1.

17. **Hamilton M.** 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry 23:56.*
18. **Beck A.T., C.H. Ward and M. Mendelson.** 1961. An inventory for measuring depression. *Arch. Gen. Psychiatry 4:561.*
19. **Beck A.T., M. Kovacs and A. Weissman.** 1979. The Scale for Suicide Ideation. *J. Consult. Clin. Psychol. 47:343.*
20. **Ledue T.B., D.L. Weiner, J.D. Sipe, S.E. Poulin, M.F. Collins and N. Rifai.** 1998. Analytical evaluation of particle-enhanced immunonephelometric assays for C-reactive protein, serum amyloid A and mannose-binding protein in human serum. *Ann. Clin. Biochem. 35:745.*
21. **Lanquillon S., J.C. Krieg, U. Bening-Abu-Shach and H. Vedeer.** 2000. Cytokine production and treatment response in major depressive disorder. *Neuropsychopharmacology 22:370.*
22. **Sluzewska A., J. Rybakowski, E. Bosmans, M. Sobieska, R. Berghman, M. Maes and K. Wiktorowicz.** 1996. Indicators of immune activation in major depression. *Psychiatry Res. 64:161.*
23. **Ford D.E. and T.P. Erlinger.** 2004. Depression and C-reactive protein in US adults: data from the Third National Health and Nutrition Examination Survey. *Arch. Intern. Med. 164:1010.*
24. **Douglas K.M., A.J. Taylor and P.G. O'Malley.** 2004. Relationship between depression and C-reactive protein in a screening population. *Psychosom. Med. 66:679.*
25. **Kop W.J., J.S. Gottdiener, C.M. Tangen, L.P. Fried, M.A. McBurnie, J. Walston, A. Newman, C. Hirsch and R. Tracy.** 2002. Inflammation and coagulation factors in persons > 65 years of age with symptoms of depression but without evidence of myocardial ischemia. *Am. J. Cardiol. 89:419.*
26. **Penninx B., S.B. Kritchevsky, K. Yaffe, A.B. Newman, E.M. Simonsick, S. Rubin, L. Ferruci, T. Harris and M. Pahor.** 2003. Inflammatory markers and depressed mood in older persons: results from the health, aging and body composition study. *Biol. Psychiatry 54:566.*
27. **Steptoe A., R. Kunz-Ebrecht and N. Owen.** 2003. Lack of association between depressive symptoms and markers of immune and vascular inflammation in middle-aged men and women. *Psychol. Med. 33:667.*
28. **Modai I., A. Valevski, S. Dror and A. Weizman.** 1994. Serum cholesterol levels and suicidal tendencies in psychiatric inpatients. *J. Clin. Psychiatry 55:252.*
29. **Kunugi H., N. Takei, H. Aoki and S. Nanko.** 1997. Low serum cholesterol in suicide attempter. *Biol. Psychiatry 41:196.*
30. **Huang T.L.** 2005. Serum lipid profiles in major depression with clinical subtypes, suicide attempts and episodes. *J. Affect. Disord. 86:75.*
31. **Atmaca M., M. Kuloglu, E. Tezcan and B. Ustundag.** 2003. Serum leptin and cholesterol levels in schizophrenic patients with and without suicide attempts. *Acta Psychiatr. Scand. 108:208.*
32. **Repo-Tiihonen E., P. Halonen, J. Tiihonen and M. Virkkunen.** 2002. Total serum cholesterol level, violent criminal offences, suicidal behavior, mortality and the appearance of conduct disorder in Finnish male criminal offenders with antisocial personality disorder. *Eur. Arch. Psychiatry Clin. Neurosci. 252:8.*
33. **Tripodianakis J., M. Markianos, D. Sarantidis and M. Agouridaki.** 2002. Biogenic amine turnover and serum cholesterol in suicide attempt. *Eur. Arch. Psychiatry Clin. Neurosci. 252:38.*
34. **Cassidy F. and B.J. Carroll.** 2002. Hypocholesterolemia during mixed manic episodes. *Eur. Arch. Psychiatry Clin. Neurosci. 252:110.*
35. **Neaton J.D., H. Blackburn, D. Jacobs, L. Kuller, D.J. Lee, R. Sherwin, J. Shih, J. Stamler and D. Wentworth.** 1992. Serum cholesterol level and mortality findings for men screened in the Multiple Risk Factor Intervention Trial. *Arch. Internal Med. 152:1490.*
36. **Steegmans P.H.A., A.W. Hoes, A.A.A. Bak, E. van der Does and D.E. Grobbee.** 2000. Higher prevalence of depressive symptoms in middle-aged men with low serum cholesterol levels. *Psychosom. Med. 62:205.*
37. **Huang T.L., S.C. Wu, Y.S. Chiang and J.F. Chen.** 2003. Correlation between serum lipid, lipidprotein concentrations and anxious state, depressive state or major depressive disorder. *Psychiatry Res. 118:147.*
38. **Muldoon M.F., S.B. Manuck, A.B. Mendelsohn, J.R. Kaplan and S.H. Belle.** 2001. Cholesterol reduction and non-illness mortality: meta-analysis of randomised clinical trials. *Br. Med. J. 322:11.*
39. **Horsten M., S.P. Wamala, A. Vingerhoets and K.**

Orth-Gomer. 1997. Depressive symptoms, social support, and lipid profile in healthy middle-aged women. *Psychosom. Med. 59:521.*

40. **Chen C.C., F.H. Lu, J.S. Wu and C.J. Chang**. 2001. Correlation between serum lipid concentrations and psychological distress. *Psychiatry Res. 93:93.*
41. **Huang T.L. and J.F. Chen**. 2004. Lipid and lipoprotein levels in depressive disorders with melancholic feature or atypical feature and dysthymia. *Psychiatry Clin. Neurosci. 58:295.*