

RELATIONSHIP BETWEEN LOWER SERUM CHOLESTEROL LEVEL AND PSYCHIATRIC DISORDERS

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ABSTRACT

The study applies the General Health Questionnaire (GHQ-60) to 50 consecutive patients attending Psychiatry-O.P.D., Medical College, Calcutta provided they meet the inclusion and exclusion criteria. Subjects were between 15 to 55 years, literate, and did not have any physical disease or condition specially those which can alter serum cholesterol level. Every patient was physically examined and interviewed. Subjects scoring less than 11 on GHQ were taken to have no psychiatric disease. Serum cholesterol level of these subjects was contrasted with subjects scoring 11 or more on GHQ, who were considered to have psychiatric diagnosis. The study showed that male psychiatric patients had statistically significant lower serum cholesterol than normal subjects while no significant lowering was observed in female psychiatric patients.

Key words : Cholesterol, psychiatric disorders

High serum cholesterol level is a definite risk factor for coronary artery disease and lowering serum cholesterol by diet or drugs is a logical corollary in strategy for prevention of myocardial infarction. However the issue became somewhat controversial when meta-analysis of cholesterol-lowering trials undertaken by Muldoon et al. (1990) showed that such intervention did not decrease the overall mortality rate. The reduction in mortality due to cardiovascular cause was offset by increase in non-illness mortality (e.g. suicide, accidents, violence). This was followed by a number of reports linking low-cholesterol level with suicidal ideation (Gallerani et al., 1995), depression (Morgan et al., 1993), aggressive behaviour (Spitz et al., 1994; Band, 1993).

While large number of studies had been conducted for individual psychiatric conditions, results were not clear as yet, indeed results were conflicting (Ernst, 1994).

Relationship between cholesterol level and psychiatric disorders were studied only in few studies and results of such studies did not show significantly lower cholesterol value (Wardle, 1995). Cholesterol level also depends on large number of factors which act as potential confounders and very few studies excluded all the possible confounders (Ernst, 1994).

The present study was undertaken to compare serum cholesterol level of psychiatric (non-psychotic) patients with psychiatrically normal subjects. It aimed to exclude as many confounding variables as possible so as to make direct comparison possible.

MATERIAL AND METHOD

All patients attending Psychiatry Out Patients Department, Medical College, Calcutta were included in the study, subject to the patients satisfying the inclusion criteria as described below. Study period was 15th

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September to 15th December, 1996.

The aim was to strictly separate psychiatric patients from patients who have no psychiatric disease. For this, investigators interviewed patients at the onset clinically and then used the General Health Questionnaire (GHQ-60) (Goldberg, 1972) Bengali version with previously tested validity & reliability (Sarkar et al., 1990) which patients were required to fill up themselves.

Since GHQ-60 was used to separate psychiatrically normal patients from psychiatrically ill patients (physical illness ruled out), patients included in the study were required to be-

- i) Have literacy upto class IV and able to read Bengali and understand questions in the form (as GHQ is self-rating instrument).
- ii) Age within 15 to 55 years (as the validity of the instrument was not standardised in age groups beyond that). This age group had additional benefit of avoiding variation of cholesterol value that could occur if extreme ages were included.
- iii) Psychotic disorders, past disease under partial remission, patients who behaved defensively when filling up questionnaires were detected during preliminary interview and excluded as GHQ gives incorrect scores in such situations.

Investigators also decided to include in this study only patients belonging to urban area (Calcutta & Howrah City limits) and belonging to lower socioeconomic class (Kuppuswamy, 1962) as these patients were more common and such restriction lowers the number of confounding variables.

Each patient who met the preliminary criteria were further examined by careful history taking, physical examination, laboratory investigations according to a predetermined format. This helped to exclude patients who had disorders or conditions which could influence serum cholesterol level -

1. Dietary abnormality or peculiarity - for the purpose of this study only those patients were taken who take usual Bengali diet which is

- mixed type. Pure vegetarians were excluded.
2. Patients life style/occupation were usual ones, i.e. neither sedentary nor excessive hard work.
 3. Severe physical or mental strain of recent (1 month) origin caused exclusion of subjects from study.
 4. Patients taking alcohol, tobacco, or any psychotropic or narcotic substance were excluded from the study.
 5. Physical disorders included were hypertension, hypotension, diabetes mellitus, renal disorders, hepatic disorder, thyroid disorders, anaemia, malabsorption.

Patients thus included were asked to fill up the GHQ-60 form, and those scoring below 11 were considered to be psychiatrically normal and assigned to Group A (22 patients) of the study. Patients scoring 11 and above were clinically interviewed to verify psychiatric diagnosis and the entire group was assigned to Group B (28 patients). Fasting blood sample was drawn in the morning from each patient for estimation of serum cholesterol. Since investigators measured serum cholesterol using a single random sample, it was needed to keep provision for day to day inpatient variation of upto 11% (Denmacker, 1983). It was decided to account for this by taking 27.5 mg/dl (i.e. 11% of maximum normal value of 250 mg/dl) as minimum difference needed for clinical relevance in confidence interval analysis.

The cholesterol values of A and B group were compared statistically with separate gender wise comparison. Student's t-test was used (unpaired t-test).

RESULTS

Table 1 shows the age distribution for subjects included in the study. Chi-square test on the table is not significant, hence we may conclude that Group A and B did not differ significantly with regard to age of subjects constituting them. Values of mean age further proves that regardless of gender, age wise Group A & B were well matched.

TABLE 1
AGE DISTRIBUTION FOR SUBJECTS
INCLUDED IN THE STUDY

Age in years	Group A	Group B
16-35	10	16
36-55	12	12
Total	22	28
	Mean age in years	Mean age in years
	Overall - 36.5	Overall - 36.4
	In males - 35.8	In males - 35.8
	In females - 37.4	In females - 37.3

$\chi^2 = 0.287$ (Using Yates continuity correction)
d.f.=1, N.S.

Table 2 shows the gender wise distribution for subjects included in the study. Chi-squared test on the table is not significant, hence we may conclude that Group A and B did not differ significantly with regard to gender of the subjects constituting them. Thus Group A and B are gender wise well matched.

Table 3 shows serum cholesterol level of subjects belonging to Group A and Group B. It has been seen that Group B subjects (overall) had extremely significant lower cholesterol level compared to Group A subjects (Overall). However since lower range of the confidence interval for difference between means is less than predetermined value of 27.5 needed to achieve clinical relevance, hence the observed difference is not clinically relevant. It can also be seen the male Group B subjects had significant lower cholesterol level compared to male subjects of Group A. Confidence interval upholds the clinical relevance of the observed difference. However while female subjects of Group B did show lower cholesterol levels compared to female subjects of Group B, the observed lowering of cholesterol levels was statistically insignificant. This was upheld by confidence interval, even though quite a large lowering might also be predicted from the confidence interval.

DISCUSSION

The present work indicated that

TABLE 2
GENDERWISE DISTRIBUTION FOR SUBJECTS
INCLUDED IN THE STUDY

Sex	Group A	Group B
Male	12	16
Female	10	12
Total	22	28

$\chi^2 = 0.01$ [with Yates continuity correction]
d.f.=1, N.S.

relationship between low cholesterol levels and psychiatric disease existed only in male subjects but not in females. Such gender wise difference was not observed in few studies that showed relationship between psychiatric disorder and lower cholesterol level (Wardle, 1995). Interestingly study conducted by Benton and Fordy (1992) had indicated that there was no relationship between cholesterol concentrations and rating of subjects as per GHQ. However a subgroup of women-namely those with lowest 5% of cholesterol concentration had significantly poorer mental health as indicated by their questionnaire scores.

Cholesterol is specially abundant in nervous system, where it plays important role per different aspects of cellular structure (e.g. fluidity of cell membranes) and function (e.g. membrane permeability and exchange processes) (Boston *et al.*, 1996).

Membranes and plasma cholesterol concentration are kept in equilibrium by homeostatic mechanisms. However lower plasma concentration of cholesterol may lead to lower cholesterol concentration in brain which in turn reduce serotonergic neuronal activity as hypothesized by Hawton *et al.* (1993) had also postulated that serotonergic activity is reduced in two distinct ways-

- (i) Action at presynaptic sites by causing increase in serotonin reuptake.
- (ii) Action at post synaptic sites by causing decrease in number and function of serotonin receptors.

Studies conducted in animals by Muldoon

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TABLE 3
SERUM CHOLESTEROL LEVEL OF SUBJECTS BELONGING TO GROUP A & GROUP B

	N	Groups B Mean \pm S.D. (in mg/100ml)	N	Groups A Mean \pm S.D. (in mg/100ml)	Significance			Confidence Interval C.I. 95%
					t	d.f.	p	
Overall	28	175.9 \pm 19	22	209.4 \pm 18.6	6.25	48	<.001	-22.78 to -44.22
Male	16	163.1 \pm 20.6	12	213.3 \pm 21.0	6.33	26	<.001	-30.53 to -69.87
Female	12	192.8 \pm 20.7	10	204.6 \pm 19.8	1.36	20	N.S.	-29.96 to 6.36

(i) Un-paired t-test was used.

(ii) For each t-test condition of equality of variance was satisfied according to Levene's test.

et al. (1992) upheld such hypothesis. Lowering of serotonergic neuronal activity may be the cause of higher psychiatric morbidity seen in patients with lower serum cholesterol.

Genetic factors may also play an important role in making a person more prone to psychiatric disorders in situation of lower serum cholesterol (Boston et al., 1996).

Another theory proposed by Penttinen (1995) suggested that interleukin -2 which can cause decrease in serum cholesterol. It can also cause depression (by suppressing melatonin secretion from pineal gland). Interleukin 2 thus may have a role to play.

None of the hypothesis mentioned above has been fully confirmed as yet.

In the present work due to the stringent exclusion criterion the study sample was small. Such exclusion criterion perhaps created an artificial subgroup in target population, which might have differed from real population. The present study could have been further improved by matching the patients belonging to normal and disease group more accurately. Rigorous analysis considering various biochemical and physical characteristics taken together was not attempted by the investigators in this study and no attempt was made to relate disease intensity with cholesterol level in this study.

It can be concluded that the issue of relationship between low cholesterol and psychiatric disorders is of great concern due to the implications on cholesterol lowering strate-

gies for prevention of ischaemic heart disease. However more detailed studies are needed to arrive at any definite conclusion. Perhaps this will also help in better understanding of aetiopathogenesis of psychiatric disorders.

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