UNIVERSITY OF GONDAR
COLLEGE OF MEDICINE AND HEALTH SCIENCES
SCHOOL OF BIOMEDICAL AND LABORATORY SCIENCES
DEPARTMENT OF CLINICAL CHEMISTRY

WAIST CIRCUMFERENCE CUTOFF POINT DETERMINATION FOR DEFINING METABOLIC SYNDROME AMONG TYPE II DIABETIC MELLITUS PATIENTS AT AYDER COMPREHENSIVE SPECIALIZED HOSPITAL, MEKELLE UNIVERSITY, TIGRAY REGION, NORTHERN ETHIOPIA

By: Shewit Hailemariam
Advisors: Mr. Molla Abebe (Ass.prof)
Mr. Tadele Melak (MSc)

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Waist circumference cutoff point determination for defining metabolic syndrome among type II diabetic mellitus patients at Ayder Comprehensive Specialized Hospital, Mekelle University, Tigray Region, Northern Ethiopia

By: Shewit H/Mariam

Date: _____/_____/_____ Signature: _____

Approved by: _____Signature: _____

Advisors:

1. Mr. Molla Abebe (Ass.prof) Date: ___/___/____ Signature: _____
2. Mr. Tadele Melak (Msc) Date: ___/___/____ Signature: _____

Examiners

Internal Examiner: Habtamu wendifraw Signature _____

External Examiner :Zerihun Ataro Signature _____

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LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

AUC…….Area Under the Curve

BMI……..Body Mass Index

BP..... Blood Pressure

CT…….Computed Tomography

CV……Cardiovascular

CVD…….Cardiovascular Disease

EGIR……European Group for the study of Insulin Resistance

FBG……..Fasting Blood Glucose

HDL-c……..High Density Lipoprotien cholesterol

HOMA-IR……Homeostasis Model Assessment of Insulin Resistance

HT……Hypertensive

IDF……...International Diabetic Federation

IR……..Insulin Resistance

LDL-c……Low Density Lipoprotein cholesterol

MetS…….Metabolic syndrome

NCD……..Non Communicable Disease

NCEP/ATPIII…….....National Cholesterol Education Program Adult Treatment Panel III

NT……..Normotensive

ROC……...Receiver Operating Characteristics

SSA……Sub-Saharan Africa

SOP……Standard Operating Procedure

T2DM…….Type two Diabetic Mellitus

TG……..Triglyceride

VAT ……..Visceral Adipose Tissue

WC…….....Waist Circumference

WHO……..World Health Organization

TABLE OF CONTENT

Contents **Page**

ABSTRACT

Back ground: Metabolic syndrome (MetS) is a complex disorder which is characterized by clustering of interrelated risk factors of cardiovascular disease and diabetic mellitus. So far, cutoff point variability for one of the cluster to define MetS, which is waist circumference, based on ethnicity was documented.

Objective: To determine waist circumference cutoff point to define MetS among type II diabetic patients.

Methods: Institution based cross sectional study was conducted from March to April 2017 at Ayder Comprehensive Specialized Hospital among type II diabetic mellitus (T_2DM) patients. Systematic sampling technique was used to select study participants and 520 of them were assumed to be included in the study. Data were collected by checklist, anthropometric measurements and biochemical analyses. Fasting blood sample was collected for the biochemical evaluation. Data were entered to Epi-info 3.5.1 and transferred to SPSS 20 for analysis. Participants having more than one abnormal MetS components were categorized as cases. The classification power of waist circumference (WC) to distinguish cases from controls was determined by ROC curve analysis. WC cutoff point was determined by taking the point which was having maximum Youden Index.

Results: A total of 520 participants were included in the study, of whom 308(59.2%) were females. The mean age of the participants was 56 ± 10.8 years and 55 ± 11.4 years for males and females respectively. The classification power of WC was 0.67 (0.58-0.75) for male and 0.63 (0.52-0.73) for females. The optimal waist circumference cutoff point to predict the presence of at least two other components of the MetS was 95.5 cm (sensitivity 39.8%, specificity86.3%, *p* value < 0.001) for males and 87.5 cm (sensitivity73.1%, specificity54.5%, *p* value < 0.017) for females.

Conclusion: The power of WC value to classify cases from controls was poor and the cutoff points of WC were 87.5 cm and 95.5 cm for female and male respectively. WC cutoff points need to be reconsidered for these patients using a prospective cohort study. In addition, studies which can consider the confounders such as lipid lowering medications, age of the participants and duration of diabetes are advisable in order to increase the classification power of WC.

Keywords: *Diabetic mellitus; Metabolic syndrome; Waist circumference*

1. INTRODUCTION

1.1 Background

Metabolic syndrome (MetS) is a complex disorder which is characterized by clustering of a number of interrelated risk factors that increase the risk of cardiovascular disease (CVD), type II diabetic mellitus (T2DM) and other non communicable diseases. The probability of risk is increasing when they appear together (1) and even it increases the complication rate when it combines with DM (2) .

Historically, cluster of MetS were including insulin resistance, hypertension, triglyceridemias, reduced high density lipoprotien cholesterol (HDL-c), shifting of low density lipoprotien (LDL-c) to small dense particles, increased procoagulant state, increased vascular abnormalities, increased inflammatory markers, and hyperuricemia. However, today various international organizations have defined MetS using five components alone including elevation of waist circumference (WC), blood pressure (BP), triglycerides(TG), fasting blood glucose(FBG), and reduced HDL-c level (3).

Elevated WC is one of the components of MetS. It is accumulation of fat in the central region of the body. It is commonly associated with insulin resistance and it is evident that the abdominal fat accumulation plays a central role for pathogenesis of MetS (4).

The fundamental cause of obesity and overweight is an energy imbalance between calories consumed and calories expended (5). Factors that contribute to the preferential accumulation of fat in certain body regions as well to the development of insulin resistance involve modifiable (physical activity levels, nutritional surplus and hormonal status) and non-modifiable factors (age, gender, genetic predisposition and ethnic background)(6).

Compared to the subcutaneous fat, the visceral abdominal fat confers more risk of metabolic and cardiovascular complications. This may be explained by, visceral fat has a six times higher lipolytic activity which directly releases free fatty acids into the portal circulation, and this considerably contributes to insulin resistance (7).

To precisely assess the visceral fat volume, abdominal computed tomography (CT) has been considered as the most accurate and reproducible technique (8). However, CT scans are costly and time consuming, and exposes to ionizing radiation (9). Because of this limitation a variety of

alternative methods are being used to assess abdominal obesity. Waist to hip ratio, WC and body mass index (BMI) had good correlation with abdominal imaging. Among them, WC is considered to be simple and inexpensive measure with excellent correlation with CT (10). In addition, it is used to define MetS based on various organizational criteria and different scholars indicted that WC appears to be a better central obesity indicator than BMI and waist to hip ratio (11).

World Health Organization (WHO) recommends BMI, but all organizations and expert groups uses WC as one of the criteria to define MetS. International Diabetic Federation (IDF), particularly, needs elevation of WC as obligatory criteria with different cutoff point in accordance with ethnicity and gender. Different literatures also supported that WC cutoff point is much variable among different ethnic groups and between genders. However, based on ethnicity and gender, until now, IDF have stated WC cutoff point for the general populations to two regions alone to define MetS, for the European and Asian populations.

The African region had no cutoff point for WC to define MetS yet because there is lack of representative data (12). However, different literatures supported that WC cutoff point is much variable among different ethnic groups and between genders. Different literatures also support the necessity of local based WC cutoff points in the study among T_2DM patients. Consequently, due to lack of properly determined WC cut points among T_2DM patients in our population, we decided to determine WC cut points to define MetS among T_2DM patients in Ayder Comprehensive Specialized Hospital, Mekelle University, Tigray Region, Northern Ethiopia.

1.2 Statement of the problem

Elevated WC is one of the major components of MetS and it is also positively associated with the development of chronic non-communicable diseases (NCDs) such as CVDs, T2DM, musculoskeletal disorders and cancers. Those diseases have been reported as the major causes of death globally and they accounted for 36 million (63 %) of the 57 million deaths in 2008(13, 14).

From recent estimates of the IDF, the number of adults with diabetes in the world currently stands at 415 million. An estimated 14.2 million people aged 20–79 have diabetes in the sub-Saharan Africa (SSA) region; by 2040 this figure will be more than double (15). In developing countries, mainly in Asia and Africa, DM may represent as much as 70% of all cases and about 90 – 95% of the diabetes cases are T2DM (16). In 2015, over 1.33 million cases were diabetes in Ethiopia. Of these, 23,145 deaths of adults aged 20-79 were due to diabetes (17).

In addition, obese people are at increased risk for many serious diseases and health conditions including mental illness such as clinical depression, anxiety, and other mental disorders(18, 19). Obese people are also at higher risk for body pain and difficulty with physical functioning as compared to non obese individuals (20).

Worldwide prevalence of overweight and obesity is increasing at an alarming rate in developed and developing countries, and they become a major global health challenges (21, 22). In 2014, more than 1.9 billion adults aged 18 years and older were overweight. Of these over 600 million adults were obese. Overall, about 13% of the world's adult populations (11% of men and 15% of women) were obese and 39% of adults (38% of men and 40% of women) were overweight. The worldwide prevalence of obesity was more than doubled between 1980 and 2014 (5). The highest prevalence of overweight and obesity was also recorded in African region particularly in South African and Ugandan (23, 24). Economic globalization and western life style in developing countries have driven changes in dietary patterns and food choices (25). According to the 2013 Global Burden of Disease study, obesity is already a major public health challenge in many middle income countries such as in Kenya; It was estimated that about 36% and 49 % of men and women aged 20 years or older, respectively are either overweight or obese (23).

Obesity is prevalent in patients with type II diabetic mellitus. In some area such as in United kingdom, approximately 86% of patients with T_2DM are overweight or obese (26). In Australia

53% of patients with T_2DM are obese and 32.8% are overweight (27). In Saudi Arabia, the prevalence of overweight among patients with T_2DM is around 87.5% (28).

Obesity has an economical implication of once country. It has direct consequence in medical spending on diagnosis and treatment of obesity related diseases. The indirect consequence also involves loss of productivity due to increased death and illness, and the need for informal care.

(29).

It is estimated that around 20-25 % of the world's adult population have MetS and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome (30). MetS is extremely common among diabetic patients and it is a risk factor for the development of diabetes and its complications (31). In addition, people with MetS have a fivefold greater risk of developing T_2DM patients (32). In 2004, MetS was present in 25.2% of T_2DM patients in Nigeria(33). In sub-Saharan Africa, 71.1% of T_2DM patients had MetS, the prevalence was significantly higher in women than in men (34).

Measurement of abdominal obesity is strongly associated with increased cardiometabolic risk, cardiovascular events, and mortality. A normal WC differs for specific ethnic groups due to different cardiometabolic risk. For example, Asians have increased cardiometabolic risk at lower body mass indexes and with lower waist circumferences than other populations (35).

Despite elevated WC being one of the basic components of MetS, the real value of WC hadn't been estimated in T_2DM of the study area. Absence of WC cutoff point in our population may affect estimation for prevalence of MetS. As a result, the aim of this study was to determine WC cutoff point for defining MetS in T_2DM patients in Ayder Comprehensive Specialized Hospital, Tigray Region, Northern Ethiopia.

1.3. Literature review

According to the harmonized definition for MetS, the optimal WC cutoff point to predict the presence of at least two other components of MetS is ≥94 cm and ≥80cm for Europeans, ≥90cm and ≥80cm for South Asian and Chinese people, ≥85cm and ≥90cm for Japanese, and ≥90cm and 85cm for Korean population (i.e. proposed by Korean Society for the Study of obesity) for males and females, respectively. In addition, South and Central Americans are recommended to use the cutoff point proposed to South Asians, and Sub Saharan Africans, Eastern Mediterranean and middle East are recommended to use European data until more specific data are available (36).

The classification power of WC to discriminate individuals with MetS and without MetS is determined using ROC curve analysis and the accuracy of the measurement is measured by the area under the ROC curve (AUC). Different studies reported different classification power of WC for males and females. For instance, in study from Mexico, the AUC of WC was 0.90 and 0.80 for males and females, respectively (37). In study conducted in T2DM patients in Korea, the AUC value was 0.616 for males and 0.611 for females (38). In addition, age specific study conducted in Korean population, in elderly population the AUC was 0.620 in males and 0.626 in females, and for those who were 65 to 74 years old AUC was 0.664 and 0.658 for males and females respectively(37). Moreover, in study conducted in Japan showed that the AUC was 0.669 and 0.739 for males and females respectively (39), and in China 0.736 and 0.705 for females and males respectively (40). The AUC in South Africa was 0.75 in males and 0.68 in females (41), in Egypt 0.693 in males and 0.683 in females (42), in Angola 0.85 for males and 0.79 for females (43) and in Congolese community 0.899 in males and 0.844 in females (44).

Different literatures supported that WC cutoff point is much variable among different ethnic groups and between genders. This is due to different cardiometabolic risk in different ethnic groups (35). For instance, a study of optimal WC cutoff point determination in relation to the amount of visceral adipose tissue in Five Latin American countries: Mexico, El Salvador, Venezuela, Colombia and Paraguay identified a WC threshold of 94 cm and 90-92 cm for men and women, respectively (37). Moreover, age specific study conducted in elderly Korean population, 2,224 participants aged 65 years and older found that optimal WC cutoff point to define MetS was 89.6 cm for males and 90.5 cm for females, and for those who were 65 to 74 years old, it was 89.9 cm and 87.9 cm for males and females respectively (39).

The optimal cutoff points for WC for identifying the presence of IR and visceral obesity, as well as two or more metabolic components in Korean T_2DM patients, were 87 cm for males and 81 cm for females (38).

A study conducted in general population in Japanese people using CT had also showed that cut off points of WC was 82.1cm for men and 78cm for women (40). Another study conducted in urban communities in Jinan and Jining Cities in China showed the WC cutoff point was 83.8 cm and 91.1 cm for females and males respectively (45).

A cohort study was conducted on South African women to determine ethnic specific WC cutoff point for the diagnosis of the MetS. The result had found 91.5 cm cutoff point of WC for defining MetS (41). On the other side, WC cutoff point was lower in South African study, which was 86 cm for men and 92 cm for women (46).

Similarly, another cohort study conducted in South Africa reported that the cutoff points were91cm for males and 84cm for females. The report for Caucasian (white) men and women also showed WC cutoff point variation among Caucasian and African women; which was 97cm and 84cm, respectively (47).

Another study was also done in T_2DM black South African diabetic men. From the study, WC cutoff point above >90 cm was reported for T_2DM black South African diabetic men as a predictor for the presence of at least two elements of the MetS (48).

Egyptian has conducted a study aimed to identify WC cutoff points in normotensive and hypertensive patients. The result has indicated that WC value to define MetS was 93.5 cm for both Normotensive and hypertensive men and 91.5 and 92.5 cm for Normotensive and hypertensive women, respectively (49). Another study in adult Egyptians also showed that the optimal WC cutoffs were 100.5 and 96.25 cm for men and women, respectively (42).

A cross sectional study in university employee in Luanda, Angola found an optimal WC cutoff point of 87.5 cm and 80.5 cm for men and women respectively (50). In Congolese community, the highest values of WC for men and women were obtained for a threshold value of 95 cm for men and 99 cm in women (44).

1.4 Significance of the study

International Diabetes Federation guidelines and the new harmonized guidelines have defined population specific WC cutoff point to define MetS. However, for African population IDF has recommended to use the cutoff points derived from European population until the appropriate cutoff point is determined for African population. As a result, this study will provide insight about appropriateness of using the cutoff point of WC set by IDF.

Moreover, different literatures support variation of WC cutoff points to define MetS among ethnicity difference and different segment of population. Therefore, the aim of this study is to determine WC cutoff point among T_2DM patients in Ayder Comprehensive Specialized Hospital. This will help clinicians to avoid misclassification of T_2DM who are at risk of MetS. The result will also be used as a baseline data for researchers to perform further studies.

2. OBJECTIVES

2.1 General objective

- To determine WC cutoff point for defining MetS among T_2DM patients in Ayder Comprehensive Specialized Hospital, Mekelle University, Tigray Region, Northern Ethiopia.

2.2 Specific objectives

- To determine the classification power of WC among male T_2DM patients for defining MetS
- To determine the classification power of WC among female T_2DM patients for defining MetS
- To determine the cutoff point of WC among male T_2DM patients for defining MetS
- To determine the cutoff point of WC among female T_2DM patients for defining MetS

3. HYPOTHESIS

We hypothesized that there was a difference in WC cutoff point between T_2DM patients in the study area and the IDF value recommended for the study population.

4. MATERIALS AND METHODS

4.1 Study area

The study was conducted in Ayder Comprehensive Specialized Hospital, Mekelle University, which is located in the Northern part of Ethiopia in Mekelle city, Tigray Region. It is 783 km far from Addis Ababa. Ayder Comprehensive Specialized Hospital is a teaching hospital for College medicine and Health Sciences, Mekelle University. The Hospital is rendering its referral and non-referral services for around 8 million populations in its catchment areas of the Tigray, Afar and north-eastern parts of the Amhara regional state with total patient flow of above 100,000 per year. The Hospital is equipped with as the most advanced medical facility in the northern part of the country and it stands as the second largest hospital in the nation with a total capacity of 500 inpatient beds. In diabetic clinic unit of the hospital, on average, about 2100 diabetic mellitus patients were serving in the hospital. Of these, 1600 (76.2%) diabetic patients were T_2DM.

4.2 Study design and period

Institution based cross sectional study was conducted from March to April 2017 in Ayder Comprehensive Specialized Hospital among T_2DM patients.

4.3 Population

4.3.1 Source population

All T_2DM patients registered at the diabetic clinic of Ayder Comprehensive Specialized Hospital.

4.3.2 Study population

All type II diabetic patients who were attending to the diabetic clinic of Ayder Comprehensive Specialized Hospital during the study period

4.4 Inclusion and exclusion criteria

4.4.1 Inclusion criteria

All T_2DM patients 30 years and above who gave the informed consent were included in the study.

4.4.2 Exclusion criteria

Diabetic patients who were not in the fasting state, patients with mental disorders and seriously ill patients were excluded from the study. Participants with any health condition or procedure that may alter the distribution of body fat compartments or the anatomy of the abdominal cavity such as pregnancy, recent laparotomy (≤8 days), invasive procedures in the abdomen, ascitis, and peritonitis were excluded from the study. Patients with co-morbidities such as TB and HIV were also excluded from the study.

4.5 Variable

4.5.1 Dependent variable

Waist circumference

4.6 Operational definitions

Components of Mets are elevated Tg, BP, FBG, WC and reduced HDL-c

- **Elevated Tg** means_ Tg level ≥150 mg/dl or under treatment for hyper triglyceridemia.
- **Reduced HDL-c** means HDL-c level < 40 mg/dl in men and < 50 mg/dl in women
- **Elevated BP** means systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or being under treatment for hypertension
- **Elevated FBS means** FBS ≥100 mg/dl or being under treatment for diabetes or being positive for T_2DM.

Cases mean T_2DM patients with ≥1 abnormal components of MetS, excluding WC and FBS.

Controls means T_2DM patients without MetS components, excluding WC and FBS (51).

Under weight: BMI <18.5 kg/m^2

Normal weight: BMI 18.5-24.99 kg/m^2

Over weight: BMI 25-29.99 kg/m^2

Obese: BMI ≥30kg/m^2

Youden index means (sensitivity + specificity – 1).

4.7 Sample size and sampling technique

Sample size was calculated based on the following formula:

$$n = \frac{\left(Z_{\frac{a}{2}}\right)^2 v(AUC)}{d^2}$$

Where: n= number of study participants who were selected for each group (case and control)

$v(AUC)$=$\left(0.0099\, X\, e^{-(a^2)/2}\right) X(6a^2 + 16)$

$a = {}^{\varphi^{-1}}(AUC)\, X\, 1.414$

$^{-1}_{\varphi}$ = the inverse of standard cumulative normal distribution of AUC value (52).

It is calculated by considering the assumptions of 5% margin of error, 95% level of confidence and, 0.899 and 0.844 AUC value of WC to classify cases from controls for male and female, respectively (44). A total of 520 study participants were selected using systematic sampling technique every 3 T_2DM patients. The interval was obtained from the following formula and assumptions K^{th} =N/n, 1500/520=2.88~3 Where, "K" is the interval,

"N" is the total number of registered T_2DM patients in the hospital who fulfilled the inclusion criteria which was 1500

"n" is the sample size (520).

4.8 Data collection and laboratory methods

4.8.1 Socio-demographic data

WHO modified STEPS questionnaire for NCD risk factors (version 1.4 questionnaires) was customized to collect socio-demographic and behavioral information. Patient data was obtained from routine hospital records of the diabetic clinic. During the study period, three clinical nurses were participated in collecting the patient information, and in measuring the anthropometric and clinical measurements.

4.8.2 Anthropometric and blood pressure measurements

Based on WHO STEPS protocol, WC measures were obtained from individuals wearing underwear at the end of several consecutive natural breaths, at a level parallel to the floor, midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the mid axillary line (53, 54). Measurements were taken in duplicate and an average was calculated. If the difference between the two measurements was >1 cm, a third measurement was performed and the two closest values were used.

The classification power of WC was measured by the AUC, which has a meaningful interpretation for disease classification from healthy subjects. The AUC interpreted as the probability that a randomly chosen diseased subject is rated or ranked as more likely to be diseased than a randomly chosen non diseased subject. This interpretation was based on nonparametric Mann-Whitney U statistics that is used in calculating AUC (55). Based on Mann-Whitney U statistics, the maximum AUC=1 means that the diagnostic test is perfect, the AUC=0.8-0.9 is very good, the AUC= 0.7-0.8 is good and AUC=0.6-0.7 is poor in the differentiation between the diseased and non diseased (56).

Height and weight were measured with the subject in light clothing and no shoes, and BMI was calculated (kilograms per meter squared).Body mass index was measured as weight in kilograms divided by the square of their height in meter. Weight was measured while patients were wearing light clothing without shoes by using the weighing scale. Height measurement was taken using portable tape meter without shoes.

Blood pressure was measured with a mercury sphygmomanometer after a 10 minute rest in the sitting position and the measurements was taken twice, 5 minute apart. The systolic and diastolic

blood pressures were measured. When the first two measurements differed by more than 5mmHg, additional readings were measured and the average was taken (57). Participants were abstained from smoking and ingesting caffeine preceding 30 minutes measurement.

4.8.3 Sample collection and laboratory methods

After an overnight fasting, 3 ml of venous blood sample was collected in a tube, preferably with gel following standard operating procedures (SOPs) by a qualified laboratory technologist. Blood samples were centrifuged after 30 minute of collection and serum sample was separated in to another test tube. Glucose, triglyceride and HDL-c levels in serum sample were analyzed on the day of sample collection by Pentra C400 clinical chemistry analyzer (HORIBA ABX SAS, France).

Fasting serum glucose was measured using glucose oxidase method by colorimetry and triglyceride was determined based on an enzymatic colorimetric assay. In addition, HDL-c was measured using homogeneous enzymatic method for directly measuring of HDL-c level in serum without the need for any off-line pretreatment or centrifugation steps. The blood specimen was collected, processed and analyzed by two laboratory technologists.

4.8.4 Data quality control and management

Pre-test was carried out in 10% of the total sample in the diabetic clinic of University of Gondar to evaluate the validity of the tool. Training was given to the data collectors by the principal investigator. In addition, the principal investigator had closely followed and frequently checked the data collection process to ensure the completeness and consistency of the collected data. Laboratory assays was carried out after running quality control samples. All procedures were done in accordance with the SOPs. The raw data (laboratory, clinical and demographic) was checked for completeness prior to entry to the software. The data was analyzed and interpreted by the principal investigator.

4.9 Data analysis and interpretation

Data were entered using Epi-info 3.5.1 and analyzed using SPSS version 20. Participants who had one or more abnormal MetS components (excluding WC and FBS), were code as case and the other as control (12, 58). The classification potential (AUC) of WC to distinguish cases from control was determined using ROC curve for both sexes separately. Sensitivity and specificity of WC to distinguish cases from controls was calculated at several WC points. For each WC point again, YI was computed. The WC point having the maximum YI was taken as the optimum cutoff point of WC to classify case from controls. In all conditions, *P*-value of < 0.05 was treated as statistically significant.

4.10 Ethical consideration

Ethical clearance was obtained from the Research and Ethical Committee of School of Biomedical and Laboratory Sciences, University of Gondar. Letter of support was also secured from Ayder Referral Hospital. Written consent was obtained from the study participants after briefing on the aim and the voluntary nature of the study. Codes were used to keep the confidentiality of the study participants. The study participants were informed that they could receive their test results. Only the investigators were able to link the study participant's identity with the code number.

5. RESULTS

5.1. Socio-demographic characteristics of T_2DM patients

Among the 520 study participants, 308 (59.2%) were females. The mean (± SD) age of the participants was 56 ± 10.8 years and 55 ± 11.4 years for males and females respectively. Majority of the participants 457/520 (87.9%) were from urban area (Table 1).

Table 1: Socio-demographic characteristics of diabetic patients at Ayder Comprehensive Specialized Hospital, Northern Ethiopia, 2017 (N=520)

Variables		Male n (%)	Female n (%)	Total N(%)
Age (years)	30-39	11(5.2)	18(5.8)	29(5.6)
	40-49	45(21.2)	81(26.3)	126(24.2)
	50-59	78(36.8)	95(30.8)	173(33.3)
	60-69	55(26.0)	76(24.7)	131(25.2)
	≥ 70	23(10.8)	38(12.4)	61(11.7)
Occupation	Governmental	80(37.7)	68(22.1)	148(28.5)
	Non- governmental	19(9.0)	13(4.2)	32(6.1)
	Self employee	68(32.0)	56(18.2)	124(23.8)
	House wife	0(0.0)	128(41.5)	128(24.6)
	Farmer	22(10.4)	11(3.6)	33(6.35)
	No	23(10.9)	32(10.4)	55(10.6)
Marital status	Single	17(8.0)	9(6.2)	36(6.9)
	Married	181(85.4)	212(68.8)	393(75.6)
	Divorced	8(3.8)	19(6.2)	27(5.2)
	Widowed	6(2.8)	58(18.8)	64(12.3)
Ethnicity	Tigray	208(98.1)	305(99.0)	513(98.6)
	Other	4(1.9)	3(1.0)	7(1.4)
Educational level	No formal schooling	29(13.7)	79(25.7)	108(20.7)
	Less than Primary school	14(6.6)	43(13.9)	57(10.8)
	Primary school completed	47(22.2)	60(19.5)	107(20.6)
	Secondary school completed	38(17.9)	53(17.2)	91(19.0)
	College/university completed	84(39.6)	73(23.7)	157(28.9)
Residence	Rural	29(13.7)	34(11.1)	63(12.2)
	Urban	183(86.3)	274(88.9)	457(87.8)
Religion	Orthodox	191(90.1)	288(93.5)	479(92.1)
	Muslim	18(8.5)	18(5.8)	36(6.9)
	Other	3(1.4)	2(0.7)	5(1.0)

5.2 Clinical, behavioral and biochemical measurements of T_2DM patients

The mean duration of diagnosed diabetes was 4.7 ± 2.9 years for males and 4.6 ± 2.5years for females. All of the study participants have taken anti-diabetic drugs. Seventy two (35%) male and 144(46.8%) female participants were overweight and obese (Table 2).

Table 2: Frequency of clinical, behavioral and anthropometric measurements of T_2DM patients at Ayder Comprehensive Specialized hospital, Northern Ethiopia, 2017 (N=520)

Variables		Male n(%)	Female n(%)	Total N (%)
Medication status	Anti-DM Only	123(58.02)	170(55.19)	293(56.35)
	Anti-DM +Anti-HT	34(16.04)	27(8.77)	61(11.73)
	Anti-DM +Anti-Dyslipidemia	25(11.79)	58(18.83)	83(15.96)
	Anti-DM + HT + Anti-Dyslipidemia	30(14.15)	53(17.21)	83(15.96)
Duration of diabetes (Yrs)	Less than one year	20(9.43)	25(8.13)	45(8.65)
	1-5 years	101(47.64)	154(49.99)	255(49.05)
	6-10 years	39(18.39)	75(24.35)	114(21.92)
	More than10 years	52(24.54)	54(17.53)	106(20.38)
Alcohol consumption	Yes	46(21.69)	14(4.55)	60(11.54)
	No	166(78.31)	294(95.45)	460(88.46)
Cigarette Smoking	Yes	5(2.35)	0(0.00)	5(0.96)
	No	207(97.65)	308(100)	515(99.04)
BMI	Under weight	11(5.00)	10(3.20)	21(4.00)
	Normal weight	129(60.00)	154(50.00)	283(54.50)
	Over weight	65(31.70)	116(37.70)	181(34.80)
	Obese	7(3.30)	28(9.10)	35(6.70)

DM= diabetic mellitus, HT= hypertension

Four hundred thirty six (275 Females and 161 Males) of the study participants were cases. Reduced HDL-c was the most prevailing abnormal component of MetS in both sexes which was 221(42.5%), whereas, high blood pressure was the least, 157(30.2%) **(**Table 3).

Table 3: Frequency of individual components of MetS among T_2DM patients in Ayder Comprehensive Specialized Hospital, Northern Ethiopia, 2017 (n=520).

Variables	**Male**		**Female**		**Total (N%)**
	n(%)	**95 % CI**	**n(%)**	**95 % CI**	
High TG	79(37.3)	30.7-44.0	134(56.5)	37.1-49.0	213(40.9)
high BP	75(35.4)	28.9-42.3	82(26.6)	21.2-31.3	157(30.2)
low HDL-c	116(54.7)	47.6-61.7	105(34.1)	20.6-47.6	221(42.5)
Clusters of abnormal components					
At least 1 component	161(75.9)	70.2-81.6	275(89.3)	85.4-92.4	436(83.8)
At least 2 components	78(36.8)	30.7-43.5	131(42.5)	36.7-47.7	209(40.2)
At least 3 components	57(26.9)	20.6-32.9	99(32.1)	27.3-37.2	156(30.0)
All components	26(12.3)	7.9-16.7	45(14.6)	11.0-19.2	71(13.6)

BP: Blood Pressure, HDL-c: High density lipoprotein cholesterol, TG: Triglyceride,

5.3 AUC, sensitivity and specificity of WC cutoff point to define MetS and metabolic risk factors

The classification power of WC to define hypertension among the other MetS components was higher (0.67 in males and 0.63 in females) in both sexes in our study. However, the classification power of WC to define the reduced HDL-c was lower as compared to the other MetS components in both sexes (0.60 in males and 0.53 in females) (Table 4).

Table 4: Characteristics of ROC curves used for the identification of optimal WC cutoff values to define cases and MetS components among T2DM patients in Ayder Comprehensive Specialized Hospital, Northern Ethiopia, 2017 (N=520)

Sex	MetS components	AUC (95% CI)	Sensitivity	Specificity	*P* value
Male	Hypertension	0.67(0.60 -.75)	0.51	0.76	≤0.001
	Hypertriglyceridemia	0.67(.60 -.74)	0.49	0.76	≤0.001
	Low HDL-c	0.60(.52 -.67)	0.39	0.73	0.013
	Cases	0.67(.58 -.75)	0.40	0.86	≤ 0.001
Female	Hypertension	0.63(.56 -.70)	0.79	0.33	0.001
	Hypertriglyceridemia	0.57(.52 -.65)	0.75	0.34	0.010
	Low HDL-c	0.53(.44 -.61)	0.72	0.59	≤0.001
	Cases	0.63(.52-.73)	0.73	0.45	0.017

5.4 Classification power and optimum WC cutoff point of WCs to discriminate cases from controls

Among the participants, 89.3% (275/308) of females and 75.9% (161/212) of males had at least one abnormal component of MetS (cases). The power of WC (AUC) to discriminate cases from control were 0.67(0.58-0.75) and 0.63(0.52-0.73) for males and females respectively; (Figure1).The optimal WC cutoff point to classify cases from controls was 95.5 cm and 87.5 cm for males and females respectively (Table 5).

Table 5: Performance of different WCs for discriminating cases from controls among T_2DM patients at Ayder Comprehensive Specialized hospital, Northern Ethiopia, 2017 (N=520)

	WC cutoff points (cm)	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Youden index
Male (n=212)	90	63.4	60.8	83.6	34.4	0.242
	92	54.4	70.6	85.3	32.7	0.250
	94	44.1	80.4	87.7	31.3	0.245
	95.5	**39.8**	**86.3**	**90.1**	**31.2**	**0.261**
	98	27.9	88.2	88.2	27.9	0.161
	100	21.7	92.2	89.7	27.2	0.139
Female (308)	80	88.4	24.2	87.3	20.0	0.126
	82	84.4	30.3	91.0	18.9	0.147
	85	81.4	36.4	91.4	19.0	0.178
	87.5	**73.1**	**54.5**	**93.0**	**19.6**	**0.276**
	88	70.9	54.5	92.8	18.4	0.254
	90	61.8	57.6	92.4	15.3	0.194

CI= confidence interval, PPV= positive predictive value, NPV=negative predictive value

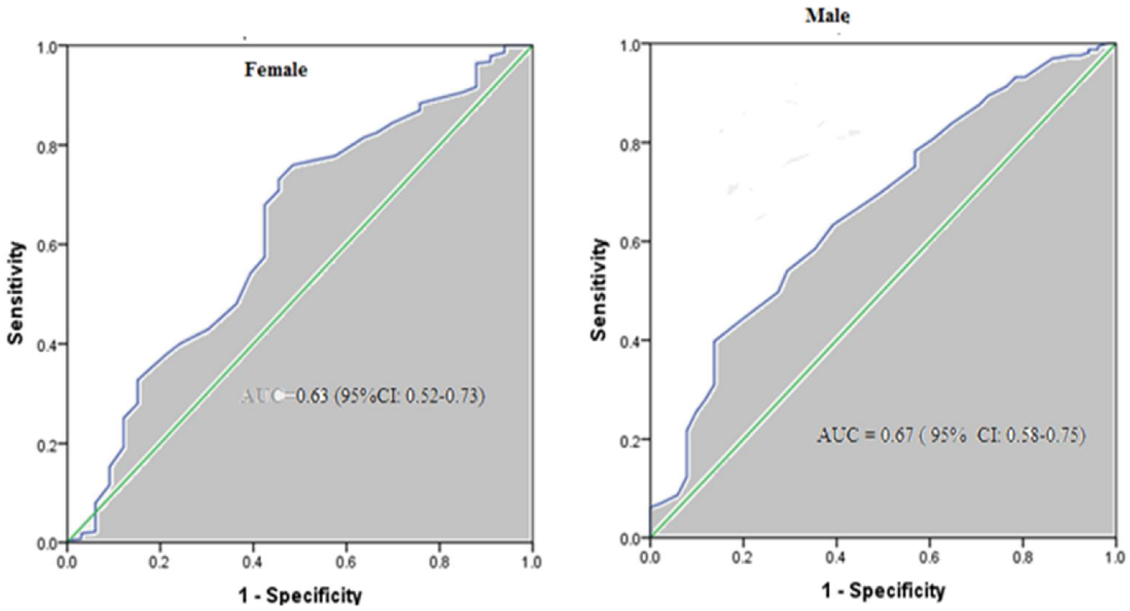

Figure 1 : ROC curves of WC to discriminate cases from controls among T_2DM patients for both sexes in Ayder Comprehensive Specialized Hospital, Northern Ethiopia.

6. DISCUSSION

Central obesity is the major component of metabolic risk factors. WC is considered to be simple and inexpensive measure with excellent correlation with CT. As a good indicator of visceral fat, WC is widely used to predict the outcome of MetS by different organizations. In addition, WC cutoff values are age, gender and ethnicity specific for MetS. This study was aimed to determine WC classification power and cutoff point among T_2DM patients for defining MetS.

In the current study, WC had classified cases from controls with statistically significant power for both sexes (P-value= <0.001 and < 0.017 for males and females, respectively), and it had a poor classification power to categorize cases from controls in both sexes. The optimal WC cutoff value was 87.5 cm (sensitivity 73.1% and specificity 54.5%) for females and 95.5 cm (sensitivity 39.8% and specificity 86.3 %) for males for identifying cases from controls.

Even though the classification power of WC was statistically significant, it had poor classification power (for males AUC=0.67;95% CI: 0.58-0.75, for females AUC =0.63;95% CI 0.52-0.73) to discriminate cases from controls (56). Similar to our study, the classification power of WC to classify cases from control was poor in a study conducted on Benin. It was 0.67 for males and 0.68 for females (59). Moreover, a finding reported from Egypt was also 0.69 for males and 0.63 for females (60).

On the contrary, in several studies such as in Angola (0.85 in males and 0.79 in females) (43), and in Congolese adults (0.899 in males and 0.844 in females) (44), WC had a good classification power to classify cases from control in both sexes.

In our study, the optimal WC cutoff point that best predicts cases was 95.5 cm for the T_2DM males, which is relatively higher than the value for females. The finding from the present study is slightly higher than the IDF recommended value for males, which is 94 cm (12).

In contrast to our study, WC cutoff point in urban African teachers was 90cm in men (61) and the same to that in black South African T_2DM male patients were also 90cm (48). These values were somewhat different to that found in T_2DM male patients in our study area.

The WC cutoff value for T_2DM females determined in this study is 87.5cm which is similar to study in university employee in Angola (87.5cm) (62). The result from this study was higher than the recommended cutoff points to define cases for African females, which is ≥80cm. In contrast, our finding is lower than the study conducted for African females, which was 98 cm (61) and in study from Egyptian adults, which was 96.25cm (60).

The present study suggested that WC cutoff point for females shows lower than males, which is in line to the recommended value. Some studies report shows that WC cutoff point for African population is higher in rural south African females (92cm) than males (86cm)(41),in Cape Town 94cm for females and 83.9cm for males (63). Similarly, in Benin 94 cm for females and 80cm for males, which is the exact reverse of the recommended value (64). Furthermore, a study in Congolese community also shows high WC value in females (99 cm) as compared to males (95cm) (44).

In general, several studies in Africa that conducted to determine WC cutoff point showed an increased WC value in females as compared to males. On the contrary, our finding is higher in males than females, which is in line to the IDF. On the other hand, study from Tunisian adults showed equal value of WC for both males and females which was 85 cm (65). Although the WC value in adult Egyptian females (96.25cm) wasn't higher than males (100.5cm), it shows higher than the IDF recommended value for African females (60).

7. CONCLUSION

The power of WC value to classify cases from controls was poor and the cutoff points of WC were 87.5 cm and 95.5 cm for females and males respectively.

8. RECOMMENDATION

Further study in prospective cohort is better to determine the optimal WC cutoff point among T_2DM patients to define MetS. In addition, studies which can consider the confounders such as lipid lowering medications, age of the participants and duration of diabetes are advisable in order to increase the classification power of WC.

9. LIMITATION

In our study the discriminating power of WC to classify cases from controls was poor. The possible reasons for the poor classification power of WC could be due to the confounders such as statin medication, age of the particpants and duration of diabetes, were not considered.

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Declaration

I, the undersigned, Clinical Chemistry MSc. student declare that this thesis paper is my original proposal for fulfillment of the requirements for degree of Master of Science in Clinical Chemistry.

Name: Shewit H/mariam

Signature: _____

Place of submission: Department of Clinical Chemistry, School of Biomedical and Laboratory Sciences, College of Medicine and Health Science, University of Gondar

Date of submission: _____

This thesis proposal will be submitted for confirmation with my / our approval as University advisor (s)

Advisors

1. Mr. Molla Abebe (MSc.): Sign: _____ Date:_____
2. Mr. Tadele Melak (MSc): Sign: _____ Date:_____

ASSURANCE OF INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as pre-terms and conditions of the research and publications office of the University of Gondar.

Name of the student: _____

Date: _____ Signature: _____

Approval of the advisor (s)

Advisors

Name	Signature	Date
1 Mr. Molla Abebe (Ass.prof)	_____	_____
2. Mr. Tadele Melak (MSc)	_____	_____

Examiners

Name	Signature	Date
1. _____	_____	_____
2._____	_____	_____