

Association of blood lipids, cortisol and Hemodynamics Under stress: A possible role in early Atherogenesis

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Abstract:

Introduction: High blood cholesterol is claimed as a risk factor but recently it is accepted that cholesterol is increased under psychological stress. When raised in blood, cholesterol plays role in atherosclerosis formation; a role which is being debated since last many decades but still various questions is un-answered. Role of stress in early atherogenesis with association to alteration in blood lipids has been proposed but the available literature is scanty on the subject.

Objective: To explore the association of alterations in blood lipids, cortisol level and hemodynamics under mental stress in youth with no apparent heart disease.

Methodology: 114 male participants were selected from 397 volunteers as per 'selection criterion' approved by scientific committee. The volunteers were examined two times: during stress task as 'stress-study' and during non-stress period as 'control' according to 'paired sample' design. Thus, 56.54% apparently healthy subjects were included with exclusion ratio of 43.58%. All experiments were conducted under standard methods at LINAR-Larkana and Physiology Department of Sindh University, Jamshoro. Blood sample were taken between 9.00 am to 12.00 pm.

Results: Cortisol, systolic and diastolic blood pressures and heart rate were significantly increased during stress session. Different lipid levels were changed with different significant values. Correlations of some altered lipid levels with raised values of hemodynamics and cortisol detected were positive and significant.

Conclusion: Most changes in the level of variables were found prone to be "atherogenic in pattern" due to psychological stress. This work may pave a way for better understanding of relationship in between lipid alterations, mental stress and early atherogenesis. For that further studies are needed.

Key Words: Cholesterol, Hemodynamics, Cortisol, psychological stress.

Introduction:

In humans, anxiety mostly occurs with strength during stressful situation for instance this happens with many students during exam-event¹⁻⁴. Mental stress and anxiety have been recently blamed to be a risk factor for heart problems including development and progress of atherosclerosis⁵⁻⁶. The process of 'atherogenesis' starts in early life and matures into the 'atherosclerotic lesion' in late ages. As complication it may affects coronary function /cardiac activity, leadings to occurrence of ischemic heart disease (IHD) or myocardial infarction (MI) usually in older ages⁷⁻⁹. To determine possible mechanisms of psychological stress that may lead to early atherogenesis, the studies on stress-linked changes in blood biological factors and hemodynamics in subjects with no apparent heart disease and the consequences of alterations found in variables particularly in youth were substantial. But, very scanty work has been conducted on relation of stressful life events, work stress or job strain with atherogenesis process in earlier life of subjects¹⁰. Furthermore, little is known about 'hidden after effects of mental stress" on health particularly heart activity of the youth who face stressful situations¹¹. This may reason the atherogenesis by affecting blood constituents e.g. blood cells, coagulation factors, blood lipids and interleukins including cardio-

vascular re-activities¹². This cross-sectional study was designed to explore the association of alterations in blood lipids, cortisol level and hemodynamics under mental stress of exam-event in healthy adults.

Methodology:

Initially 397 male medical students belonging to 1st and 2nd year MBBS were registered as volunteers for this study at Chandka Medical College, Larkana. The purpose of project was explained in detail to all volunteers. All volunteers were tested for proneness to stress as "trait-anxiety" by applying TAI and their "health condition" was checked before actual study. Finally, 114 participants were selected as per 'selection-criterion' approved by scientific committee constituted on members from Larkana Institute Nuclear medicine and Radiotherapy Larkana (LINAR-Larkana), Department of Physiology, University of Sindh, Jamshoro and Department of Biochemistry CMC Larkana. Thus, 56.542 % of apparently healthy subjects as participants were included in the study with exclusion ratio of 43.58 % of volunteers. All were instructed to avoid heavy exercise and were restricted to take proposed diet and no medication was allowed for one day before and on the day of selection / blood sampling. The participants were allocated to both stress and non-stress session (control) and all participants were

subjected to same and identical environment. They were studied twice: first time during exam-event as “stress study” and after taking conditional rest with in 1 to 1.5 months as ‘control study’. For control session, volunteers were not subjected to any serious academic activity pertaining stress. Blood samples were taken from them during both sessions during 9.00 am to 12 pm. statistically, ‘paired sample’ design was applied. Heart rate (HR), Systolic and Diastolic blood pressure (SBP and DBP) along with Electrocardiography (ECG) were recorded by standard methods. Radio-immune assay was carried out on gamma counter at LINAR-Larkana to estimate blood cortisol according to instructions of the manufacturer. These diagnostic kits were purchased from Immunotech, a Beckman coulter company through LINAR Larkana. While, the cholesterols were determined on spectrophotometer machine, the spectronic - 21 made by Interlabs instruments of Bausch and Lomb USA. The reagent and standards available in concerned kits, were used to estimate Low density Lipoprotein (LDL-C), High density Lipoprotein (HDL-C), Triglycerides (TG) and Cholesterol (TC), and methods to estimate blood lipids were applied accordingly.

Results:

The selected participants were 18 to 23 years aged (mean 19.45 years). Blood cortisol was increased by value of 22.780ng/ml during stress period. While, HR.SBP and DBP were increased in order of increments of 12.097 beats/minutes,13. 590 mm Hg and 11.009 mm Hg as shown in table 1.

Table.No:1. The affects of stress on the Blood cortisol and hemodynamics variables along with percentage increments in stress (n= 114 subjects).

Sr. No	Variables	During Stress “Mean ± SEM”	After Stress “Mean ± SEM”	Mean of Difference	Increment percentage during stress
01.	Blood Cortisol (ng /ml)	179.55 ± 2.680	156.77 ± 2.210	22.780**	14.53%
02.	Heart Rate (beats/min)	83.360 ± 0.776	71.263 ± 0.618	12.097**	16.97%
03.	Systolic Blood Pressure (mm Hg)	135.960 ± 1.080	122.37 ± 0.790	13.590**	11.11%
04.	Diastolic Blood pressure (mm Hg)	86.930 ± 0.792	75.921 ± 0.796	11.009**	14.15%

** = P<0.001

Table.No:2. The affects of stress on Blood lipid profile variables along with percentage increments in stress (n=114 subjects).

Sr. No	Variables	During Stress “Mean ± SEM”	After Stress “Mean ± SEM”	Mean of Difference	Percentage change in stress
01.	TC (mg/dl)	170.65 ± 1.69	171.15 ± 1.73	- 0.5	00.29% Decrease
02.	LDL-C (mg/dl)	94.20 ± 1.53	91.56 ± 2.0	+ 2.64*	2.88% Increase
03.	HDL-C (mg/dl)	36.41 ± 1.07	39.55 ± 0.76	- 3.14**	7.94% Decrease
04.	TG (mg/dl)	114.49 ± 1.48	112.31 ± 1.63	+ 2.18*	1.94% Increase

* = P<0.01

** = P<0.001

TC and HDL-C were decreased due to effect of stress with percentage decrease of 0.29% and 7.94%, respectively. Whereas, negative mean of difference detected was -0.5 mg/dl for TC decrease and -3.14 mg/dl in respect to HDL-C decrease. The LDL-C and TG were increased in order of +2.64 mg/dl and +2.18mg /dl under stress. Percent change of LDL-C and TG increments were found as 2.88% and 1.94%, respectively as shown in table 2.

Under effects of stress, the correlation of increased LDL-C with raised DBP was detected with correlation co-efficient value of r= +0.20 and with SBP by coefficient value of r =+0.28. The raised level of LDL-C became non-significantly correlated with increased HR. Under stress, the decreased level of HDLC was negatively correlated with increments of SBP and DBP by negative correlation coefficient values of r = -0.35 and r = -0.27 respectively. A non-significant correlation was observed in between increased HDL-C and raised HR due to stress. While, in case of TC, its correlation with HR, SBP and DBP detected were non-significant in stress. The correlation of raised blood cortisol with increments of LDL-C and decrease HDL-C level were found significant with P-Value of P<0.048 and P<0.05, respectively in stress as shown in table 3.

Table.No:3. Correlations of lipid profile variations with hemodynamic responses and blood cortisol under affects of stressful life event (n= 114 subjects).

Sr. No:	VARIABLES FOR CORELATION		STATISTICAL ANALYSIS	
			Co-Relation Coefficient (r)	P-level Significance (P)
01	Total Cholesterol (TC)	HR	- 0.001	NS
		SBP	-0.001	NS
		DBP	- 0.004	NS
02.	LDL Cholesterol (LDL-C)	HR	+ 0.16	NS
		SBP	+ 0.28	P < 0.01
		DBP	+ 0.20	P < 0.05
03.	HDL Cholesterol (HDL-C)	HR	- 0.17	NS
		SBP	- 0.35	P < 0.001
		DBP	- 0.27	P < 0.01

04.	Blood Cortisol	LDL Cholesterol	+ 0.27	P < 0.048
		HDL Cholesterol	- 0.294	P < 0.05

NS = Non- Significant.

Discussion:

The studies that examined lipids and lipoproteins under different stressors has reported variable results, some of these have shown increase while others had detected decrease of some blood lipids and lipoproteins¹³⁻¹⁸. Generally, TG, LDL-C, TC and HDLC were increased in most of studies¹⁹. The result of current study showed that only LDL-C and TG were increased in stress session with different percentage and at different levels but with identical p value of <0.01 (Table No: 2). While, TC was decreased as non-significant change, and HDL-C was decreased significantly during stress with p value of <0.001. The results of LDL-C and TG were consistent with results of some previous works^{13,18}. As per available literature, on one side, the lipids were consistently associated with IHD and on other side their levels were altered during stress. Hence, stress related mechanisms of lipid alterations associated with increased cardiovascular reactivity under life-disturbing situations may have clinical significance. With this assumption, the special attention was given in present work to assess blood-lipid changes and correlations of such altered lipid levels with cardiovascular responses (Table No: 3).

Anxiety and excitement tend to increase the stroke volume under sympatho-adrenergic activation without causing increase in pre-contraction length of cardiac muscle. In such states, the fast HR associated with increased cardiac contractility results into increase of cardiac out put (C.O) to meet homeostatic demands¹⁸⁻²¹. In humans, the cardiac out put (C.O) may be increased up to two to three-fold under stress due to increase in HR²⁰. Whereas, the major increase in C.O up to 41% to 74% was suggested to be due to modest increase in HR²²⁻²³. In this study not only, HR was increased with highly significant level but also blood cortisol, SBP and DBP were significantly increased (p-value of <0.001 under stress as shown in table No: 1. Raised levels of blood cortisol and CVR e.g. HR, SBP and DBP found in present study under stress were in consistent with some previous works²⁴⁻²⁷.

Increased SBP, DBP along with raised cardiac out put causes the changes in hydrostatic pressure, and in turn this may cause fluid shift from circulatory system. By this mechanism of increasing hydrostatic pressure under psychological stress, the acute intravascular hemoconcentration might occur^{24, 28, 29}. Some investigators argued that increased lipoproteins in circulation were because of such haemoconcentration. In such studies the altered values of lipid levels and increased blood viscosity (raised haematocrit) remained for short duration and disappeared after stress^{15,29} indicating the occurrence of haemoconcentration at the time of stress²⁸⁻³⁰. During current study both, altered findings of lipid-levels and their associations with SBP

& DBP were also found for 'short duration' and disappeared during 'control session'. However, the non-correlative findings of altered lipid values with raised HR observed under effect of stress-task indicated that haemoconcentration may not be only reason of lipid alteration. Furthermore, packed cell volume and Hemoglobin (PCV & HB %) were not determined during our study. Therefore, it is difficult to conclude from the available data of this study that alterations in lipid values are due to hemoconcentration. Even though, a few of lipid findings (e.g. HDL-C) observed in present are not in agreement with results of a study conducted by Joseph in medical students at time of exam-stress. However, present work is in agreement with its suggestions that the increments of lipids and lipo-protein under stress may not be solely due to hemoconcentration^{9, 10}.

Wolf et al studied work-stress, and to find its relationship with ratio of low density to high-density lipoprotein in younger men and women³¹. We did not examine this ratio during current study but results of current research showed that stressful event (mental stress) did alter lipid levels adversely (prone to be atherogenic in form) in apparently healthy and young adults. For instance, the risk factor or bad lipids like LDL-C was more increased (2.88%) than TG (1.49%). The increment of LDL-C was significant and positively correlated with increased responses of SBP and DBP (Table No: 2 &3). While, the protective or good lipids (HDL-C) were reduced by 7.94%, and became negatively correlated with increased response of SBP and DBP during stress. Yet for better understanding of biochemical risk factors in early atherogenesis under stress, further studies are warranted in young age group. Surprisingly, it is recently reported that in these important areas very limited knowledge has been searched out, and particularly there is lack of such studies in subjects round about 30 with no apparent IHD^{8,32}. On other hand, exact physiological mechanisms, working under stress that may influence the cholesterol metabolism are not fully known and in turn possible clinical significance of acute alterations in lipid levels under stress remain uncertain. The possibility is that stress do affect plasma lipid concentrations have been the subject of recent investigation^{15, 16}.

Conclusion:

The changes in levels of blood lipids and lipoproteins were found in association with cardiovascular reactivity as "prone to be atherogenic pattern" due to effect of real-life stressful situation (anxiety-task) in healthy young persons. Further work is needed to evaluate many specific details e.g. exact mechanisms regarding changes in levels of biochemical risk factors and their associations with CVR under stress on basis of regular follow up and coherent broad base study. Then, this in turn may reveal the possible role of mental stress in creation, development and progress of early atherogenesis.

Limitation of the Study:

This study was not continued as 'follow-up' for a long period as all subjects were students.

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