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ASSOCIATION OF NECK CIRCUMFERENCE WITH LIPID PROFILE IN POSTMENOPAUSAL WOMEN ATTENDING TERTIARY CARE HOSPITAL.

Physiology

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ABSTRACT

Introduction: Metabolic syndrome is believed to increase the risk of cardiovascular disease and postmenopausal women are more prone to develop cardiometabolic risk, most probably due to change in body fat distribution due to deficiency of estrogen. Evidence regarding the clinical significance of neck circumference in cardio-metabolic syndrome is limited. Also there is inconsistency in the results of studies regarding the relationship between neck circumference and lipid profile. Therefore, present study was conducted with an objective to examine association between neck circumference and lipid profile to find the independent contribution of neck circumference to cardiometabolic risk. **Materials and Methods:** This was a hospital based cross-sectional, observational study. A total of 129 postmenopausal women, age > 45 years were selected consecutively after applying the inclusion and exclusion criteria. Anthropometric and biochemical parameters taken in our study were height, weight, BMI, neck circumference, waist circumference, fasting blood glucose, lipid profile. Neck circumference >=34cm was considered as abnormal. Metabolic syndrome was defined based on (AHA/NHLBI+IDF) 2009 criteria. **Result:** Mean neck circumference was found to be 32.52 ± 2.67cm. 40% of total subjects had neck circumference >=34cms. NC was found to be significantly associated with components of metabolic syndrome ($p<0.001$). NC was also found to be significantly associated with cardiometabolic risk factors like low density lipoprotein cholesterol (LDL), triglycerides (TG), total cholesterol (TC) (all p- value < 0.001). NC showed significant but negative correlation with high density lipoprotein cholesterol (HDL) ($p<0.001$). **Conclusion:** NC showed significant correlation with lipid profile (TC, TG, LDL, HDL). NC can serve as clinical marker to easily identify individuals, with a higher risk of developing cardiometabolic disorders, such as in postmenopausal women.

KEYWORDS

Lipid profile, Metabolic syndrome, Cardiovascular disease(CVD), Waist circumference

INTRODUCTION

The metabolic syndrome (MetS)—also called syndrome X, Reaven syndrome, "the deadly quartet," and insulin resistance syndrome—was originally described in 1988 [1] and refers to the commonly occurring disorder comprising central obesity, systemic hypertension, insulin resistance, and atherogenic dyslipidemia (specifically hypertriglyceridemia and reduced levels of high-density lipoprotein cholesterol).

Postmenopausal status is associated with a 60% increased risk of the metabolic syndrome, even after adjusting for confounding variables, such as age, body mass index (BMI), household income, and physical inactivity.[2]

A large variation has been found in the global prevalence of metabolic syndrome ranging from 7.1% to 41.6% across studies.[3,4] The prevalence of metabolic syndrome is quite high worldwide - 35% in USA,[5] 24.9% in Latin America[6] and 20.7%–37.2% in the gulf countries**[7]** as per ATP III criteria. Available data indicate that the prevalence of metabolic syndrome in India varies according to socioeconomic and cultural factors, lifestyle pattern, extend of urbanization [8]. It has been reported in one of the study in india that prevalence varies upto 24.9% in northern India and 41% in Southern India using different definitions.[9]

Women are at a higher risk of developing CVDs after menopause due to estrogen deficiency and dysregulated lipid metabolism [10]. Estrogen, especially E2, exert a protective role in the cardiovascular system and are produced primarily in the ovaries via a process that uses low-density lipoprotein (LDL) cholesterol (LDL-C) as a substrate. However, circulatory LDL-C cannot be utilized to synthesize estrogen during menopause, thereby resulting in decreased estrogen production. Therefore, menopause is associated with increased blood LDL-C levels and enhanced CVD risk [11].

The aetiology of the metabolic syndrome in postmenopausal females is not clearly known but may be because of increased abdominal obesity as a result of decrease in estrogen production. During menopause, reduction in estrogen level causes decrease basal metabolism and this causes weight gain. Another factor responsible for the control of body weight are the estrogen receptors. These estrogen receptors, activated by estradiol, has inhibiting effect on the development of adipose tissue; therefore, there is an increase in adipose tissue during the menopause as a result of the deficiency of estrogen.[12]

Measurement of neck circumference (NC) has been identified as a reliable tool and has been used as an index for upper body obesity. It is easy to measure, reproducible and not affected by phases of respiration or stomach fullness. It can be taken without removal of clothing and is therefore convenient for both the examiner and the subject. [13-15]

There are not sufficient evidences regarding the clinical significance of neck circumference in cardio-metabolic syndrome. Also there is inconsistency in the results of studies regarding the relationship between neck circumference and lipid profile. Furthermore the studies conducted in postmenopausal women in this regard, especially in india, are very less. Therefore, present study was conducted with an objective to examine association between neck circumference and lipid profile in postmenopausal women to find the independent contribution of neck circumference to cardiometabolic risk.

AIMS AND OBJECTIVES:

AIMS:

To examine the independent contribution of neck circumference to cardiometabolic risk in postmenopausal women.

OBJECTIVES:

Primary objective:

To investigate whether there is any association of neck circumference with various components of lipid profile like TC, TG, LDL, HDL.

Secondary objective:

To evaluate individual components of metabolic syndrome in postmenopausal women and their relation with neck circumference.

MATERIALS AND METHODS

This study was a hospital based cross-sectional observational study, conducted over a period of one year (June 2021- May 2022). Purposive sampling was used. A total of 129 postmenopausal women, attending obstetrics and gynaecology OPD were selected for this study after taking their consent and after applying inclusion and exclusion criteria. Detailed medical history, general and physical examination was done in study subjects. Anthropometric and biochemical parameters were measured as per standard methods.

Ethical consideration:
Study was approved by the local medical ethics committee of CNMC&H Kolkata.

Study tools:
Patient information sheet, Informed consent form, case record sheet, Weighing machine, Measuring tape, Aneroid manometer, Syringe and vials.

Inclusion and exclusion criteria:

Inclusion criteria	Exclusion criteria
• Women age >45 years who have attained menopause • Women who want to participate willingly.	• Women who are not willing to participate • Severely ill • Mentally challenged • who have undergone hysterectomy • Women on - antihypertensive drugs --antilipid drugs --anti diabetic drugs • Women on estrogen replacement therapy • History of neck surgery, malignancy or thyroid dysfunction

Anthropometric measurements:
Digital scale weighing machine corrected to 0.5 Kg was used to measure body weight of subjects with light clothing on and without shoes. Machine was checked for zero error prior to each measurement. Height was measured with the commercial fixed stadiometer corrected to 0.5cm with the subject standing with arms at the sides with head held erect and in a Frankfurt plane. BMI was calculated by dividing body weight in kilogram (kg) by height in meters squared. BMI = weight in Kg / (height in meters)^2 [16]. Waist circumference was measured in horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest, using a standard measuring tape at the end of gentle expiration. Normal value for Indian male is 85 cm and for Indian female 80 cms [Rosner PS et al]. Blood pressure was measured with mercury sphygmomanometer.

Neck circumference (NC): Participants were asked to stand erect with their head positioned at Frankfort horizontal plane. NC was measured by placing superior border of a tape measure just below the laryngeal prominence and perpendicular to the long axis of the neck [17]. Neck circumference >=34 cm was considered as abnormal and this cut off was taken from the study conducted by Nagendran Vijaya Kumar et al [18].

Metabolic syndrome was defined based on (AHA/NHLBI+IDF) 2009 criteria [19]. Any three of the following:
WC > 80cm
Fasting plasma glucose >= 100
BP >= 130/85
TG >= 150
HDL < 50
[AHA; American Heart Association; NHLBI, National Heart, Lung, and Blood Institute; IDF, International Diabetes Federation]

Biochemical parameters:
Venous blood samples were collected in the morning after an overnight fasting. The samples were centrifuged for 15 min at 2500 rpm, and aliquots of serum were kept at minus 20°C until assays for analysis.

Triglyceride level was measured using GPO-POD (glycerol phosphate dehydrogenase) method.[20, 21, 22]

High density lipoprotein cholesterol (HDL) was estimated by direct HDL method. [23, 24]

Total cholesterol (TC) was estimated by CHOD-POD (cholesterol oxidase/hydrogen peroxidise). [25, 26]

Fasting plasma glucose:
Trinder's method was used for glucose estimation where glucose was oxidised to gluconic acid and hydrogen peroxide by the enzyme glucose oxidase. The formed hydrogen peroxide was detected by a chromogenic oxygen acceptor, phenol, 4- aminophenazone (4-AP) in the presence of peroxidase (POD). The intensity of the colour formed was proportional to the glucose concentration in the sample. [27,28] All the above mentioned parameters were measured in an automated analyser using a Tersaco kit.

LDL was calculated by using the FRIEDWALD's equation.
Calculated LDL = TC – (TG/5 + HDL)
TC = Total cholesterol in mg/dl.
TG = Triglyceride in mg/dl.
HDL = High density lipoprotein.
This equation can be used as long as TG value is ≤ 400mg/dl. For TG value > 400mg/dl
direct LDL method is used. Friedwald's equation was used in this study as TG values of all our subjects were less than 400mg/dl.

Statistical analysis:
The statistical software SPSS version 22 has been used for the analysis. Continuous variables are expressed as Mean, Median and Standard Deviation. Association between continuous variables were captured using Spearman's Rank Correlation Coefficient. An alpha level of 5% has been taken, i.e, if any p value is less than 0.05 it has been considered as significant.

RESULTS
This study was conducted in total of 129 postmenopausal women. Majority of women were in age group of 56-60 years. Baseline characteristics of study subjects is given in table 1.

Mean neck circumference in study subjects was found to be 32.52 ± 2.67cm. Abnormal neck circumference (>=34cm) was found in 40% of total subjects. Based on (AHA/NHLBI+IDF) 2009 criteria, 51% of total subjects were found to have metabolic syndrome. Among the women with abnormal neck circumference, 98% had metabolic syndrome.

Reduced HDL cholesterol level was found to be the most common individual component of lipid profile found in 57% of total subjects followed by increased LDL cholesterol level found in 40% of total study subjects and increased triglyceride level found in 33% of total study subjects. 58% of total study subjects were found to be overweight.

Table/figure 1: Anthropometric and biochemical characteristics of study subjects:

	Mean	Median	Std. Deviation
Age in years	57.68	58.00	2.40
Weight	57.77	58.00	5.70
Height	146.92	147.32	3.20
BMI	26.76	26.50	2.44
Total cholesterol	201.63	199.00	17.65
LDL	131.15	127.00	16.82
HDL	46.53	48.00	5.66
Fasting glucose	107.40	102.00	14.86
Neck circumference	32.52	32.00	2.67

Table/figure 2: components of MetS among study subjects

Metabolic syndrome components	Number of subjects	Percentage
WC > 80cm	86	66.7%
Fasting plasma glucose >= 100	76	58.9%
BP >= 130/85	70	54.3%
TG >= 150	43	33.3%
HDL < 50	73	56.6%

Abnormal waist circumference (>80cm) was found to be the most common individual component of metabolic syndrome found in 67% of total subjects followed by Increased fasting blood sugar which was found in 59% of total subjects. [table 2]

Neck circumference was found to be significantly associated with individual components of metabolic syndrome [table/figure 3].

Neck circumference showed moderate positive correlation with triglyceride level ($p<0.001$, $r = 0.629$) [fig 4], moderate positive correlation with total cholesterol ($p<0.001$, $r = 0.469$) [fig5], strong positive correlation with LDL cholesterol ($p<0.001$, $r = 0.727$) [fig 6]. Strong negative correlation was found between neck circumference and HDL cholesterol ($p<0.001$, $r = -0.745$). [fig 7]

[Table/figure 3]. Correlation of NC with individual components of MetS:

		Neck circumference
Total cholesterol	Correlation Coefficient	0.469
	p Value	<0.001
Triglycerides	Correlation Coefficient	0.629
	p Value	<0.001
LDL	Correlation Coefficient	0.727
	p Value	<0.001
HDL	Correlation Coefficient	-0.745
	p Value	<0.001
Fasting glucose	Correlation Coefficient	0.721
	p Value	<0.001
SBP	Correlation Coefficient	0.799
	p Value	<0.001
DBP	Correlation Coefficient	0.756
	p Value	<0.001
Waist circumference	Correlation Coefficient	0.798
	p Value	<0.001

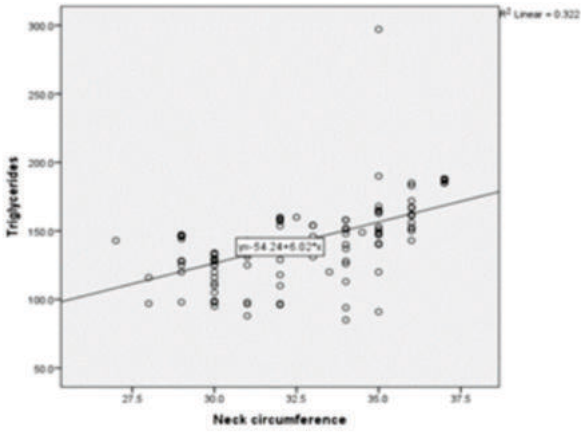

Figure 4: Correlation between NC and TG (p<0.001, r = 0.629)

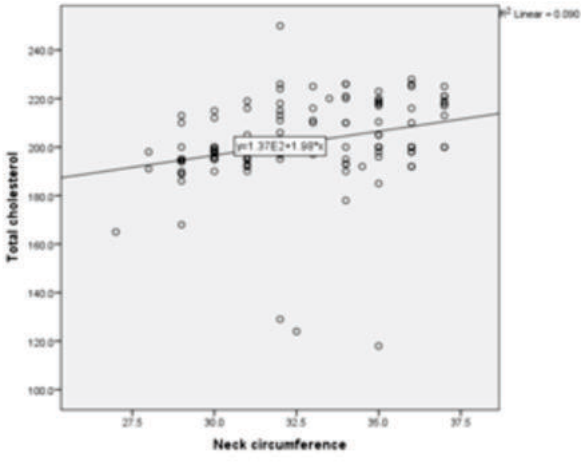

Figure 5: Correlation between NC and TC (p<0.001, r = 0.469)

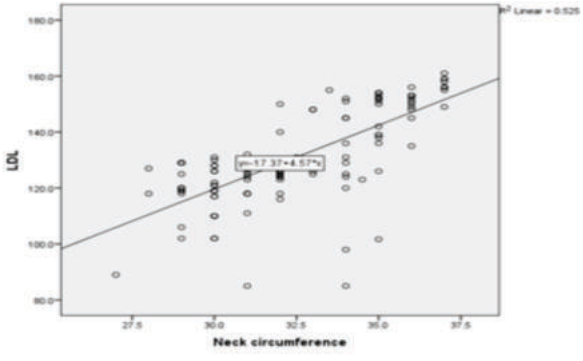

Figure 6: Correlation between NC and LDL cholesterol (p<0.001, r=0.727)

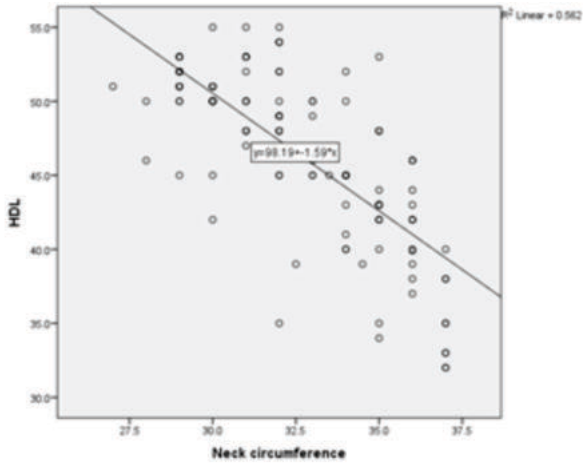

Figure 7: Correlation between NC and HDL cholesterol (p<0.001, r=-0.745)

DISCUSSION

Present study was undertaken to evaluate the relationship of NC with lipid profile in postmenopausal women and to find its independent contribution to cardiometabolic risk. In the present study, among the subjects with abnormal neck circumference, 98.08% had MetS. This clearly shows that upper body fat may have some contribution in pathogenesis of MetS. Nagendran Vijaya Kumar et al also found that among the women with abnormal NC, higher proportion of women (71.9%) had metabolic syndrome.

Data in the literature indicate that subcutaneous fat in the upper body, as well as visceral fat, is associated with cardiometabolic risks [Rosner PS et al]. This is possibly due to the fact that visceral fat is not the main source of concentrations of circulating free fatty acid (FFA). Systemic free fatty acid concentrations are known to be primarily determined by upper-body subcutaneous fat, suggesting that this fat depot may play an important role in risk factor pathogenesis. Since this upper-body subcutaneous fat can be easily assessed by NC, this measurement may be an important predictor of cardiometabolic risks.

The present data demonstrated that NC could be an indicator of cardiometabolic risk by showing its significant correlation with triglycerides, total cholesterol, LDL-C, HDL-C and also with metabolic syndrome and its individual components. These findings were in line with previous studies.[15,18,29,30]

In the Framingham Heart Study, 3307 participants (mean age 52 years) were followed for 10 years for the development of each component of MS. It was found that NC positively correlated with low HDL-c cholesterol and high triglyceride, TC, LDL-c along with other cardiometabolic risk factors Rosner PS et al. Study conducted by Nagendran Vijaya Kumar et al showed that all individual parameter of cardiometabolic risk factor including HDL & TG were found to be correlated with NC. Yan Q et al. in a cross-sectional study on 2,092 elderly Chinese subjects found NC to be highly correlated with anthropometric indices of obesity, such as BMI and WC as well as to MetS [29]. Zhou JY et al. examined a total of 4,201 male and female subjects between the ages of 20 to 85 years and found significant association of NC with cardiometabolic risk factors. In men NC was found to be positively correlated with TG, TC, and LDL-C and negatively correlated with HDL-C. [30]

However in the same study conducted by Zhou JY et al correlation between neck circumference and total cholesterol was not found to be significant in female subjects. Similarly, in a study conducted by Satomi AOI et al, [31] in japanese postmenopausal women, neck circumference contributed to both an increase in TG and a decrease in HDL-C. However total cholesterol and LDL cholesterol were not correlated to neck circumference. This inconsistency in results of lipid profile may be due to racial difference.

The precise biological mechanisms of neck adipose tissue on metabolic abnormality are not fully understood. Neck region has a unique anatomical characteristic and metabolic profile. A specificity of neck fat depot is the presence of brown adipose tissue. In adults, this adipose tissue is predominantly located in the neck and supraclavicular

regions and plays an important role in energy homeostasis. Although brown adiposities can uptake glucose and produce heat rather than store energy, the activity of brown adiposities is significantly lower in individuals with overweight or obesity [32]. In addition, the neck region includes two perivascular fat depots surrounding bilateral carotid vessels in a relatively small area. These fat depots are recognized as an ectopic fat, which can secrete various adipokines, leading to stimulation of metabolic abnormality [33, 34].

All of these novel findings apparently reflect that NC could be an indicator of cardio-metabolic risk factors and metabolic syndrome as a whole.

CONCLUSION

NC was found to be significantly correlated to lipid profile and individual components of cardiometabolic syndrome. NC measurement was found to be a simple, time saving, reproducible and least invasive measurement tool that can serve as clinical marker to easily identify individuals, with a higher risk of developing cardiometabolic disorders, such as postmenopausal women, for early diagnosis and timely management and prevention of cardiovascular complications which has become a major health burden in a developing countries like India.

Drawbacks:

All participants were from same health center and a selection bias could not be excluded. Sample size was small. So further studies which are multicentric and with more number of subjects and among different races are required to clarify whether NC is a suitable anthropometric index to predict cardio-metabolic disorders.

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