ORIGINAL ARTICLE

RELATIONSHIP OF LIPIDS, C-REACTIVE PROTEIN AND SIALIC ACID IN THE HEALTHY INDIVIDUALS

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Background: Raised levels of cholesterol and triglycerides are major risk factors for atherosclerosis, which can lead to coronary heart disease. Both the CRP and Sialic Acid levels are elevated in response to acute as well as chronic inflammatory conditions. This study was conducted to determine the serum lipid profile, CRP and Sialic Acid levels and their relationship with each other in healthy individuals. **Methods:** This was a cross-sectional study performed by the Department of Biochemistry, Institute of Basic Medical Sciences (IBMS), Khyber Medical University (KMU) Peshawar. Two hundred healthy subjects in the age group of 18–50 years of either gender was recruited through consecutive sampling. Blood sampling were taken from all the participants and analysed each for serum lipid profile, CRP and Sialic Acid levels through standardized methods. **Results:** A total of 200 individuals were included, 53.5% being male. Mean age was 33.39±9.76 years. Mean height was 167.86±10.8 cm. Mean weight was 66.87±11.39kg. Mean Hip-Waist ratio was 0.93±0.16 whereas mean BMI was 24.12±3.65. The simultaneous raised levels of serum lipids, CRP and Sialic Acid were observed more commonly in females as compared to males. CRP and Sialic Acid has got statistically significant correlation with HDL. Sialic Acid had statistically significant correlation with triglycerides in the study population with a significant *p*-value (<0.05), while having a non-significant correlation with total cholesterol and LDL. CRP had got significant correlation with total cholesterol and LDL and non-significant correlation with triglycerides. **Conclusion:** The study showed that serum CRP and Sialic Acid had a significant negative correlation with serum HDL. A significant positive correlation was found between serum Sialic Acid and triglycerides. CRP and Sialic Acid though expensive but are useful predictors of atherosclerotic disease.

Keywords: Triglycerides; HDL; LDL; Cholesterol; CRP; Sialic Acid

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INTRODUCTION

Atherosclerosis is a major cause of disease-related mortality around the globe. Atherosclerosis has a number of risk factors associated with it: hypertriglyceridemia and hypercholesterolemia in particular are major risk factors and a positive correlation between dyslipidaemia and atherosclerosis has been described.[1] However, recently, it has been shown that atherosclerosis is an inflammatory condition, a synergistic effect of endothelial dysfunction and inflammation results in responses at cellular and molecular level.[2,3] These responses can be identified in an atherosclerotic plaque. Atherosclerosis results in generation of acute phase reactant proteins, phagocytes and cytokines in addition to chemotactic materials leading to potentiation of host-defence systems.[4]

Acute phase reactants (APRs) are the markers of inflammation. They are synthesized in response to tissue damage and inflammation. During inflammation, their concentrations increase thousand-fold over the normal levels. They are mainly produced by hepatocytes, but they can also be synthesized by adipocytes, fibroblasts, and endothelial cells. It has been shown in recent research that inflammation plays an important role in the pathogenesis of coronary artery disease and development of other manifestations of atherosclerosis. Early atherosclerotic lesions predominantly show abundant immune cells whose effector molecules play a key role in an accelerated progression of the atherosclerotic lesions and acute coronary syndromes can develop secondary to activation of inflammation.[5]

A major acute phase reactant, C-reactive protein or CRP as it is commonly known, is found to be raised many times in acute illness. The CRP is elevated in response to acute as well as chronic inflammatory conditions[6] Raised level of high-sensitivity CRP (hs-CRP) is a reliable marker of inflammation in patients with atherosclerosis[7]. A number of studies have shown a strong association between high serum levels of CRP and future cardiovascular events.[8]

The association between inflammation and causation of diabetes mellitus has been reported earlier and inflammation has also been proposed as an aetiologic agent in the pathogenesis of diabetes mellitus, which, on its own, has been identified as a risk factor for coronary artery disease such as myocardial infarction in addition to ischemic cerebrovascular incidents.[9–12] Sialic acid is a "terminal component of the non-reducing end of the carbohydrate chains of glycoproteins and glycolipids".[13] Plasma Sialic acid is another acute phase reactant which is also a strong predictor of the risk of coronary heart disease.[14–16]

It is unlikely that the CRP or any other marker can actually cause coronary artery disease and this notion is supported by the fact that at the same time many different inflammatory markers have been found contributing to the risk of occurrence of coronary artery disease. Instead, circulating levels of all these inflammatory markers reflect the local inflammatory process in the vessel wall and other tissues including the adipose tissue. Further research is needed to ascertain the role played by these inflammatory markers in disease incidence and progression. This cross-sectional study was performed with a view to determine the lipid profile, CRP and Sialic acid levels and their relationship with each other in the healthy individuals belonging to Khyber-Pakhtunkhwa province of Pakistan.

MATERIAL AND METHODS

This cross-sectional study was conducted from January 1 to December 31 2013, after obtaining approval from ethical committee of Advanced Study and Research Board (ASRB) of Khyber Medical University (KMU) Peshawar. Two hundred (200) consecutive healthy subjects were recruited. Main centre of study was the Department of Biochemistry, IBMS, Khyber Medical University Peshawar. Individuals with chronic diseases like diabetes mellitus, hypertension, ischemic heart disease, cancer and pregnant females were excluded. Five cc of fasting blood sample was taken from each of the 200 healthy individuals. Each sample was analysed for serum lipid profile, C-reactive protein and Sialic Acid levels. Lipid profile was determined by Cobas CIII (Roche). Estimation of CRP was done by Chemi Luminescence Immuno Assay (CLIA) on Lumax by Monobind USA, and the serum Sialic Acid level was determined by Natelson technique using spectrophotometer at the Institute of Basic Medical Sciences (IBMS), Khyber Medical University Peshawar.

According to the guidelines of National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), the reference values for LDL Cholesterol, HDL Cholesterol, Total Cholesterol and triglyceride given below in table 1 were adopted in the present study.[17]

The classification of Body Mass Index recommended by the Centre of Disease Control, USA was used as a reference for body mass index for the study participants.[18] The criteria are in table-2. In table-3 are the expected values for the hs-CRP assay.[19]

The reference values for Serum Sialic Acid were taken as 68.12±6.70 mg%.[20]

Data was analysed using SPSS 17.0. All the results were presented in the form of tables and graphs. Mean±SD were calculated for age, anthropometric parameters as well as the clinical profile of the patients enrolled in the study. Pearson-Correlation coefficient was used to determine correlation of CRP and Sialic Acid with the lipid profile of the study subjects. A p-value ≤ 0.05 was considered to be significant.

RESULTS

There was a total of 200 study participants with a mean age of 33.39±9.76 years. Mean height was 167.86±10.8 cm. Mean weight was 66.87±11.39 Kg. Mean Hip-waist ratio was 0.93±0.16 whereas mean BMI was 24.12±3.65.

The anthropometric and laboratory data are presented according to the sex of the study participants (Table-4). The simultaneous raised levels of serum lipids, CRP and Sialic Acid were observed more commonly in females as compared to males (Table-5).

The correlation of serum Sialic Acid and CRP levels with the lipid profile of all the study population shows that there was a significant correlation between CRP levels and total cholesterol (r value= -0.17, p-value=0.02), HDL (r value= -0.40, p-value=0.00), LDL levels (r value= -0.21, p-value=0.00) in the study population. There was no correlation between CRP levels and serum triglyceride levels in the study population. However, correlation between Sialic Acid and lipid profile did not follow the same pattern. For Sialic Acid, there was significant correlation between HDL (r value= -0.19, p value=0.01) and triglyceride levels (r value= 0.15, p-value=0.04) only. Among the male healthy study subjects, there was no correlation between Sialic Acid levels and the serum lipid profile while CRP levels were found to be correlated with HDL (r value= -0.41, p value=0.00) and LDL levels (r value= -0.23, p-value=0.02). Among the female healthy study subjects, only HDL was found to have a significant correlation with the CRP levels (r value= -0.39, p-value=0.00). The Sialic Acid levels were found to be significantly correlated with HDL (r value= -0.27, p-value=0.01) and triglycerides (r value= 0.25, p-value=0.02).

Table-1: Reference range of lipid profile

Range	Total cholesterol (mg/dl)	High density lipoprotein (mg/dl)	Low density lipoprotein (mg/dl)	Triglyceride (mg/dl)
Low	-	<40	<100	<150
Desirable	<200	-	-	-
Above Optimal	-	-	100–129	-
Border line high	200–239	-	130–159	150–199
High	240	>60	160–189	200–499
Very high	-	-	>190	500

Table-2: BMI values according to CDC

BMI (Kg/m^2)	Weight category (Kg)
18.5–24.99	Normal weight
25.00–29.99	Over weight
30.00–34.99	Obese Class I
35.00–39.99	Obese - class II
Above 40	Morbid Obese

Reference range of CRP Values

Table-3: Reference values for hs-CRP in blood

Low Risk	≤ 1.0 µg/ml
Normal	≤ 1–3 µg/ml
High Risk	≥ 3.0 µg/ml

Table-4: Anthropometric data

Sex	Parameter	Age (Year)	Height (cm)	Weight (Kg)	Hip-waist ratio	Body Mass Index (Kg/m^2)
Males (n= 107)	Mean	33.24	172.24	69.94	0.99	23.95
	Standard Deviation	10.13	9.31	10.39	0.16	3.27
	Standard Error of Mean	0.97	0.90	1.00	0.016	0.31
	Coefficient of Variance	30.5	5.41	14.86	16.83	13.68
Females (n=93)	Mean	33.55	162.81	63.34	0.86	24.31
	Standard Deviation	9.34	10.23	11.52	0.11	4.05
	Standard Error of Mean	0.96	1.06	1.19	0.01	0.42
	Coefficient of Variance	27.85	6.28	18.2	13.81	16.7

Table-5: Clinical profile of 107 healthy male study subjects of Khyber-Pakhtunkhwa given as Mean±SEM

Sex	Parameter	Total Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Triglycerides (mg/dl)	CRP (mg/L)	Sialic Acid (mg/dl)
Males (n=107)	Mean	168.64	37.60	108.74	136.86	5.65	85.29
	SD	48.88	12.50	45.55	77.34	12.30	28.91
	Standard Error of Mean	4.72	1.20	4.40	7.47	1.18	2.79
	Coefficient of Variance	28.98	33.25	41.89	56.50	217.3	33.90
Females (n=93)	Mean	172.16	39.50	105.60	160.47	5.58	88.17
	Standard Deviation	48.04	11.75	38.19	102.98	8.84	27.00
	Standard Error of Mean	4.98	1.21	3.961	10.67	0.92	2.80
	Coefficient of Variance	27.91	29.75	36.17	64.18	78.28	30.63

DISCUSSION

CRP and Sialic acid have statistically significant correlation with HDL. Low HDL, CRP and Sialic Acid are inflammatory/atherogenic markers. Rest of the other lipid profile have got different association with Sialic Acid and CRP. Sialic Acid has got statistically significant correlation with triglycerides, while having a non-significant correlation with total cholesterol and LDL. CRP has got significant correlation with total cholesterol and LDL. It has non-significant correlation with triglycerides.

These results are similar to other results reported in different studies from Pakistan and neighbouring countries. Ichiro *et al.* reported that Serum triglycerides has a positive significant correlation with serum Sialic Acid and HDL Cholesterol showed a negative significant correlation in healthy subjects.[21] These findings suggest that the serum concentration of Sialic Acid is affected by serum lipids. Rehnuma *et al*. reported that Bangladeshi healthy adults have a positive association with their serum triglycerides and negative association with their HDL cholesterol levels.[22] Klisic *et al.* reported significantly higher triglycerides and hs-CRP levels together with their lower HDL cholesterol levels in overweight compared to normal weight women.[23] Similarly Shivananda *et al.* found that significant correlations were observed between Sialic Acid concentration and cardiovascular risk factors like LDL and triglycerides in the diabetic subjects.[24] Recently, Ahuja *et al.* reported that there was a significant correlation between CRP and serum lipid profile in patients with acute stroke.[19] These results vary from the results of our study due to the fact that we found no correlation between Triglycerides and CRP levels, while Ahuja *et al.* reported a correlation between these two. Unlike our study, they had conducted the research in 100 cases of ischemic stroke and hypertension while this study was done on 200 healthy subjects. The results reported by Ahuja *et al.* are similar to the results reported by Waheed *et al*.[25] This study differs from the study by Waheed *et al.* in that there was no correlation between triglycerides and CRP and that the study participants were 200 healthy subjects of Khyber-Pakhtunkhwa, while Waheed *et al.* recruited 30

patients who were already diagnosed with type 2 diabetes mellitus.[25]

It was a small-scale study and needs a bigger sample to calculate estimate of the population at large.

CONCLUSION

The study showed that serum CRP and Sialic Acid has a significant negative correlation with serum HDL. Low HDL, CRP, and Sialic Acid are inflammory/atherogenic markers. A significant positive correlation was found between serum Sialic Acid and triglycerides. Raised CRP and Sialic Acid levels are associated with low HDL. All these are predictors of atherosclerosis. CRP and Sialic Acid though expensive, so readily available HDL assay can be considered as a useful test in assessing the risk of atherosclerosis. In view of the relationship between triglycerides and Sialic Acid, further large-scale studies to establish the role of Sialic Acid as a predictor of cardiovascular disease and its associated morbidity and mortality.

AUTHORS' CONTRIBUTION

MI, CG: Conceived the study, collected data and did literature review. AUR: Literature Rev, data collection, statistical analysis. ASK, MS, SR: data collection and literature review. MA: Chemical analysis.

REFERENCES

1. Schoen F, Cotran R. The Blood Vessels. In: Kumar V, Cotran RS, Robbins SL, editors. Robbins Basic Pathology. 7th ed. New Delhi: Harcourt (India) Pvt Ltd, 2003; p.335–7.
2. Libby P. Atherosclerosis: the new view. Sci Am 2002;286(5):46–55.
3. Ross R. Atherosclerosis--an inflammatory disease. N Engl J Med 1999;340(2):115–26.
4. Taubes G. Cardiovascular disease. Does inflammation cut to the heart of the matter? Science 2002;296(5566):242–5.
5. Steel DM, Whitehead AS. The major acute phase reactants: C-reactive protein, serum amyloid P component and serum amyloid A protein. Immunol Today 1994;15(2):81–8.
6. Mazer SP, Rabbani LE. Evidence for C-reactive protein's role in (CRP) vascular disease: atherothrombosis, immuno-regulation and CRP. J Thromb Thrombolysis 2004;17(2):95–105.
7. Francisco G, Hernández C, Simó R. Serum markers of vascular inflammation in dyslipemia. Clin Chim Acta 2006;369(1):1–16.
8. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, *et al*. Low-grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ 2000;321(7255):199–204.
9. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001;286(3):327–34.
10. Pickup JC, Crook MA. Is type II diabetes mellitus a disease of the innate immune system? Diabetologia 1998;41(10):1241–8.
11. Vilbergsson S, Sigurdsson G, Sigvaldason H, Sigfusson N. Coronary heart disease mortality amongst non-insulin-dependent diabetic subjects in Iceland: the independent effect of diabetes. The Reykjavik Study 17-year follow up. J Intern Med 1998;244(4):309–16.
12. Kannel WB, D'Agostino RB, Wilson PW, Belanger AJ, Gagnon DR. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990;120(3):672–6.
13. Stary HC, Chandler AB, Glagov S, Guyton JR, Insull W Jr, Rosenfeld ME, *et al*. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation 1994;89(5):2462–78.
14. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997;349(9063):1436–42.
15. Libby P, Ridker PM. Inflammation and atherosclerosis: role of C-reactive protein in risk assessment. Am J Med 2004;116(Suppl 6A):S9–16.
16. Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull W Jr, *et al*. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Arterioscler Thromb Vasc Biol 1995;15(9):1512–31.
17. Schuster H. Managing the high-risk patient: therapeutic approaches in 2002. Atherosclerosis Suppl 2003;4(1):15–20.
18. About Adult BMI, Healthy Weight. [Internet]. Centre for Disease Control 2014 [cited 2014 Dec 6]. Available from: http://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html
19. Ahuja A, Basu A. Study of C-Reactive Protein Level in Patients of Acute Ischemic Stroke and Its Correlation with Serum Lipid Profile. Int J Health Sci Res 2012;2(3):40–8.
20. Hangloo VK, Kaul I, Zargar HU. Serum sialic acid levels in healthy individuals. J Postgrad Med 1990;36(3):140–2.
21. Wakabayashi I, Sakamoto K, Yoshimoto S, Masui H. Relation of serum sialic acid to lipid concentration. BMJ 1991;305(6853):562–3.
22. Rehnuma B, Hassan Z, Ibrahim M, Ali L. Serum levels of high sensitivity C-reactive protein and its association with lipidemic status in Bangladeshi healthy adults. J Pathol Nepal 2014;4(8):644–8.
23. Klisic AN, Vasiljevic ND, Simic TP, Djukic TI, Maksimovic MZ, Matic MG. Association between C-reactive protein, anthropometric and lipid parameters among healthy normal weight and overweight postmenopausal women in Montenegro. Lab Med 2014;45(1):12–6.
24. Nayak SB, Bhaktha G. Relationship between sialic acid and metabolic variables in Indian type 2 deabetic patients. Lipids Health Dis 2005;4:15.
25. Waheed P, Naveed AK, Farooq F. Levels of inflammatory markers and their correlation with dyslipidaemia in diabetics. J Coll Physicians Surg Pak 2009;19(4):207–10.

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