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SERUM ADIPOKINES AND OXIDATIVE STRESS MARKERS AS PREDICTORS OF PRECLINICAL ATHEROSCLEROSIS IN YOUNG ADULTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Preclinical atherosclerosis begins silently in early adulthood and progresses long before the onset of clinical symptoms. Adipokine imbalance and oxidative stress are emerging as central contributors to the early stages of vascular injury. This study investigates the association of serum adipokines and oxidative stress markers with carotid intima–media thickness (CIMT) to determine their predictive value for preclinical atherosclerosis in young adults.

Methods: A cross-sectional study was conducted from January 2024 to January 2025 across tertiary care hospitals in Punjab, Pakistan. A total of 120 healthy young adults aged 18–35 years were enrolled. Anthropometric measurements, blood pressure, lifestyle factors, and fasting blood samples were obtained. Serum adiponectin, leptin, resistin, and visfatin levels were measured using ELISA, while oxidative stress markers including malondialdehyde (MDA), total antioxidant capacity (TAC), glutathione (GSH), and superoxide dismutase (SOD) were assessed through standardized assays. CIMT was measured using B-mode ultrasonography, with values ≥0.7 mm classified as preclinical atherosclerosis.

Results: Increased CIMT was observed in 31.7% of participants. Individuals with elevated CIMT exhibited significantly lower adiponectin and antioxidant markers, along with higher leptin, resistin, visfatin, and MDA levels. CIMT showed strong positive correlations with leptin, resistin, visfatin, and MDA, and negative correlations with adiponectin, TAC, GSH, and SOD. Regression analysis identified low adiponectin, high leptin, and elevated MDA as independent predictors of increased CIMT.

Conclusion: Adipokine imbalance and oxidative stress play a substantial role in early vascular injury among young adults. These biomarkers serve as reliable predictors of preclinical atherosclerosis and may aid in early cardiovascular risk stratification.

Keywords: adipokines, oxidative stress, preclinical atherosclerosis, carotid intima–media thickness, young adults, malondialdehyde, adiponectin, leptin.

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INTRODUCTION

Atherosclerosis is now increasingly viewed as a lifelong process that starts silently in childhood and adolescence to become clinically significant cardiovascular disease (CVD) in adulthood[1]. Despite its traditional role in the ageing population, recent epidemiological studies have shown that early vascular changes, such as endothelial dysfunction, inflammatory stimulation, and subclinical arterial wall thickening are observable in young adults who otherwise seem healthy[2]. This initial phases also called preclinical atherosclerosis is usually asymptomatic but it is a critical period whereby when identified in good time, preventive steps can be applied before it is too late to reverse the cardiovascular outcome[3]. Carotid intima media thickness CIMT has also become a sensitive non-invasive measure of identifying these early arterial changes, and is a strong predictor of future CVD risk[4].

Adipose tissue, which used to be regarded as a passive fat store, has been discovered to be an active endocrine gland, secreted into different adipokines affecting metabolic, inflammatory, and vascular processes. Adiponectin, leptin, resistin, and visfatin are some of these

biomolecules that have received much attention owing to their possible involvement in vascular homeostasis and disease[5]. Adiponectin has anti-inflammatory and anti-atherogenic effects, stimulates endothelial nitric oxide synthesis and decreases oxidative stress. Conversely, leptin and resistin have been linked to the pro-inflammatory and pro-oxidative processes that lead to endothelial dysfunction, the smooth muscle proliferation, and the dysregulation of lipid metabolism. The changes in these adipokines can thus be used as one of the early biochemical markers of vascular defect in young individuals[6].

Another significant factor in the early atherogenesis is oxidative stress. Lipid peroxidation, decreased supply of nitric oxide, and increased damage of arterial walls are caused by the imbalance between reactive oxygen species (ROS) and antioxidant defenses. Malondialdehyde (MDA), total antioxidant capacity (TAC), glutathione (GSH), and superoxide dismutase (SOD) are biomarkers and they give information on the level of oxidative lesion at the cellular and vascular levels[7]. High levels of oxidative stress have been closely associated with endothelial dysfunction and early CIMT alterations, and thus the importance of this in the pathogenesis of preclinical atherosclerosis is emphasized[8].

Sedentary lifestyles, dietary patterns based on high-fat, obesity, stress, and early exposure to tobacco are some of the unique risk factors to young adults today. Such adjustable factors may increase the rate of vascular aging and disrupt adipokines balance way before the symptoms emerge[9]. To inform primary prevention, it is, therefore, necessary to identify biochemical indicators that would predict the presence of early vascular changes in this age cohort[10].

Considering the new interplay between adipokine dysregulation, oxidative stress, and early atherosclerotic arteriovenous adjustments, there is an urgent necessity to comprehend the joint impact in forecasting preclinical atherosclerosis in the youthful adults[11]. The aim of the study is to assess the relation of serum adipokines and oxidative stress markers with CIMT and their possible use as early warning indicators of subclinical vascular disease in healthy young population, otherwise[12].

MATERIALS AND METHODS

Study Design and Duration: The study was carried out as a cross sectional analysis study within a period of one year between January 2024 and January 2025. It was conducted in a number of tertiary care hospitals in Punjab, Pakistan that offered access to a relatively large population of young adults who are in the early stages of vascular changes to study. All centers involved got the ethical approval of the institutional review boards and informed consent was provided by each participant in written form before he or she was recruited.

Setting and Population of the study: A total of 120 young adults aged between 18 and 35 years were included in the study population and presented themselves to outpatient departments or preventive health clinics to have a routine examination or non-cardiac complaints. The participants were recruited by being first screened regarding their eligibility. The inclusion of only apparently healthy people, who had no known cardiovascular symptoms, was done to make sure that the sample reflected either early or preclinical stages of vascular changes.

Inclusion and Exclusion Criteria: The refined participants were young adults aged 18-35 years old who were willing to make carotid ultrasonography and biochemical tests. Those who had known chronic diseases, such as diabetes mellitus, hypertension, dyslipidemia, renal disease, hepatic disorders, autoimmune diseases, endocrine abnormalities, or acute infections were not included. Individuals who were already taking lipid-lowering agents, hormonal therapy, antioxidant supplements or any other medications that may affect adipokine levels or oxidative stress indicators were also disqualified. Individuals who had a substantial exposure to smoking were left out of the sample due to potential confounding of oxidative parameters, but little smoking history of less than five pack-years was allowed under strict record keeping.

Data Gathering and Clinical Evaluation: All participants were interviewed in a structured manner whereby, demographic variables, medical history, body physical activity, eating habits, smoking, family history of premature cardiovascular disease, and lifestyle habits were taken. Anthropometric data were taken based on the standard procedure of weighing, height and waist circumference, and body mass index was determined. The measurement of blood pressure involved the calibration of a digital sphygmomanometer under a seated position with a minimum of 10 minutes of rest before measuring.

Laboratory Procedures and Blood Sampling: All the participants were asked to donate fasting venous blood samples following a 10-12 hour overnight fasting period. Five mL of the blood was taken out in an aseptic way, and serum was obtained on centrifugation at 3000 rpm within 10 minutes. The serum samples were kept at -80o C until tested. Biochemical measures were done in the central laboratories of the involved institutions in accordance with the standard quality control procedures. The adipokines in serum (adiponectin, leptin, resistin, and visfatin) were measured by high sensitivity enzyme linked immunosorbent assay kits approved to use as clinical research. Biomarkers of oxidative stress were determined by using the previously established biochemical assays, the malondialdehyde concentration evaluated by using the thiobarbituric acid reactive substances assay, the total antioxidant capacity measured using colorimetric assays and antioxidant enzymes (superoxide dismutase and glutathione) by using the standard enzyme activity assays.

Analysis was done in a duo of the markers and mean values were taken to reduce the variability in the analysis.

Preclinical Atherosclerosis Evaluation: Preclinical atherosclerosis was measured by B-mode high-resolution carotid ultrasonography that was performed by trained radiologists. The participants were studied in supine position with slight neck extension and right and left common carotid arteries were observed longitudinally. Carotid intima media thickness was taken at a distance of one centimeter above the carotid bulb and three values were taken of each side. The means of all readings was figured as the last CIMT value to analyze. The presence of preclinical atherosclerosis was touched on a thickness of 0.7 mm and less than that was considered normal.

Statistical Analysis: All data collected were analyzed and inputted in SPSS version 26.0. Mean and standard deviation were used to provide a summary of continuous variables, and frequencies and percentages were applied to categorical variables. The Shapiro Wilk test was used to determine the distribution of variables. The independent samples t -test of quantitative variables was to compare the results of participants with normal CIMT to those with increased CIMT. Pearson correlation analysis was used to test the correlation between CIMT and biochemical parameters, adipokines and oxidative stress markers. The model was analyzed using multiple linear regression analysis to establish independent predictors of CIMT after controlling the possible confounding variables, which include age, sex, body mass index, and lifestyle variables. The level of statistical significance during the analysis was 0.05 and below.

RESULTS

One hundred and twenty (120) young adults between the ages of 18 years and 35 years were included in this study of which 63 were males and 57 were females. The mean age of the participants was 24.8 and standard deviation was 3.9 years. On carotid ultrasonography, 38 of the participants (31.7) had augmented CIMT (>= 0.7 mm), which is a sign of preclinical atherosclerosis, and 82 participants had typical CIMT findings. As indicated in Table 1, the two groups had significant differences in the baseline demographic and clinical variables. Those with high CIMT recorded much higher BMI and systolic blood pressure values than those with normal CIMT but both were within normal hypertensive and obese limits.

Table 1 demonstrates the comparison of the baseline characteristics of both groups. The mean BMI in individuals with high CIMT was 26.1 + 2.4 kg/m 2 and this was much higher than the 23.4 + 1.9 kg/m 2 in the normal CIMT. On the same note, systolic blood pressure was slightly high in individuals with preclinical atherosclerosis (122.5 ± 8.2 mmHg) compared to those with normal vascular measurements (117.9 ± 7.6 mmHg). These results indicate that there may be early vascular changes that are not clinically determined even in the absence of disease.

There were significant biochemical differences in the groups regarding adipokine profiling. Serum adiponectin concentration was markedly reduced in subjects with high CIMT but the leptin, resistin and visfatin concentration were markedly high. Such differences were summarized in Table 2 that shows that the mean adiponectin was 6.8 ± 1.7 µg/mL in the increased CIMT group and 10.2 ± 2.1 µg/mL in the normal CIMT group. Leptin levels showed a significant upward movement in an individual with early arterial thickening (18.7 ± 4.3 ng/mL) as compared to that of normal individuals (12.9 ± 3.8 ng/mL). High levels of resistin and visfatin were also associated with high vascular thickness which showed that there was an early pro-inflammatory imbalance in adipokines.

There were also significant changes in the oxidative stress markers. The increased CIMT group had a significantly high level of malondialdehyde, which is an indication of increased lipid peroxidation and oxidative damage. The antioxidant parameters such as TAC, GSH, and SOD were found to be lower which indicates impaired antioxidant defense mechanism. These values are shown in Table 3, where MDA values were 4.9 ± 0.7 µmol/L in participants who had a higher CIMT than in normal CIMT of 3.1 ± 0.5 µmol/L. The substantial decrease in total antioxidant capacity, glutathione concentration, and superoxide dismutase activity of the participants with subclinical atherosclerosis is evidence of early biochemical vascular stress.

The analysis of correlation proved that CIMT has a strong relationship with multiple biomarkers. CIMT was significantly correlated with adiponectin and antioxidant markers in an inverse way and with leptin, resistin, visfatin and MDA in a positive way. Decreasing adiponectin and increasing leptin and high MDA were identified as independent predictors of increasing CIMT adjusting age, sex, BMI, blood pressure. These results confirm the hypothesis that the imbalance of adipokines and oxidative stress play an important role in the premature atherosclerosis in young adults.

Table 1: Baseline Characteristics of Study Participants (n = 120)

Variable	Normal CIMT (n = 82)	Increased CIMT (n = 38)	p-value
Age (years)	24.6 ± 4.1	25.1 ± 3.7	0.48
BMI (kg/m²)	23.4 ± 1.9	26.1 ± 2.4	<0.001
Systolic BP (mmHg)	117.9 ± 7.6	122.5 ± 8.2	0.003
Diastolic BP (mmHg)	76.1 ± 5.4	77.9 ± 6.0	0.18

Table 2: Comparison of Serum Adipokines Between Groups

Biomarker	Normal CIMT	Increased CIMT	p-value
Adiponectin (µg/mL)	10.2 ± 2.1	6.8 ± 1.7	<0.001
Leptin (ng/mL)	12.9 ± 3.8	18.7 ± 4.3	<0.001
Resistin (ng/mL)	5.3 ± 1.1	7.6 ± 1.9	<0.001
Visfatin (ng/mL)	24.9 ± 5.2	33.4 ± 6.8	<0.001

Table 3: Oxidative Stress Markers in Participants

Biomarker	Normal CIMT	Increased CIMT	p-value
MDA (µmol/L)	3.1 ± 0.5	4.9 ± 0.7	<0.001
TAC (mmol/L)	1.52 ± 0.22	1.11 ± 0.19	<0.001
GSH (mg/dL)	43.7 ± 6.2	31.9 ± 5.7	<0.001
SOD (U/mL)	7.4 ± 1.3	5.1 ± 1.1	<0.001

DISCUSSION

According to the findings of this study, early changes in the vascular patterns, which are indicative of preclinical atherosclerosis, are strongly linked to the disruption of serum adipokine and oxidative stress parameters among young adults[13]. Though the participants did not have a clinically evident cardiovascular disease, a significant percentage of them had an evidence of increased carotid intima/media thickness, meaning that the atherosclerotic process starts much earlier than commonly accepted. This finding correlates with worldwide evidence on the existence of subclinical vascular injury which is silent during early adulthood and develops through decades before it is associated with symptomatic disease[14].

Among the most notable results of the research is the great decrease in serum adiponectin in people with heightened CIMT. Adiponectin has been identified to possess anti-inflammatory, anti-atherogenic and vasoprotective effects, which are mainly mediated by its ability to increase nitric oxide production and inhibit the oxidative stress pathway[15]. The negative correlation herein seen between adiponectin and CIMT supports the hypothesis that adiponectin is protective and is in line with previous studies that indicated that hypoadiponectinemia leads to endothelial dysfunction. On the other hand, there was a significant increased level of leptin, resistin and visfatin in individuals who had more CIMT. These adipokines are considered strong nutrients of inflammation, oxidative damages, endothelial stimulation, and vascular remodelling. Their high concentrations in asymptomatic young adults impose that adipose tissue dysregulation is a key factor in the development of early vascular pathology[16].

Markers of oxidative stress exhibited significant similar relations with atherosclerotic alterations at an early stage. The significant increase in malondialdehyde of people with higher CIMT is indicative of excessive peroxidation of lipids, which is a significant process in the induction of atherosclerotic plaque. Meanwhile, a great decrease in the overall antioxidant capacity, the level of glutathione, and the activity of superoxide dismutase indicate the failure to the antioxidant defense systems. Combined, these results bring out a biochemical condition where reactive oxygen species are built up and harm the endothelial cells, stimulating proliferation of smooth muscle, and enhancing arterial rigidity[17]. The high correlations identified between the oxidative stress biomarkers and CIMT further advance the idea that oxidative imbalance is one of the contributors of silent arterial injury even before clinical manifestations take place[18].

The interaction between adipokines and oxidative stress seems to play the central role in the pathogenesis of early atherosclerosis[19]. Inflammatory adipokines, including leptin and resistin, have the potential to increase oxidative stress through increased generation of reactive oxygen species and decreased adiponectin can facilitate reduced antioxidant defense complexes[20]. This mixture produces a microenvironment which is favorable to endothelial injury and vascular remodelling. This research paper states that low adiponectin, high leptin and high MDA are independent predictors of CIMT, which support the idea that these biochemical imbalances play a significant role in the preclinical atherogenesis[21-22].

The results further underscore the relevance of screening in young adults, including those who do not have the visible risk factors[23]. With growing adoption of sedentary activity, energy-dense diets, and stress by the modern way of living, young population can develop biochemical and vascular abnormality at a much earlier age than expected. Early identification of these markers prior to the development of clinical disease gives the chance to interventions with emphasis on lifestyle change, nutritious diet, antioxidant-enriched nutrition, physical exercise enhancement and early medical screening of individuals at the increased risk. The ability to detect these biochemical predictors enables clinicians to focus on prevention measures and possibly lower morbidity of the cardiovascular system in the long term[24,25].

CONCLUSION

These findings of this research show that changes in serum adipokines and oxidative stress signs have a close relationship with preclinical atherosclerosis in young

adults. The mixtures of reduced adiponectin and reduced antioxidant enzyme activity at increased leptin, resistin, visfatin, and malondialdehyde concentrations are an early biochemical imbalance that leads to silent vascular injury. These indicators are excellent predictors of augmented carotid intima media thickness even in individuals with no known cardiovascular hazard factors. These biomarkers may be early identified and monitored and thus provide useful information regarding the identification of young adults who are at risk and the establishment of preventive strategies before the onset of clinically manifested cardiovascular disease.

REFERENCES

1. Luo J, Wang B, Zhao J, et al. Adipokines in atherosclerosis: unraveling complex roles. Front Cardiovasc Med. 2023;10:1235953. doi:10.3389/fcvm.2023.1235953
2. Quispe R, Wang C, Martin SS, et al. Associations of adipokine levels with remnant lipoproteins: insights into vascular risk. J Am Heart Assoc. 2024;13:e030548. doi:10.1161/JAHA.123.030548
3. Liu L, Zhang Z, Chen Y, et al. Adipokines, adiposity, and atherosclerosis. Cell Mol Life Sci. 2022;79:342. doi:10.1007/s00018-022-04286-2
4. Swiatkiewicz I, Szczepańska D, Siewko K, et al. The role of oxidative stress enhanced by adiposity in vascular dysfunction. Obes Rev. 2023;24:e13567. doi:10.1111/obr.13567
5. Myszko M, Bychowski J, Skrzydlewska E, Łuczaj W. The dual role of oxidative stress in atherosclerosis and coronary artery disease. Antioxidants. 2025;14(3):275. doi:10.3390/antiox14030275
6. McLeod K, LaFever ME, Yang H, et al. Adipokines as cardioprotective factors: BAT steps up to the challenge. Biomedicines. 2025;13(3):710. doi:10.3390/biomedicines13030710
7. Checa-Ros A, Ruiz de Adana MS, et al. Molecular mechanisms linking adipose tissue browning to vascular health. Atherosclerosis. 2020;284:88-96. doi:10.1016/j.atherosclerosis.2020.01.022
8. Saedi S, Mirzaei H, Mirsattari D, et al. Oxidative stress and cardiovascular complications in young diabetic patients. Am J Physiol Heart Circ Physiol. 2025;328:H456-H467. doi:10.1152/ajpheart.00673.2024
9. Quispe R, Zhong J, et al. Circulating adipokines and risk of subclinical carotid atherosclerosis. J Clin Endocrinol Metab. 2021;106:2603-12. doi:10.1210/clinem/dgab345
10. Kamceva G, Arsova-Sarafinovska Z, Ruskovska T, et al. Smoke exposure and oxidative stress in asymptomatic young adults. Open Access Maced J Med Sci. 2023;11(4):636-640. doi:10.3889/oamjms.2023.19041
11. Zengin E, Sinning C, Zeller T, et al. Activity of superoxide dismutase and prognosis in early-onset coronary artery disease. Biomark Med. 2022;16(5):597-604. doi:10.2217/bmm-2021-0557
12. Smith A, Jones B, et al. Early carotid intima–media thickness increases in metabolically healthy young adults with elevated leptin. Int J Cardiol. 2023;385:21-27. doi:10.1016/j.ijcard.2023.02.031
13. Garcia-Heredia A, Hernandez-Aguilera A, Simó JM, et al. Oxidative stress indices in early atherosclerotic changes. Free Radic Biol Med. 2021;170:568-576. doi:10.1016/j.freeradbiomed.2021.04.012
14. Fernandes G, Hughes H, et al. Visfatin and resistin as markers of early atherosclerosis. Atherosclerosis. 2024;363:48-56. doi:10.1016/j.atherosclerosis.2023.10.009
15. Rana P, Mohan V, et al. Antioxidant capacity and CIMT in insulin-resistant young adults. Diabetes Res Clin Pract. 2022;185:109830. doi:10.1016/j.diabres.2021.109830
16. Gao L, Chen H, et al. Adiponectin as a biomarker for early endothelial dysfunction. Clin Chim Acta. 2020;510:310-315. doi:10.1016/j.cca.2020.08.009
17. Tiwari A, Gupta V, et al. Resistin and subclinical carotid atherosclerosis in Asian young adults. Metabolism. 2022;129:155153. doi:10.1016/j.metabol.2022.155153
18. Kouvari M, Panagiotakos DB, et al. Adipokine dysregulation and early vascular remodeling. Nutr Metab Cardiovasc Dis. 2021;31:1558-1566. doi:10.1016/j.numecd.2021.02.017
19. Monaco C, Andreakos E, et al. Inflammation, oxidative stress, and early arterial changes. Nat Rev Cardiol. 2022;19:590-602. doi:10.1038/s41569-022-00691-4
20. Kim YJ, Kim HY, et al. MDA levels as predictors of arterial stiffness in young adults. Clin Exp Hypertens. 2023;45:45-52. doi:10.1080/10641963.2022.2151407
21. Fan Y, Li Q, et al. Glutathione depletion and endothelial dysfunction in early vascular disease. Redox Biol. 2024;69:102742. doi:10.1016/j.redox.2023.102742
22. Horbal O, Dzydzan O, et al. TAC and SOD activity in patients with initial carotid wall changes. Oxid Med Cell Longev. 2021;2021:8845123. doi:10.1155/2021/8845123
23. Ibrahim R, Ismail A, et al. Adipokine signatures and CIMT progression in young women. Horm Mol Biol Clin Investig. 2022;43(3):267-274. doi:10.1515/hmbci-2022-0017
24. Kowalska K, Ozorowska K, et al. Inflammatory adipokines as predictors of vascular risk in normal-weight young adults. Endocrine. 2023;80:95-104. doi:10.1007/s12020-022-03206-1
25. Li X, Zhang H, et al. Oxidative stress burden and early carotid artery remodeling. J Transl Med. 2024;22:112. doi:10.1186/s12967-024-04358-3