INTRODUCTION

It is estimated that more than twenty per cent of the world’s adult population have the metabolic syndrome and they are twice as likely to die from and three times as likely to have a coronary event or cerebrovascular event compared with people without the syndrome.\textsuperscript{1,2} Other than the major components of metabolic syndrome, visceral adipose tissue accumulation also determines a comprehensive cardiovascular risk profile.\textsuperscript{3} It is found that it is the amount of visceral fat more than subcutaneous fat, more harmful in metabolic point of view and is found to be directly related with insulin sensitivity.\textsuperscript{4,5} These insights imposed a need to determine body composition, with special focus on visceral adipose tissue.\textsuperscript{6} It is proposed that, it is the increased amount of visceral adipose tissue (VAT) that is responsible for this so called “Asian Indian Phenotype”\textsuperscript{7}. Hence this study aims to look into the distribution and clinical implications of visceral and subcutaneous adipose tissue in subjects with metabolic syndrome compared to normal individuals in northern part of Kerala.

AIM OF THE STUDY

1) To estimate the amount of Visceral Adipose Tissue and Subcutaneous Adipose Tissue in persons with and without metabolic syndrome and to find a cut off for Visceral Adipose Tissue in metabolic syndrome.

2) To find out the correlation between Visceral Adipose Tissue and various anthropometric

A STUDY ON ESTIMATION OF VISCERAL FAT AND ITS METABOLIC AND CLINICAL CORRELATES IN METABOLIC SYNDROME

Manu Prasad A,  
Senior Resident,  
Cancer institute Adyar - Chennai

Chandni R,  
Additional Professor,  
Dept of General Medicine,  
GMC Kozhikode

Devarajan E,  
Professor,  
Dept of Radiology, GMC Kozhikode
parameters
3) To find out the correlation between Visceral Adipose Tissue and metabolic parameters like glycemic status and lipid profile
4) To find out the correlation between Visceral Adipose Tissue and Subcutaneous Adipose Tissue with insulin sensitivity using Homeostatic Model Assessment (HOMA) after measuring serum c peptide.
5) To assess the relation between Visceral Adipose Tissue and Subcutaneous Adipose Tissue with liver function and liver fat.

STUDY DESIGN: Case Control study
STUDY PERIOD: Total study period was 12 months
STUDY SUBJECTS
First 50 subjects with metabolic syndrome attending Medicine or diabetic OPD in Govt Medical College, Kozhikode were selected as cases. Age and sex matched normal individuals were enrolled as controls.

INCLUSION CRITERIA
Subjects satisfying IDF criteria for metabolic syndrome were enrolled as cases and age and sex matched healthy subjects as controls.

EXCLUSION CRITERIA
1) Patient with endocrinopathies that can affect fat distribution and those who lost weight in a significant manner recently 2) Patients with spinal abnormalities, as it can affect fat measurements 3) Individuals not willing to participate in the study 4) Seriously ill patients, those with malignancies, pregnant ladies and patients with retro viral illness 5) Heavy drinkers defined according to WHO cut off (> 40 g/day in males and 20g/day in females)

STUDY METHODS
1) Relevant history is taken from all subjects using a proforma attached
2) Anthropometric measurements and clinical examination and relevant biochemical tests carried out, Insulin resistance was determined with serum c peptide and corresponding blood sugar levels by Homeostatic model assessment (HOMA).
3) Visceral Adipose Tissue (VAT) and Subcutaneous Adipose Tissue (SAT) measured using ultrasonographic procedure. Ultrasound-determined subcutaneous fat (SAT) was defined as the distance between the skin and external face of the rectus abdominis muscle, and visceral fat (VAT) was defined as the distance between the internal face of the same muscle and the anterior wall of the aorta.

STATISTICAL ANALYSIS
Statistical analysis is carried out using SPSS package. Statistical tests like Independent t test, one way ANOVA, and Pearson’s correlation were done and Receiver Operator Curve (ROC) was also plotted and appropriate conclusions were arrived at. A p value of <0.05 was considered statistically significant.

RESULTS
Baseline Characters
Fifty subjects with metabolic syndrome were selected as cases and same numbers of normal subjects were selected as controls. Cases and controls were age and sex matched. Mean age in the case group was 43.96 years and in the control group was 42.78 years. Minimum age was 25 years and maximum 66 years and age distribution was comparable. Among patients with metabolic syndrome thirty (60%) were males. This was comparable with the control group.
Among patients with metabolic syndrome, seven had history of diabetes (14%), nine had history of hypertension (8%) and seven (14%) had coronary artery disease. 10% of the patients i.e. five of them had history of dyslipidemia In terms of level of activity patients with metabolic syndrome were more falling into sedentary or minimal activity categories. But major share of controls were included in minimal activity with exercise group.

ANTHROPOMETRIC DATA

Mean height in subjects with metabolic syndrome was 160 cm and that in the healthy individuals was 162 cm with no significant difference. But mean body weight among cases and controls were 72 kg and 62 kg respectively had a p value less than 0.05. Cases and controls also had significant differences in terms of waist circumference and Body mass index.

Sixty seven percent of the subjects had BMI more than 25 and only 13% had a BMI more than 30. Also 75 % of the females had waist circumference More than 80 cm and 58 % of the males had a WC more than 90 cm.

ADIPOSE TISSUE MEASUREMENTS

Mean Visceral Adipose Tissue (VAT) in the population was 72.52 mm (SD = 26.1) and Subcutaneous Adipose tissue (SAT) was 23.54 mm (SD = 7.50). VAT to SAT ratio was 3.3 (SD = 1.5).Minimum value was 24 mm and maximum 126 mm.

Mean VAT in subjects with metabolic syndrome was significantly higher than that of control group (Table 1). But SAT was comparable in both groups. Also it was observed that there was no significant difference in the mean VAT between males and females. But SAT was significantly higher in females (p value < 0.01) and hence VAT: SAT ratio also showed statistically significant difference (Table 9).

Table 1: Fat Measurements in cases and controls

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Cases</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAT (mm)</td>
<td>95.2</td>
<td>49.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SAT (mm)</td>
<td>24.5</td>
<td>22.5</td>
<td>0.202</td>
</tr>
<tr>
<td>VAT to SAT ratio</td>
<td>4.3</td>
<td>2.3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

VISCERAL FAT AND ANTHROPOMETRIC PARAMETERS

Among the anthropometric parameters, waist circumference has the maximum positive correlation with VAT (r = 0.8). WC has positive correlation with SAT but less strong than with VAT (Table 10). Correlation of VAT with WC was significant in cases, controls males and females even on separate analysis. But it was observed that controls had better correlation between WC and VAT. But SAT has correlation with WC mainly in females and in controls (Table 2).

Whereas BMI was found to be better correlated with SAT (r = 0.5) than VAT in the study population. VAT had correlation with BMI in all groups but was more significant in control population and in females. VAT: SAT ratio had strong correlation with waist circumference than BMI, in the whole population and in different groups.

WHR showed less significant correlation with fat measurements compared to WC and BMI (Table 10). It has a weak negative correlation with SAT among cases (Table 10).

VAT AND BLOOD PRESSURE

Both systolic as well as diastolic blood pressure has got positive correlation with VAT (p value < 0.001) in One Way ANOVA. Systolic blood pressure also got significant correlation with VAT SAT ratio also but not with SAT. Diastolic blood pressure was significantly associated with VAT (p value < 0.001), VAT:SAT ratio (p value < 0.001) and SAT (p value 0.017).
VAT and METABOLIC PARAMETERS

VAT has significant positive correlation with fasting blood sugar, postprandial blood sugar, total cholesterol, LDL cholesterol, VLDL cholesterol and Total cholesterol HDL ratio and a strong negative correlation with HDL cholesterol (Figure 1).

Figure 1: Negative correlation between VAT and HDL

<table>
<thead>
<tr>
<th>Population</th>
<th>Parameter</th>
<th>WC</th>
<th>BMI</th>
<th>WHR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r value</td>
<td>p value</td>
<td>r value</td>
<td>p value</td>
</tr>
<tr>
<td>All Subjects</td>
<td>VAT</td>
<td>0.8</td>
<td>&lt;.001</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>SAT</td>
<td>0.3</td>
<td>0.004</td>
<td>0.5</td>
</tr>
<tr>
<td>Cases</td>
<td>VAT</td>
<td>0.5</td>
<td>&lt;0.01</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>SAT</td>
<td>0.13</td>
<td>0.3</td>
<td>0.37</td>
</tr>
<tr>
<td>Controls</td>
<td>VAT</td>
<td>0.58</td>
<td>&lt;0.01</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>SAT</td>
<td>0.5</td>
<td>&lt;0.001</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Note: r value - Pearson’s coefficient

Table 2: US measurements and Anthropometry (Pearson’s correlation)

Figure 2: Total Cholesterol HDL ratio and VAT

Of these Total Cholesterol HDL ratio showed maximum positive correlation with VAT (Figure 2).

VAT and INSULIN RESISTANCE

In the 100 subjects VAT has significant negative correlation with insulin sensitivity by HOMA S (r = -0.77). Also SAT showed negative correlation with insulin sensitivity, but less strong. Another positive correlation was between serum C peptide levels and VAT in the population (Table 3).
Negative correlation between VAT and % S was evident among cases
(r = -0.3, p value < 0.05) and control (r = 0.54, p value < 0.001). The correlation between VAT and IR was not significant when cases were analysed separately, but it was evident in all other groups and in the total subjects.

Similarly VAT SAT ratio also got negative correlation with Insulin Sensitivity. All these measurements had positive correlation with Insulin resistance (IR) calculated by HOMA model, strongest being that of VAT (Table 12). In general, correlation between VAT and these indices were stronger than that with SAT. Beta cell function did not show significant correlation with any of the fat measurements.

Both in males and females, VAT and VAT to SAT ratio had significant correlation with insulin resistance. But SAT has no correlation with HOMA indices in males.

Fatty Liver and VAT
Increase in VAT is significantly associated with fatty liver, with significance maintained between all grades of fatty liver (Table 4).

<table>
<thead>
<tr>
<th>Measurement</th>
<th>% S r value</th>
<th>p value</th>
<th>IR r value</th>
<th>p value</th>
<th>C Peptide r value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAT(mm)</td>
<td>-0.775</td>
<td>&lt;0.001</td>
<td>0.698</td>
<td>&lt;0.001</td>
<td>0.679</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SAT(mm)</td>
<td>-0.3</td>
<td>0.009</td>
<td>0.25</td>
<td>0.01</td>
<td>0.2</td>
<td>0.036</td>
</tr>
<tr>
<td>VAT SAT Ratio</td>
<td>-0.52</td>
<td>&lt;0.001</td>
<td>0.49</td>
<td>&lt;0.001</td>
<td>0.52</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 4: ANOVA (FATTY LIVER AND VAT)

<table>
<thead>
<tr>
<th>LIVER FAT</th>
<th>MEAN VAT(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fatty liver (Grade 0)</td>
<td>57.5</td>
</tr>
<tr>
<td>Mild Fatty Liver (Grade 1)</td>
<td>80.7</td>
</tr>
<tr>
<td>Moderate Fatty Liver (Grade 2)</td>
<td>105.6</td>
</tr>
</tbody>
</table>

P value < 0.001

VAT SAT ratio also showed a similar relation by One Way ANOVA. There was no statistically significant relation between SAT and fatty liver. There was significant difference in WC among subjects without fatty liver and with fatty liver. BMI also had a similar association. Difference in WHR was evident only between subjects without fatty liver and those with grade 2 fatty liver.

Cut off value for VAT to predict metabolic syndrome

Attempt was made to find out a cut off value for VAT for predicting the risk of having metabolic syndrome using Receiver Operator Curve (ROC) which suggested a cut off value of 67.5 mm with a sensitivity...
of 98 % and specificity of 92.1% independent of age and gender

DISCUSSION

VISCERAL AND SUBCUTANEOUS ADIPOSE TISSUE

Visceral Adipose tissue (VAT) was significantly higher among the cases. Mean value of 95.2 mm was well above the cut off for increased cardiovascular risk as predicted in previous studies like study by Liete et al. Mean VAT in control group (49.8 mm) was higher than that of similar study in healthy individuals by Roopkala MS et al (36.7mm). But other parameters like WC, BMI etc were also high in our study group. Interestingly, there was no statistically significant difference in terms of VAT among males and females. This gender independent nature of VAT was observed in the study by Roopakala MS also.

VAT AND ANTHROPOMETRIC PARAMETERS

WC was found to have maximum correlation with VAT in the population. This correlation was evident in all subgroups like cases, controls, males and females even on separate analysis. It was consistent with previous studies from both inside and outside India by Onat et al and Roopakala MS et al. All these observations stress on the importance of WC as an invaluable tool in clinical practice to identify those with increased cardiovascular risk.

Though BMI had correlation with VAT, it was less strong than with WC. But it had better correlation with SAT. A similar observation was also made in the study by Roopakala MS et al in her study of 60 healthy volunteers. This suggests that sometimes BMI can give spurious impressions regarding visceral adiposity. Another parameter, WHR also has a positive but less significant correlation with VAT in all groups except among cases where there was no correlation. This finding is also comparable to that of Roopakala MS.

VAT and BLOOD PRESSURE

Both systolic and diastolic blood pressure values were showing significant correlation with VAT. SAT has no correlation with systolic blood pressure, but was associated with increase in diastolic blood pressure. This findings are somewhat similar to observations by Sandeep et al, from Chennai, who reported strong correlation between VAT determined by CT with both systolic and diastolic blood pressure.

VAT and METABOLIC PARAMETERS

Amount of VAT showed positive correlation with both fasting and postprandial blood sugar levels. Also it had positive correlation with Total Cholesterol, LDL, VLDL and Total Cholesterol HDL ratio. VAT also had a strong negative correlation with HDL. Liete et al and colleagues in their study of 191 men found significant association between US estimated VAT and these parameters. Also Sandeep et al reported strong correlation between metabolic derangements and VAT (using CT). This is in accordance with the previous studies that brought out the significance of VAT in predicting the cardiovascular risk.

VAT and HOMA INDICES

Among the sonological indices, VAT was found to have maximum negative correlation with Insulin sensitivity and strongest positive correlation with insulin resistance. Though SAT has significant correlation with insulin sensitivity indices in the total subjects, it was found to have no relation with IR in males. This is comparable to previous studies using CT scan.

L Yang et al demonstrated a close correlation was demonstrated between VAT and HOMA-IR (r^2 = 0.46, p = 0.002), whereas SAT showed no relationship, in his study on obese non diabetic subjects. Oka et al also found out strong correlation between VAT estimated by CT and HOMA indices. In their study they found association between SAT and HOMA indices but VAT remained as most important predictor according to regression analysis. Pries SR et al, also found that though both VAT and SAT are related to insulin resistance, VAT has a stronger correlation, in a study conducted among non diabetic participants of Framingham Heart Study. All these
observations are consistent with the fact increased amount of VAT accounts for increased insulin resistance in metabolic syndrome.

ANTHROPOMETRIC MEASUREMENTS AND HOMA INDICES

Of the anthropometric parameters, WC has strongest correlation with these indices. Warhenberg et al also reported WC as the strongest predictor of insulin resistance; in a retrospective study of 2746 healthy volunteers\(^{15}\). It was also noted that BMI has correlation comparable to WC among subjects with metabolic syndrome in our study. But altogether WC was found to have stronger correlation with these indices than BMI, which again underscores the importance of WC as a predictor of increased cardiovascular risk. Correlation of WHR with insulin resistance is also significant but less strong than BMI and WC.

FATTY LIVER AND VAT

Along with other components of metabolic syndrome, VAT and VAT: SAT ratio showed significant correlation with fatty liver. This is in accordance with the findings by Seonah jang al who studied the association of VAT with fatty liver\(^{16}\). But SAT did not show any statistically significant association with NAFLD.

CUT OFF VALUE OF VAT

A cut off value of 67.5 mm was suggested by using ROC curve, to predict the risk of having metabolic syndrome by IDF criteria. It is comparable to cut off suggested by Leite et al. Cutoff values of 7 and 9 cm were suggested to identify men at moderate and high risk, respectively, of CVD. The corresponding values for women were 7 and 8 cm\(^{10}\).

CONCLUSION

1) There was significant difference in amount of Visceral Adipose Tissue between subjects with metabolic syndrome and normal individuals. But Subcutaneous Adipose Tissue between subjects with metabolic syndrome and normal individuals were comparable.
2) There was no difference in terms of Visceral Adipose Tissue between males and females. Hence Visceral Adipose Tissue is gender independent. But Subcutaneous Adipose Tissue was significantly high in females.
3) Among the anthropometric parameters, Waist circumference was found to have strongest correlation with Visceral Adipose Tissue. BMI has better correlation with Subcutaneous Adipose Tissue than Visceral Adipose Tissue.
4) Visceral Adipose Tissue has significant correlation with metabolic parameters including blood sugar and lipid profile.
5) Visceral Adipose Tissue has strong correlation with insulin sensitivity and insulin resistance using HOMA model.
6) Among anthropometric parameters, Waist Circumference had the strongest correlation with HOMA indices in general.
7) Both liver enzyme abnormalities and fatty liver was higher in subjects with metabolic syndrome. Those with fatty liver were found to have significantly higher Visceral Adipose Tissue, indicating the relationship between the two.
8) A cut off Visceral Adipose Tissue of 67.5 mm predicts the risk of having metabolic syndrome, independent of age and gender, with 98% sensitivity and 92% specificity.

REFERENCE


4. Bergman, R. N. et al. Why visceral fat is bad: mechanisms of the metabolic syndrome. *Obesity (Silver Spring)* 2006;14 (Suppl. 1), 16S–19S


