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Original Article

Biochemistry Section

Role of Anthropometric Measurements in Development of CVD and Stroke among T2DM in East Godavari District, Andhra Pradesh, India

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ABSTRACT

Introduction: Cardiovascular morbidity and mortality have been associated with different variables of anthropometric measurements.

Aim: To find out the association of anthropometric measurements in the development of Cardiovascular Disease (CVD) and stroke among Type 2 Diabetes Mellitus (T2DM).

Materials and Methods: Three hundred subjects were included in the study out of which 100 subjects were known Type 2 diabetics with CVD or Stroke (Group 1), 100 subjects were Type 2 diabetic patients (Group 2) and 100 subjects were normal and healthy (Group 3). Blood Pressure (BP), Body Mass Index (BMI) Neck Circumference (NC), Waist Circumference (WC), Hip Circumference (HC), Glycated haemoglobin (HbA1c), high sensitive- C-Reactive Protein (hsCRP), Malondialdehyde (MDA), Homocysteine (Hcy), microalbuminuria and estimated Glomerular Filtration Rate (eGFR) were compared between all three groups by using one-way ANOVA test, comparison between males and females by t-test and association was done by using Chi-square test.

Results: There were a significant difference in the means of anthropometric and biochemical parameters of the three groups ($p<0.05$). Diastolic BP, NC, WC, HC and homocysteine, are higher in T2DM obese patients than T2DM over weight and normal weight patients are statistically significant ($p<0.05$). The mean of levels systolic BP, Diastolic BP, hsCRP are higher in T2DM over weight patients than T2DM obese and normal weight patients are statistically significant ($p<0.05$). Association of physical activity, snoring and interrupted sleep with BMI was statistical significant ($p<0.05$).

Conclusion: Obesity and overweight in T2DM patients play important role in elevation of blood pressure and inflammation markers like hsCRP, homocysteine. Snoring and interrupted sleep also involved development of CVD and Stroke among T2 diabetes.

Keywords: Body mass index, Diabetic complications, Obesity

INTRODUCTION

Diabetes Mellitus (DM) is the most complex metabolic disorder among the world's population currently affecting around 171 million people globally in 2000 [1]. In 2013, 382 million people had diabetes; this number is expected to increase to 592 million by 2035 [2]. Obesity has been related with a dyslipidemia hypertension, intolerance of glucose, and even CVD. Most extensively used method to measure visceral fat accumulation is waist circumference measurement and it is considered as influential risk factor for CVD [3]. According to guidelines, cut-offs for waist circumference will now be 90 cm for Indian men and 80 cm for Indian women as per the consensus, the currently recommended cut-offs for BMI include 18-22.9 kg/m^2 for normal, 23.0-24.9 kg/m^2 for overweight and >25 kg/m^2 for obesity [4]. The aim of the study was designed to assess the incidence of overweight and obesity in T2DM of subjects in East Godavari, Andhrapradesh, India, and to assess the association of anthropometric measurements with cardiovascular and stroke markers.

MATERIALS AND METHODS

A cross-sectional study was conducted in GSL General Hospital and Medical College, Rajahmundry and Adikavi Nannaya University, Rajahmundry, Andhra Pradesh, India, within a duration of January 2015 to June 2016. Institutional Ethical Clearance was obtained. Assuming expected proportion in control as 20%, assumed odd ratio as 3, confidence level as 0.95, power as 0.8. Sample size per group calculated was 60. So for three groups minimum sample size calculated was 180. In this cross-sectional study, 300 subjects of both males and females were recruited. All the participants have voluntarily participated; written informed consent was taken from all the participants. Out of 300 subjects 100 subjects were known type 2 diabetics with CVD or Stroke (Group 1). Hundred subjects were type 2 diabetic patients (Group 2) and 100 subjects were normal and healthy considered as control group (Group 3). The participants were selected from general medicine and inpatients form cardiology and neurology departments of GSL Medical and General Hospital of East Godavari district, Andhra Pradesh. For Group 1 inclusion criteria was patients with type 2 diabetes aged above 30 years of both sexes and having any one of following conditions: 1) history of stroke; 2) A 12 lead Electrocardiography (ECG) with the positive result; 3) A history of hospital admission for either fatal or non fatal Myocardial Infarction (MI) or an episode of angina; 4) A history of coronary artery bypass grafting or percutaneous transluminal coronary angioplasty. For Group 2, inclusion criteria was, patient of both the gender (males and females) with known T2DM of aged 30-60 years. Exclusion criteria was patient with pulmonary, thyroid, liver disorders, CVD, history of stroke and with other complaints. For Group 3, normal and healthy individuals of both males and females with the age of 30-60 years were included in the study. Participants were interviewed to obtain relevant data like height, weight, age, sex, BP, duration of diabetes, Neck Circumference (NC) was measured by a measuring tape underneath the larynx and extend the tape around the neck by keeping shoulders at rest state. Waist Circumference (WC) and Hip Circumference (HC) were noted. HC and WC were measured by flexible measuring tape, maximum circumference in the area of hip region and mid-way between xiphoid

and umbilical during the midinspiratory phase. BP was noted for only one time, after keeping participant in resting position for 15 minutes. Approximately 10 ml of fasting blood was collected from the subjects. Approximately 5 ml of the blood sample was collected in container without any anticoagulant, and centrifuged after 30 minutes to collected the serum, it was used for estimation of hsCRP by particle enhanced immune turbidimetric assay [5], homocysteine by enzymatic colorimetric method [6], MDA by thiobarbituric acid method [7]. Approximately 2 ml of blood in EDTA container and immediately used for the HbA1c estimation by Latex enhanced immunoturbidimetry [8] and blood glucose estimation by glucose oxidase/glucose peroxidase method [9]. Spot urine was collected to measure microalbuminuria by immunoturbidimetry assay method [10] and eGFR was calculated by MDRD equation [11] and BMI was calculated by body weight in kg/height in m^2.

STATISTICAL ANALYSIS

All the data were analysed by using SPSS software (trail version) and comparison between all three groups was made by using one-way ANOVA test, comparison between males and females by t-test and association was done by using Chi-square test. The level of significance used for all the above analyses was two tailed, $p<0.05$ considered statistically significant and p-value<0.001 was considered statistically highly significant.

RESULTS

There were 300 individuals recruited in the study. In Group 1, 100 individuals were T2DM with CVD or stroke with the mean age of 48±6.7 years ranging from 34 years to 60 years. In Group 2, there were 100 individuals with known T2DM with the mean age of 47±7.8 years ranging from 30 years to 60 years. In Group 3, there were 100 healthy individuals with mean age of 44.4±6.9 years ranging from 31 to 60 years. The clinical characters of all the three groups were listed and compared in [Table/Fig-1].

All three study groups were compared, there was a statistically significant difference was noticed in mean values of age, BMI, systolic blood pressure, diastolic blood pressure, neck circumference, waist circumference, hip circumference, FBS, HbA1c, hsCRP, homocysteine, MDA and eGFR ($p<0.05$) [Table/Fig-1].

Anthropometric and Biochemical Parameters	T2DM with CVD or Stoke n=100	T2DM n=100	Healthy controls n=100	p-value
Age (years)	48.09 ±6.7	47±7.8	44.48±6.9	<0.05
BMI (kg/m^2)	25.1±3.4	26.4±4.8	24.6±3.7	<0.05
Systolic BP (mm/Hg)	135.4±10.8	128.4±14.1	115.6±7.2	<0.001
Diastolic BP (mm/Hg)	85.9±7.3	82.8±9.0	76.2±5.6	<0.001
Neck circumference (cm)	36.4±.3.8	38.1±3.7	36.7±2.9	<0.05
Waist circumference (cm)	93.3±8.0	98.2±13.3	89.5±9.3	<0.001
Hip circumference (cm)	100.7±8.2	104.5±12.4	100.7±9.1	<0.05
FBS (mg/dL)	189.4±64.2	188.0±55.0	85.7±8.2	<0.001
HbA1c (%)	9.96±2.1	8.71±1.4	5.16±0.34	<0.001
hsCRP (mg/l)	1.98±2.04	1.1±0.7	0.48±0.3	<0.001
Homocysteine (µmol/l)	14.69±6.3	14.12±7.1	9.71±2.5	<0.001
MDA (µmol/l)	8.1±1.3	7.2±1.9	5.3±1.1	<0.001
Microalbuminuria (mg/g of Creatinine)	41.98±30.34	60.73±69.7	11.9±5.1	<0.001
eGFR (ml/min per 1.73 m^2)	75.32±20.8	85.45±15.1	99.2±18.9	<0.001

[Table/Fig-1]: Morphometric measurements, clinical characteristics and biochemical measurements in type 2 diabetes patients with CVD, type 2 diabetes patients and healthy controls.
One-way ANOVA test applied
BMI- Body Mass Index, BP – Blood Pressure, FBS – Fasting Blood Sugar, HbA1c - Glycated Haemoglobin, hsCRP- High Sensitive Creactive Protein, MDA- Malondialdehyde, eGFR – Glomerular Filtration Rate

Characteristics	Males n=53	Females n=47	p-value
Age (years)	48.5±6.9	45.5±8.4	<0.05
BMI (kg/m^2)	25.7±3.9	27.1±5.6	>0.05
Systolic BP (mm/Hg)	126.8±12.8	130.2±15.3	>0.05
Diastolic BP (mm/Hg)	84.4±8.9	82.2±8.0	>0.05
Neck circumference (cm)	39.8±3.2	36.0±3.2	<0.001
Waist circumference (cm)	98.6±11.7	97.7±15.0	>0.05
Hip circumference (cm)	99.9±6.1	109.7±15.4	<0.001
FBS (mg/dL)	185.5±55.1	190.9±55.7	>0.05
HbA1c (%)	8.4±1.2	9.0±1.5	<0.05
hsCRP (mg/l)	1.10±0.8	1.10±0.8	>0.05
Homocysteine (µmol/l)	16.9±7.7	11.3±4.6	<0.001
MDA (µmol/l)	7.5±1.8	6.9±1.9	>0.05
Microalbuminuria (mg/g of Creatinine)	71.9±87.0	48.0±40	>0.05
eGFR (ml/min per 1.73 m^2)	86.0±16.5	84.4±13.4	>0.05

[Table/Fig-2]: Morphometric measurements, clinical characteristics and biochemical measurements in type 2 diabetic male and female patients.
BMI - Body Mass Index, BP – Blood Pressure, FBS – Fasting blood sugar, HbA1c - Glycated Haemoglobin, hsCRP - High Sensitive Creactive Protein, MDA - Malondialdehyde, eGFR – Glomerular Filtration Rate

T2DM male patients have significantly higher mean levels of age, neck circumference, and homocysteine in comparison to T2DM female patients ($p<0.05$). T2DM female patients have significantly higher mean levels of hip circumference, HbA1c in comparison to T2DM male patients ($p<0.05$) [Table/Fig-2].

In this current study, 22 were in the normal weight category, 19 were in over weight category, and 59 were in obese category. There was a statistically significant difference in mean levels of systolic BP, diastolic BP, NC, WC, HC, FBS, hsCRP and homocysteine, when study Group 2 (T2DM) were stratified according to BMI ($p<0.05$). The mean levels of age, eGFR, HbA1c, MDA and microalbuminuria were statistically insignificant, when study Group 2 were stratified according to BMI ($p>0.05$) [Table/Fig-3].

In current study association of physical activity, snoring and sleep disturbances with BMI was statistically significant ($p<0.05$). Association of smoking, alcohol consumption, family history of diabetes, family history of stroke, family history of CVD, hypertension with BMI was statistical insignificant ($p>0.05$). All the risk factors were analysed in only Group 2 because T2DM have two to three folds of risk toward CVD than non-diabetes [Table/Fig-4].

DISCUSSION

The present study was conducted to assess the levels of various biomarkers in T2DM patients compared with T2DM with CVD or stroke patients and healthy individuals controls and their role in primary prevention of CVD and stroke.

BMI was the established measurement index in assessing obesity which is a major risk factor for CVD [12]. The present study showed significant difference in means of BMI of T2DM subjects who has higher levels than patient with T2DM with CVD or stroke and healthy controls. The different findings were observed when compared with study done by Tan MC et al., [13]. Female patients with T2DM having high BMI when compared with male patients with T2DM, these findings were comparatively less when compare with the other studies [14,15]. In this current study 59% of T2DM (Group 2) are obese (≤25 kg/m^2), 19% of T2DM are overweight (23-24.9 kg/m^2) similar finding were observed in a study done by Daousi C et al., [16]. Hypertension was present in about half of all overweight

Characteristics	Normal weight (n=22)	Overweight (n=19)	Obese (n=59)	p-value
Age (years)	45.9±9.3	46.6±7.1	47.5±7.5	>0.05
Systolic BP (mm/Hg)	124.9±8.8	136.2±19.9	127.2±12.7	<0.05
Diastolic BP (mm/Hg)	80±5.4	87.6±12.2	83.0±7.6	<0.05
Neck circumference (cm)	34.9±3.6	38.9±3.2	39±3.2	<0.001
Waist circumference (cm)	84±8.2	96.5±13.3	104±10.6	<0.001
Hip circumference (cm)	101.5±18.3	99.4±5.3	107.3±10.7	<0.05
FBS (mg/dL)	215.1±62.7	169.6±46.3	183.9±51.6	<0.05
HbA1c (%)	8.7±1.4	8.4±1.5	8.7±1.3	>0.05
hsCRP (mg/l)	0.80±0.14	1.42±1.22	1.1±0.75	<0.05
Homocysteine (µmol/l)	10.7±3.6	14.8±5.7	15.4±7.9	<0.05
MDA (µmol/l)	7.3±1.2	7.1±2.0	7.2±1.8	>0.05
Microalbuminuria (mg/g of Creatinine)	87.6±102.8	47.4±35.3	59.9±61	>0.05
eGFR (ml/min per 1.73 m^2)	86.1±14.7	85.3±16.3	85.2±15.1	>0.05

[Table/Fig-3]: Mean values of morphometric measurements and CVD risk factors in type 2 diabetes patients when stratified according to Body Mass Index (BMI).
One-way ANOVA test applied

Character-istics	Status	Normal weight (n=22)	Over-weight (n=19)	Obese (n=59)	p-value
Smoking	No(86)	20(23.2%)	14(16.3%)	52(60.5%)	>0.05
	Yes(14)	2(14.3%)	5(35.7%)	7(50.5%)	
Alcohol consumption	No(80)	18(22.5%)	13(16.3%)	49(61.3%)	>0.05
	Yes(20)	4 (20%)	6(30%)	10(50%)	
Physical activity	No(79)	21(26.6%)	12(15.2%)	46(58.2%)	<0.05
	Yes(21)	1(4.8%)	7(33.3%)	13(61.9%)	
Sleep	Interrupted (41)	6(14.6%)	4(9.8%)	31(75.6%)	<0.05
	Uninterrupted (59)	16(27.1%)	15(25.4%)	28(47.5%)	
Family history of diabetes	No(47)	9(19.1%)	12(25.3%)	26(55.3%)	>0.05
	Yes(53)	13(22.9%)	7(13.2%)	33(62.3%)	
Family history of stroke	No(83)	19(22.9%)	16(19.3%)	48(57.8%)	>0.05
	Yes(17)	3(17.6%)	3(17.6%)	11(64.7%)	
Family history of CVD	No(87)	18(20.7%)	14(16.1%)	55(63.2%)	>0.05
	Yes(13)	4(30.8%)	5(38.5%)	4(30.8%)	
Hypertension	No(67)	17(25.4%)	12(17.9%)	38(56.7%)	>0.05
	Yes(33)	5(15.2%)	7(21.2%)	21(63.6%)	
Snoring	No(62)	20(32.3%)	13(21%)	29(46.8%)	<0.05
	Yes(38)	2(5.3%)	6(15.8%)	30(78.9%)	

[Table/Fig-4]: Association of demographic characteristics of type 2 diabetes patients when stratified according to BMI.
Chi-square test applied

individuals [17] and obesity alone accounts for about 70% of essential hypertension [18]. In worldwide 21% of ischemic heart diseases were attributed to BMI above 21 kg/m^2 [19]

In this present study, there was a significant relation was observed between systolic BP and diastolic BP. Blood pressures were higher in obese and overweight T2DM patients.

In the present study, systolic BP was more in females and diastolic BP was more in males in T2DM patients. These findings are similar to the study done by Tesfaye F et al., where it stated Indonesia women having high systolic BP and Vietnamese men having low diastolic BP [19]. Similarly, the mean BP levels increased with increased BMI. Mungreiphy NK et al., founded that mean SBP and DBP increased with increasing BMI from lowest to highest BMI [20]. Positive relationships between BMI and BP also reported in the other populations [21]. Hypertension in overweight is associated with increase sympathetic activity [22] and sympathetic blocker has a large effect in obesity [23].

In this current study, BMI had a significant relationship with NC, WC and HC in T2DM in normal weight, over weight and obese patients. The mean levels of NC, WC and HC were higher in obese T2DM patients than over weight and normal weight T2DM patients. It was consider that NC is a better parameter for prediction of cardiovascular risk compared to fat which was stored in visceral region [24], but when body fat is located in the upper part of the body, the negative consequence in both metabolic and cardiovascular, seems to be more significant. It was proposed that NC may provide better contribution in determining future risk of CVD and stroke [25]. Yang GR et al., found no association between NC and central obesity, over weight and metabolic syndrome in Chinese T2DM patients [26].

In this study WC was higher in obese patients with T2DM when compared to overweight and normal weight patients with T2DM. Male patients with T2DM were having higher WC than female patients with T2DM and patients with T2DM having higher WC compared to patients with T2DM and CVD and healthy controls. Slightly less WC mean levels of T2DM patients were noted when compared with another study [3].

In this present study, WC of patients with T2DM and T2DM with CVD patients was>90 cm. WC of males had higher mean levels than females in T2DM patients and it was also similar to other studies [27]. Many epidemiological studies have shown increase fat accumulation to be an independent risk factor for future CAD, stroke in T2DM and in general population [3].

WC is highly associated with visceral adiposity. Visceral fat is the casual factor and a simple marker of cardio metabolite. From adipocytes, there is a secretion of anti-atherosclerotic, anti-inflammatory substance called adiponectin. Its secretion is lowered with an elevation of visceral fat resulting in increased in the prevalence of CVD. Higher the frequency of fat in the body at visceral region, more amount of inflammatory substances are secreted. This adversely affects the blood vessels and insulin action and increased the CVD risk [28].

The mean levels of HC were higher in obese T2DM patients than overweight and normal weight patients with T2DM. In this study HC was more in patients with T2DM compared with patients with T2DM with CVD and healthy controls. It was noticed that obese individuals were also in healthy controls (data not given). T2DM female patients are having high HC levels than male T2DM patients. Similar findings are noted in the study done by Snijder MB et al., [27].

In this present study, hsCRP a proinflammatory prototypic cardiac risk marker in overweight and obese subjects in T2DM. Serum hsCRP levels were raised significantly in overweight and obese patients with T2DM. This hsCRP had the strong relationship with BMI [29] and obesity [30]. In this present study, subjects with abnormal hsCRP had high proportion of hypertension, obesity and hypercholesterolemia which shows similar results by the study done by Amanullah S et al., [31].

In this present study there was a significant difference in the level of serum Hcy among the normal weight T2DM patients, overweight T2DM patients and obese T2DM patients. Obese T2DM patients have elevated homocysteine levels when compare with overweight T2DM patients and normal weight T2DM patients. Similar finding was observed in the study done by [32]. Study shows obesity had been a causative factor for hypertension, dyslipidemia [33] and there was a significant relationship between Hcy and BMI and insulin resistance [34].

In this study, there was a significant association between BMI and physical activity in the patients with T2DM. There was the slight difference in the percentage of individuals having physical activity

and not having physical activity. A study done by Tan MC et al., [13] concluded that low and moderate physical activity levels and working status to be a significant predictive factor of CVD among T2DM.

When compared with inactive patients, T2DM patients who walked minimum 120 minutes per week had lesser frequency of mortality with CVD. It was estimated that one death per year can be prevented for every 61 individuals with diabetes who were ready to walk at least two hours per week [35].

Exercise improves insulin sensitivity in both in non diabetic and diabetic individuals [36]. Patients with diabetes have greater insulin resistance which can be mediated by other defects in the metabolism of glucose and some may be improved by physical exercise. Raised physical activity achieves higher mitochondrial enzyme activity and increases insulin sensitivity; however the number of capillaries of muscle in diabetic patients with complications of microvascular does not increase or is practically insignificant [37].

Obstructive Sleep Apnea (OSA) is characterized by repeated episodes of upper airway collapse, leading to apnoeas or hypopnoeas associated with either an oxyhaemoglobin desaturation or an arousal detected by electro encephalography [38]. There was a causal pathway for linking OSA with T2DM. The evidence that the physiologic stress imposed by intermittent hypoxia [39] may be involved in the pathogenesis of insulin resistance. A study by Shahar E et al., OSA was associated with a range of manifestations of CVD (stroke, heart failure, ischemic heart disease) [40]. Other study showed that OSA is associated with MI and in those with known coronary disease; patients with OSA have an increased risk of cardiovascular events and death [41].

LIMITATION

First it was a cross-sectional study. Second, several factors may influence BMI and other anthropometric levels which may play a role in controlling diabetes, which may help in primary prevention of CVD or stroke. Factors like education, hours of physical activity, diet maintenance (people of East Godavari mainly depend on polished rice as their food) which was not taken into consideration.

CONCLUSION

To the best of our knowledge, this is the first study that reports the BMI, neck circumference, waist circumference, and hip circumference as a predictive risk factor for future CVD and stroke in T2DM in an East Godavari population of Andhra Pradesh. Neck circumference is a novel, easily measured fat depot, which may be an important predictor of DM. WC, is highly associated with visceral adiposity. Visceral fat is the casual factor and simple marker of cardio metabolite this study provides a new insight into the underlying metabolic pathway between large anthropometric measurements and DM. Future prospective studies are needed to better understand the extent to which a reduction of BMI and anthropometric measurements may have in decreasing CVD and stroke in T2DM.

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