NECK CIRCUMFERENCE MEASUREMENT: A SIMPLE METHOD TO ASSESS THE RISK OF CARDIOVASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS

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ABSTRACT
Adipose tissue distribution and biochemical parameters of the type 2 diabetes mellitus (T2DM) patients have been investigated in association to cardiovascular disease (CVD) risk factors. Neck circumference (NC) shown to have a strong association with CVD. The aim of this study is to assess the relation between NC measurement and clinical characteristics involved in risk of CVD in T2DM. A case-control and cross sectional study were conducted with 100 T2DM patients and 100 healthy individuals of both male and female with 30-60 years of age. NC was measured using a flexible tape at the upper margin of the laryngeal prominence, HbA1C was estimated by immunoturbidimetry method, serum cholesterol was estimated by cholesterol oxidase, Triglycerides by Glycerol phosphate oxidase/peroxidase method, HDL-C by precipitation method, high sensitive C reactive protein (hsCRP) was estimated by latex immunoturbidimetry method and Homocysteine was estimated by enzymatic colorimetric method. Significant difference was observed in mean levels of body mass index (BMI), NC, waist circumference (WC), diastolic blood pressure (DBP), systolic blood pressure (SBP), fasting blood glucose (FBS), total cholesterol (TC), Triglycerides (TGL), high density lipoprotein (HDL-C), Glycated hemoglobin HbA1C, C reactive hsCRP and homocysteine (Hcy) of T2DM patients when compared with healthy controls (p<0.05). NC was positively correlated with BMI, DBP, WC, TGL and Hcy (p<0.05). NC as a novel indicator of CVD showed good predictive ability for adverse CVD events in T2DM individuals.

KEY WORDS: obesity, neck circumference, inflammatory marker.

INTRODUCTION
Body obesity is related with an elevated risk of developing metabolic syndrome (MS), T2DM, and hypertension and is consider as a major risk factor for CVD events and mortality. Excessive adiposity is involved in the pathogenesis of coronary heart disease (CHD), as it is related with the occurrence of conditions like dyslipidemias, hypertension and T2DM. The distribution of body weight, in addition to obesity consider as a vital aspect of MS, and is a great predictor of cardiovascular risk. The accumulation of body fat in particular regions is associated to disease risk. Generally, subcutaneous and visceral fat are related with IR. Visceral adipose tissue is a distinctive pathogenic fat deposit that is highly implicated in the pathogenesis of T2DM, and ischemic heart disease (IHD). Upper-body subcutaneous adipose tissue, evaluated by neck circumference (NC), is a fat depot that might be additional risk for metabolic risk factors over central and general adiposity and has shown a positive correlation with biochemical parameters of the MS. NC is a strong marker to identify obese persons and correlates with various anthropometric measurements. NC has been correlated with cardio-metabolic risk factors apart from the relationship with other adiposity measurements. NC is a simple and convenient anthropometric measurement, which is correlates with WC and BMI and has been related with components of MS in and cohort studies and cross-sectional studies in different populations. The relation between neck fat and MS and its components might be pertaining to an excess release of fatty acids from upper body subcutaneous fat into plasma. High concentration of plasma free fatty acids, in turn related with oxidative stress markers and IR, which may impact glycemia. Fat in the neck region may be highly similar to visceral fat, which is strongly associated with cardiometabolic risks when compared with subcutaneous fat. An increase in NC found to be an independent predictor of nonalcoholic fatty liver disease also. The aim of this study is to observe the relation between NC and clinical characteristics involved in risk of CVD in T2DM.

MATERIALS AND METHODS
A case-control and cross sectional study was conducted with 100 T2DM patients and 100 healthy individuals of both male and female with 30-60 years of age. NC (cm) was measured using a flexible tape positioned horizontally at the upper margin of the laryngeal prominence. Height and body weight were measured with participants standing without footwear. Body weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. BMI was calculated as weight (in kilograms) divided by height (in
meters square). WC was the minimum abdominal girth measured to the nearest 0.1 cm. BP was measured by using a mercury sphygmomanometer after the subject had rested for at least 10 min. SBP ≥140 mmHg, DBP ≥90 mmHg and participants who were on antihypertensive drugs was considered as hypertensive patients. Overnight fasting venous blood samples were collected from all subjects. The blood was transferred into glass tubes without anticoagulant and allowed to clot at room temperature. But for HbA1c estimation 0.5 ml of blood was transferred separately into glass tube containing EDTA. The serum was obtained by centrifugation of blood at 3500 rpm for 10 min. Blood glucose as estimated by glucose oxidase and peroxidase,$^{15}$ HbA1C was estimated by immunoturbidimetry method$^{16}$, Cholesterol by cholesterol oxidase$^{16}$, Triglycerides by Glycerol phosphate oxidase/peroxidase method$^{17}$, HDL-C by precipitation method$^{18}$, hsCRP was estimated by latex immunoturbidimetry method$^{19}$ and Homocysteine was measured by enzymatic colorimetric method$^{20}$. Data was expressed as mean ± standard deviation (SD). Comparisons between two groups were performed by unpaired Student t-test. Correlation was performed by Pearson’s calculation. A statistical analysis was performed by SPSS (Statistical Package for Social Sciences) software 17 trail version. $p$ value <0.05 was considered as statistically significant.

**RESULTS**

The mean levels of BMI, NC, WC, diastolic blood pressure (DBP), systolic blood pressure (SBP), fasting blood glucose (FBS), Cholesterol, Triglycerides (TGL), Glycated hemoglobin HbA1C, high sensitive C reactive protein (hsCRP) and homocysteine (Hcy) were higher but high density lipoprotein (HDL-C) levels were lower in T2DM patients than healthy controls ($p<0.05$). Table 2 shows the correlation between NC and various clinical parameters. There was significant positive correlation was found between NC and BMI, DBP, WC, TGL and Hcy ($p<0.05$).

**DISCUSSION**

In the current study an attempt was made to investigate the relation between NC and various parameters for cardiovascular disease risk. This study had shown significant positive relation between NC and WC. This result were consistent with a study conducted with a total of 3307 adults aged 20-65 years from two communities of Tongzhou, Beijing$^{21}$ and a cross-sectional study was conducted with 350 T2DM and 350 non-diabetics of >30 years of age$^{22}$. This study had shown a significant positive relation between NC and BMI. This result were consistent with longitudinal cohort study with 364 subjects who were not on major medical conditions and not receiving any medication$^{23}$ and a study with total of 3,182 diabetic subjects with 20–80 years of age were from 15 different community health centers in Beijing$^{9}$. There was a significant positive relation between NC and DBP in the present study and the similar results were also reported in a community-based cross-sectional study of descriptive design where 500 students from urban and rural areas of northern Tamilnadu$^{23}$ and in meta-analysis, that examined the association of NC with risk of MS, or at minimum, one of its components as outcomes$^{24}$. Significant positive relation was found between NC and TGL and this result was consistent with cross-sectional study in 1053 Brazilian

<table>
<thead>
<tr>
<th>TABLE 1. Clinical characteristics of all the study population</th>
<th>T2DM</th>
<th>Healthy control</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
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<tr>
<td>BMI (kg/m$^2$)</td>
<td>26.4 ±4.8</td>
<td>24.6 ±3.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>128.4 ±14.1</td>
<td>115.6 ±7.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>82.8 ±9.0</td>
<td>76.2 ±5.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NC (cm)</td>
<td>38.1 ±3.7</td>
<td>36.7 ±2.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>98.2 ±13.3</td>
<td>89.5 ±9.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>188.0 ±55.0</td>
<td>85.7 ±8.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>196.9 ±41.8</td>
<td>179.8 ±27.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TGL (mg/dl)</td>
<td>210.5 ±112.7</td>
<td>140.1 ±37.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>45.4 ±5.2</td>
<td>46.8 ±6.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>8.71 ±1.4</td>
<td>5.16 ±0.34</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>1.1 ±0.7</td>
<td>0.48 ±0.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hcy (µmol/L)</td>
<td>14.12 ±7.1</td>
<td>9.71 ±2.5</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data are shown as mean ±SD, maximum and minimum levels.

$p$ value was calculated by student, t-test

$p<0.05$ was consider as statistically significant

<table>
<thead>
<tr>
<th>TABLE 2. Simple correlation of NC with various parameters</th>
<th>r</th>
<th>$p$</th>
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</thead>
<tbody>
<tr>
<td>WC (cm)</td>
<td>0.608</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>0.553</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>0.201</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TGL (mg/dl)</td>
<td>0.239</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hcy (µmol/L)</td>
<td>0.405</td>
<td>&lt;0.05</td>
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</tbody>
</table>

$p<0.05$ was consider as statistically significant
adults (18-60 years) with BMI 18.5-40.0 kg/m², with normal glucose tolerance or T2DM² and a study from Calcutta from India with total of 451 individuals, 30–80 years age, without any co-morbid state who gave informed written consent underwent clinical, anthropometric, and biochemical assessment. To the best of my knowledge this is the first study investigated the relationship between NC and Hcy in T2DM patients of Andhra Pradesh, India and shown positive significant correlation. As Hcy is one of the marker for inflammation status and there is role development of CVD. Brazilian population-based study showed that NC was correlated with fasting glucose levels, high TGL, and low high-density lipoprotein (HDL)-cholesterol levels, and insulin resistance index. NC was associated with metabolic syndrome more strongly than WC in Turkish population. Framingham Heart Study offspring participants shown NC was related with increased carotid intima-media thickness (IMT) but neither BMI / WC was associated. Several mechanisms reported that underlying the relation between large NC and impaired glucose metabolism. Higher NC levels alter peripheral blood flow and results to endothelial function which may decrease insulin delivery and promote insulin resistance in the whole body.

In the Heinz Nixdorf Recall Study, epicardial fat associated with nonfatty and fatal coronary events, as well as CVD risk factors and occurrence of myocardial infarction in the general population. Not only accumulation of fat in visceral region but also in other regions like pericardial, liver, muscle, even perirenal and perivascular areas was associated with heart function and CVD. Free fatty acid secreted from upper-body subcutaneous fat was reported to be more than that from subcutaneous fat in lowerbody. Framingham Heart Study reported that NC is associated with CVD risk factors even after adjustment for BMI and visceral adipose tissue, and considered NC to be a measure of cardiac metabolic risk. In the Beijing Community Diabetes Study, NC was positively correlated with the MS in T2DM Chinese population. In other study NC was significantly correlated with all outcomes of cardiometabolic risk in males and females. Cardio metabolic Risk study with healthy adults, significant associations were observed between high NC and elevated risk of IR and several CVD risk factors in Chinese individuals. Dia et al. reported that a higher NC indicated a higher incidence of future fatal and non-fatal CVD events and all-cause mortality in both male and female high-risk participants. CVD risk factors increased more in the higher NC group. NC as a novel indicator of CVD showed good predictive ability for CVD events and mortality in a high-risk population.

CONCLUSION
Raised Neck circumference shown relationship with CVD risk factors such as high levels of BMI, TGL, and also with elevated levels of inflammatory marker such as homocysteine. So, neck circumference measurement may be considered as a marker to assess CVD risk in T2DM.

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REFERENCES
Neck circumference measurement to assess cardiovascular disease in type 2 Diabetes mellitus


