Section A-Research paper
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CORRELATION OF CHEMERIN BIOMARKER WITH SUBCLINICAL PARAMETERS OF ATHEROSCLEROSIS IN METABOLIC SYNDROME PATIENTS.

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ABSTRACT

Objective: Chemerin biomarker is newly identified adipokine with a contentious part in people with metabolic syndrome. Chemerin is important in the development of progressive atherosclerosis. It is still very unclear how circulating chemerin and non-invasive indicators of subclinical atherosclerosis interact. To assess serum chemerin levels and atherosclerosis parameters in patients with metabolic syndrome. **Methodology:** 75 patients in metabolic syndrome who were undergoing the comprehensive health examinations were the subject of the cross-sectional investigation. Enzyme linked immunosorbent assay (ELISA) used to detect the serum chemerin level. High resolution ultrasonography was used to measure the carotid intima medial thickness, flow mediated vasodilatation and ankle brachial index in all subjects. **Results:** Those with metabolic syndrome, who had subclinical atherosclerosis, as shown by increased carotid intima medial thickness, flow mediated vasodilatation and ankle brachial index, had significantly higher serum chemerin levels. Positive associations in serum chemerin levels and patients with the metabolic syndrome based on a straight forward linear regression analysis. The level of chemerin in the serum significantly correlated positively with CIMT right (r=0.305), CIMT left (r=0.244) and a significant inverse correlation between serum chemerin with FMD (flow mediated vasodilatation) (r=-0.316), ABI (ankle brachial index) (r =-0.312); all "P" value of < 0.05 or lower is mentioned as significant. **Conclusion:** The subclinical atherosclerotic parameters that are being studied are a good indicator of the atherosclerotic burden in different artery sites and disease stage. The blood chemerin level was found to be a reliable predictor of atherosclerosis in people with metabolic syndrome.

KEYWORDS: Carotid intima medial thickness, flow mediated vasodilatation, ankle brachial index, metabolic syndrome, chemerin, cardiovascular disease, Blood Pressure, Peripheral vascular disease.

INTRODUCTION:

Metabolic syndrome is a set of clinical and biochemical abnormalities related to metabolism. The conditions encompass being overweight, Dyslipidemia, hypertension, microalbuminuria and other major risk factors, that contribute to tolerance. Essentially, the combination of various risk factors of metabolic disease to contributes the development of cardiovascular disease.[1] Fat cells secrete a newly discovered adipokine called chemerin.

Some research has indicated that malfunctioning of adipose tissues endocrine system is a significant factor. Chemerin is linked to obesity and metabolic syndrome in terms of insulin resistance.[2] In earlier research, the possible contribution of chemerin to atherosclerosis was increasingly emphasized. Chemerin may have inflammatory effects in the early phases of the atherosclerotic process, according to several experimental studies.[3-7] The ankle brachial index (ABI), in addition to being useful in the diagnosis of peripheral artery disease (PAD), can also be utilized as a marker of atherosclerosis, with a negative correlation between ABI and the risk of CVD.[8] Chemerin's significance in attracting the immune cells to lymphoid organs and damages has been highlighted in experimental study as evidence for its involvement in inflammation .[9]FMD can serve as indicator of atherosclerosis and the risk of CVD can be determined by the ankle brachial index (ABI), it can also be utilized as a marker of atherosclerosis. This study explores the relationship between serum chemerin levels and a number of subclinical tests for atherosclerosis, such as CIMT, FMD and ABI. We believe that subclinical atherosclerosis lesions are linked to elevated plasma chemerin levels. As a simple and nonintrusive method, the measurement of CIMT is recognized as a commonly used tool for detecting atherosclerosis in its early stages.

METHODS AND MATERIALS:

Subjects:

Chettinad hospital and research institute served as the site of this cross-sectional investigation. 75 people under the age of 35 were recruited for the study. Experienced radiologist took CIMT, FMD and ABI in the department of radiology. According to the IDF (International Diabetic Federation) criteria, which stipulates that three or more of the risk factors listed below must be present, (i) Raised Triglyceride >150mg/dl, (ii) Reduced HDL cholesterol <40 mg/dl in male and <50 mg/dl in female, (iii) Raised BP Systolic BP>130 and Diastolic BP >85 mmHg, (iv) Raised FBG >100 mg/dl, (v) Waist Circumference >35 inches female and >40 inches in male. Level of FBS, HDL and TGL were determined by enzymatic methods using an auto analyzer. The enzyme linked immunosorbent assay (ELISA) was used for the quantitative determination of serum Chemerin. As per the kit instructions, the procedure of ELISA had been performed.

Inclusion Criteria:

The patient should fit into the definition of metabolic syndrome as defined by IDF guidelines, as given above.

Exclusion Criteria:

Past history of CAD, Past history of cerebrovascular accidents, Patients with inflammation, neoplasm, pregnancy, smokers, autoimmune, hepatic and renal dysfunction and terminal illness were excluded from the study.

Biochemical indicators:

The study participants underwent a thorough physical examination, including the measurement of waist circumference, ABI, FMD and CIMT using doppler, after providing their signed informed permission. Levels of fasting glucose, HDL-C, and triglycerides were determined by enzymatic methods using an auto analyser, whereas serum chemerin levels was deteceds using an enzyme immunoassay ELISA kit.

CIMT:

CIMT (carotid intima-media thickness) is a non-invasive method for assessing subclinical atherosclerosis. The methodology for CIMT measurement typically involves the following steps:

The participant is asked to lie down in supine position, and neck is slightly turned. An ultrasound probe with a high-frequency transducer (7-10 MHz) is placed on the skin over the carotid artery. The ultrasound probe is used to visualize the intima-media complex of the carotid artery. The mean CIMT, calculated as the average of the measurements taken at each segment of the carotid artery. CIMT presence >1.0 mm in the right and left CIMT was considered as subclinical atherosclerosis.

FMD: Assessment of brachial FMD was conducted among the study population in their fasting state. All the participants were instructed to lie down in a supine position before the start of the test. A BP cuff is placed around the participant's forearm, and an ultrasound probe is placed on the arm to visualize the brachial artery. The baseline diameter of the brachial artery is measured in a resting state. The blood pressure cuff is then inflated to a pressure of 200 mmHg or higher for 5 minutes to induce ischemia in the forearm. The cuff is then rapidly deflated, which leads to a reactive hyperaemic response that causes an blood flow to the arm, corresponding increasing in brachial artery diameter. The diameter of the brachial artery is measured at 60-90 seconds after cuff deflation. The change of diameters was automatically calculated using the formula as follows: (maximum diameter – baseline diameter)/baseline diameter × 100%.

A diagnosis of endothelial dysfunction was made if the FMD was less than 10%.

ABI:

Lower-limb peripheral artery disease can be evaluated using ankle/brachial index (ABI), which is the ratio of BP measured at the ankle to blood pressure in the brachial artery. It identifies those who are more likely to die from all causes, such as cardiovascular illnesses, in the future. ABI is used to identify PVD as a sign to overall atherosclerosis.

Statistical analysis

SPSS IBM software version 26 software was used for data analysis. Continuous variables were represented as the mean and standard deviation (SD). Correlation between the biomarkers were calculated by using Pearson’s correlation, ANOVA and chi-square test. p value <0.05 was taken as statistical significance.

RESULTS:

our study includes 75 patients of which 47 were male (62.7%) and 28 were women (37.3%) with a mean age of 58.0 ± 10.2 years. Abnormal FBS ranges (N=69; 92%) with a mean average of 145.05 ± 50.720. In HDL (N=62;82.7%) patients were presented with abnormal with a mean average of 37.13 ±7.780. Abnormal ranges in TGL (N=50; 66.6%) with a mean

average of 194.79±115.074. Abnormal ranges in waist circumference (N=23; 30.6%). Blood pressure in abnormal ranges(N=34;45.3%).

Table 1: Baseline characteristics of the patients

Parameters	Mean ± Std. Deviation (Range)
Age (years)	58.08±10.247 (36-85)
FBS in plasma (mg/dL)	145.05±50.720
TGL (mg/ dL)	194.79±115.074
HDL (mg/ dL)	37.13 ±7.780
Waist Circumference (inches)	77.72 ±10.147
SBP (mm Hg)	120.24±10.917
DBP (mm Hg)	81.40±10.351
CIMT-Right (mm)	1.0467±0.25697
CIMT-Left (mm)	1.0160±0.31151
FMD (%)	9.5240±2.514
Chemerin (ng/mL)	118.6400±21.549
ABI	0.968±0.20078

Table2: Correlation of Chemerin with CIMT:

Considerably enhanced the diameter of the right and left CIMT as compared to the Chemerin with CIMT

CHEMERIN	CIMT	
	RIGHT	LEFT
118.6400±21.549	1.04±0.25**	1.01±0.31**

Values expressed as mean standard deviation with pearson correlation significant levels of *p value <0.05 **p value <0.01(r value of right CIMT r=0.305 and left CIMT r=0.244).

Table 3: Chemerin with FMD using pearson correlation:

Inverse correlation exists between the serum chemerin with FMD.

CHEMERIN	FMD
118.6400±21.549	9.52±2.51*

Values expressed as mean standard deviation with pearson correlation significant values of *p value<0.05* (r= -0.316).

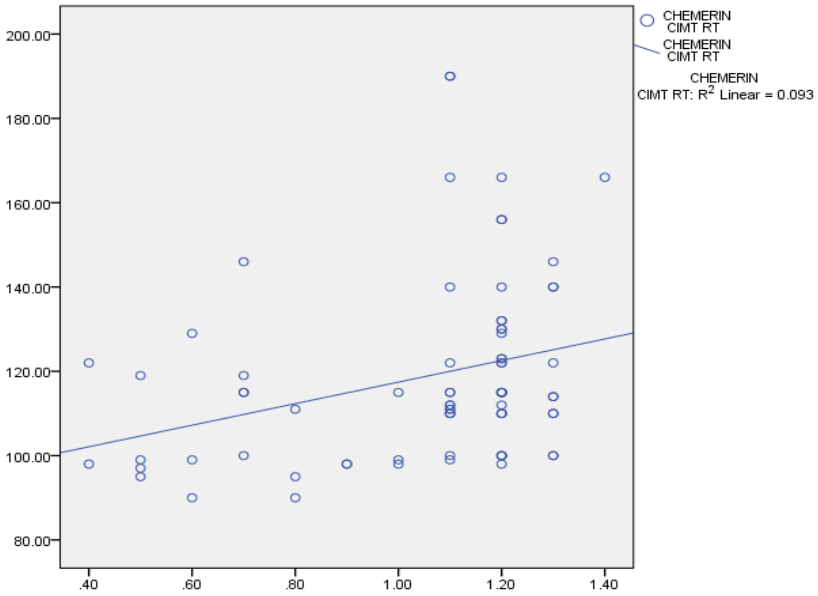
Table 4: Correlation of Chemerin with ABI:

Inverse correlation exists between the serum chemerin with ABI.

CHEMERIN	ABI
118.6400±21.549	0.968±0.20078

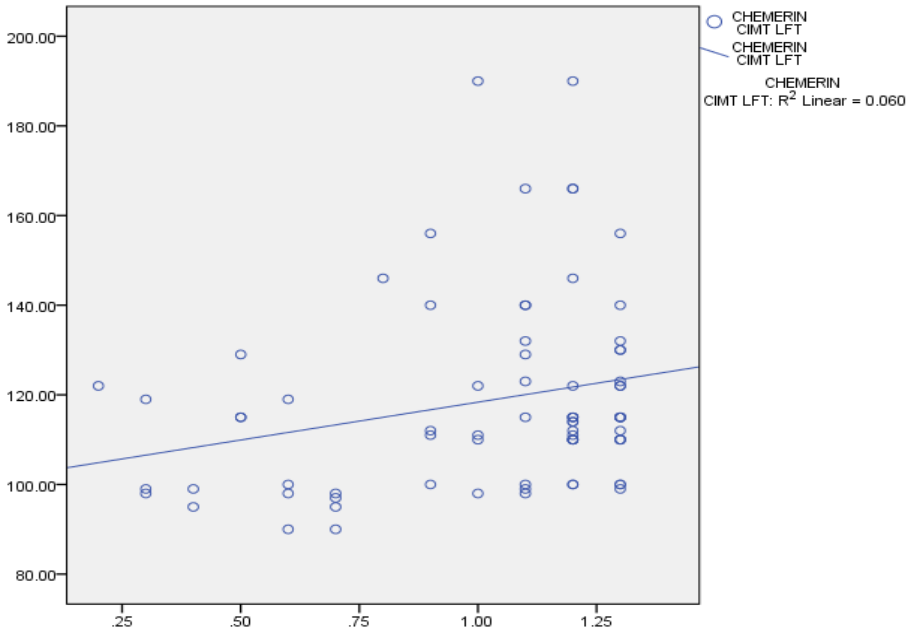
Values expressed as mean standard deviation with pearson correlation significant values of *p value<0.05* (r= -0.312).

FIGURE 1: CIMT RIGHT



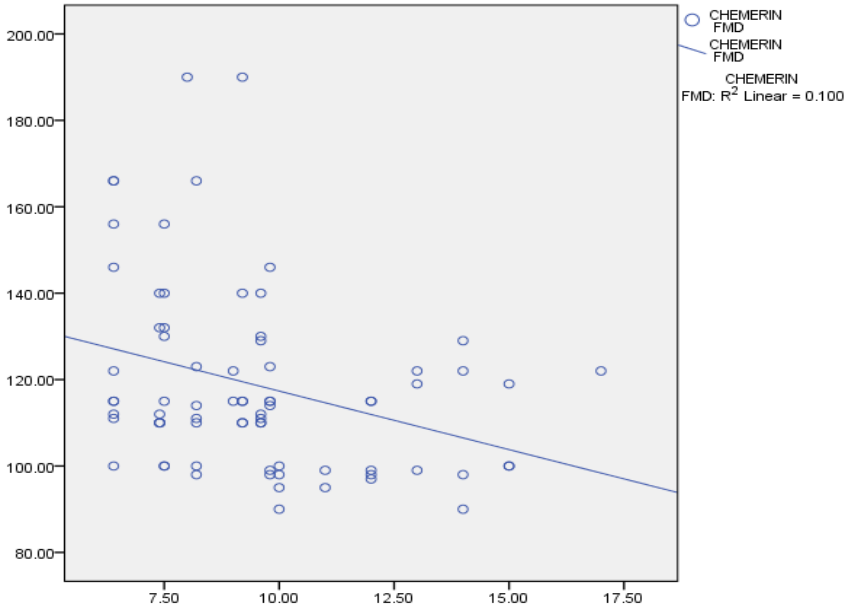
In Fig 1: **S**catter plot shows the correlation of serum chemerin levels with CIMT right with metabolic syndrome patients.

FIGURE 2: CIMT LEFT



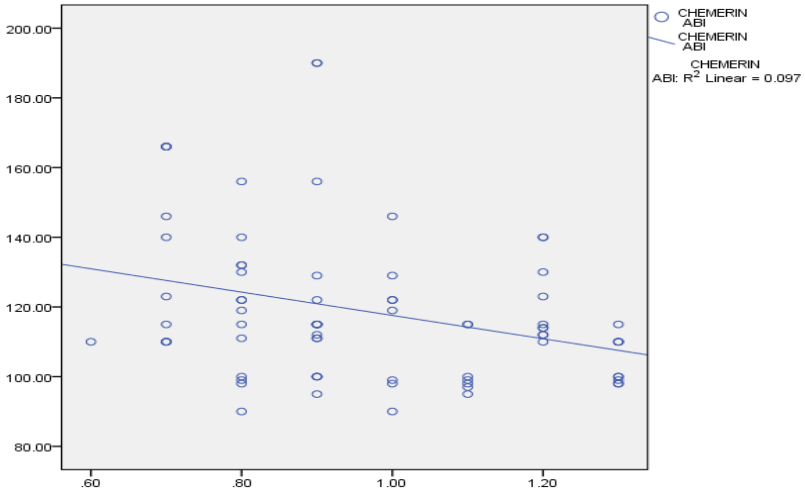
In Fig 2: **S**catter plot shows the correlation of serum chemerin levels with CIMT left with metabolic syndrome patients.

FIGURE 3: Chemerin with FMD



In Fig 3: **S**catter plot shows the negative relationship between serum chemerin levels with FMD in metabolic syndrome patients.

FIGURE 4: Chemerin with ABI



In Fig 4: **S**catter plot shows the negative relationship between serum chemerin levels with ABI in metabolic syndrome patients.

DISCUSSION:

A measure of subclinical atherosclerosis called carotid intima media thickness (CIMT) are reliable predictor to cardiovascular and cerebral vascular events. Carotid ultrasonography has been shown in studies to be a sensitive technique that produces trustworthy results.[10] Furthermore, it has been demonstrated that the onset of clinically discernible atherosclerotic plaques in the coronary arteries precedes endothelial dysfunction, which is now recognised as an early event in atherogenesis. Nitric oxide (NO), in particular, has a lower bioavailability due to endothelial dysfunction, although the bioavailability of contracting substances originating from the endothelium is increased. Many studies evaluated the endothelial function (as measured by FMD) as a predictor to future cardiovascular events.[11] ABI is recognized as a crucial cardiovascular risk indicator as well as a clinical tool for assessing

severity of PAD.[12,13] It is widely acknowledged that persons with an ABI of 0.9 or >1.4 have a greater chance of experiencing cardiovascular problems.[14]

In current study we examined the relationship between serum chemerin level with CIMT right and left side has a strong correlation between serum chemerin level and CIMT in patients with metabolic syndrome CIMT Right (r=0.305), CIMT Left (r=0.244). chemerin with FMD shows a significant inverse correlation (r=-0.316). There is evidence that carotid IMT and FMD can predict future cardiovascular events in individuals with metabolic syndrome. Impaired FMD and elevated carotid IMT are also recognized markers for early atherosclerosis.[15,16] It was discovered the serum chemerin levels also correlated with BMI, serum triglyceride levels, blood pressure, and hypothesized the chemerin encourages adipocyte differentiation and contributes to inflammation.[17]

In our study, the serum chemerin level and ABI were found to be significantly inversely correlated (Pearson correlation coefficient r=-0.312; p=0.007). The inverse correlation of serum chemerin and ABI, which is concordance with stephanie zylla et al., who found that increase of chemerin was associated with ABI are predicted for future peripheral artery disease or other cardiovascular disease.[18] A layer of perivascular adipose tissue surrounds blood vessels, and this tissue is known to secrete a variety of adipokines, including atherosclerotic plaques.[19] Human endothelial cells have been found to express chemerin and its receptor,[20] and there is evidence that chemerin may hinder vascular relaxation by decreasing NO generation in these cells.[21] According to this research, chemerin may cause endothelial dysfunction, a significant mechanism can start the atherosclerotic process.

CONCLUSION:

After adjusting for waist circumference, other metabolic and inflammatory indicators, systolic blood pressure and other factors, the current study found a moderate but significant negative correlation between serum chemerin levels with FMD and ABI that persisted. Based on this stage and location of the atherosclerotic lesion, our findings imply the chemerin may have various correlations. We presume that high serum chemerin levels are associated with the potential development to PAD given the found inverse correlation between serum chemerin with FMD and ABI. The findings showed that the amount of serum chemerin may serve as a predictor of the onset of atherosclerotic cardiovascular disease.

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