University of KwaZulu-Natal

College of Health Sciences

School of Clinical Medicine

Waist circumference, waist-to height ratio, or body mass index: Which is the better predictor of hypertension in patients living with diabetes mellitus in low-to-middle-income countries?

By

Dr Kylie Divashnee Konar

(214504785)

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As the candidate's supervisor, I have approved this thesis for submission.

Signed:  Name: Prof Somasundram Pillay Date: 14 March 2022

DEDICATION

- Thank you, dear God, Sathya Sai Baba, for the strength, wisdom, and perseverance to complete this master's degree.
- To my parents, Martha and Steven, thank you for your love, continuous faith, prayer and support in my endeavors.
- To my sister, Selina, thank you for your support, love and words of encouragement.
- To my fiancé, Rushern, thank you for your love, support, guidance and motivation.

DECLARATION

I, Dr Kylie Divashnee Konar, declare that:

(i) The research reported in this thesis, except where otherwise indicated, is my original work.

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Signed:  Date: 14 March 2022

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ABBREVIATIONS

AOR	Adjusted odds ratio
ART	Anti-retroviral treatment
BMI	Body mass index
BREC	Biomedical Research and Ethics Committee
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
GFR	Glomerular Filtration Rate
HbA1c	Glycated Haemoglobin
HIV	Human immuno-deficiency virus
HPT	Hypertension
LMIC	Low-and-middle-income countries
NCD	Non-communicable diseases
PLWD	Patients living with diabetes
PLWDHIV	Patients living with diabetes and HIV
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
SA	South Africa
SSA	Sub-Saharan Africa
T2DM	Type 2 Diabetes Mellitus
WC	Waist Circumference
WTHR	Waist-to-height ratio
WHO	World Health Organisation

EXECUTIVE SUMMARY

Approximately 80% of adults worldwide with diabetes mellitus (DM) live in low-income and middle-income countries (LMICs) [1]. In LMICs less than 1 in 10 people with DM receive coverage of guideline-based comprehensive diabetes treatment [1]. Addressing cardiovascular risk factors such as hypertension (HPT) and obesity in DM are emergent global health priorities. In South Africa (SA), comorbid HPT in DM is common [2].

Studies suggest that visceral adiposity confers a greater risk for cardiovascular disease (CVD) than body mass index (BMI) [3,4]. Better control of blood pressure, glucose, cholesterol levels and body weight in people with DM could potentially reduce the risk of diabetes-related complications and increase life expectancy [5]. With the burden of HPT in PLWD expected to rise, identifying associations between anthropometry and HPT in a LMIC in which DM is endemic would provide knowledge on better screening strategies in our setting.

The aim of this thesis is to identify and describe the associations between anthropometric indices and HPT. A review of studies from Sub-Saharan African (SSA) countries to identify the associations between HPT and anthropometric indices in PLWD. Most studies found a positive association between HPT and obesity using BMI, with limited evaluation of other anthropometric indices in PLWD. Therefore, this warranted research to find the best anthropometric index in predicting HPT in PLWD.

We conducted a cross-sectional study among 957 PLWD attending a diabetic clinic in Harry Gwala Regional Hospital (formerly known as Edendale Regional Hospital) Pietermaritzburg, SA from 1 January 2019 to 31st December 2019. In this study, we found more than 85% of hypertensive PLWD that were overweight/obese, had an increased WC and abnormal WTHR. All anthropometry was found to be significantly associated with HPT. Overall, WTHR had the highest odds for predicting HPT in PLWD (AOR 4.81 [95% CI 2.05-11.31, $p<0.001$]).

Although anthropometry may not replace a sphygmomanometer in our clinical setting, it can be used to identify patients who are at high risk of HPT. In addition, anthropometry detects patients who are obese or overweight that could be flagged for further monitoring. We hope that the results of this study can motivate other researchers to conduct more research on anthropometric indices in various regions to establish a consensus on guidelines, especially in PLWD.

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CHAPTER 1:

INTRODUCTION

Hypertension (HPT) and diabetes mellitus (DM) are components of metabolic syndrome; they coexist and affect each other's courses. HPT, DM, dyslipidemia, obesity are all well documented modifiable cardiovascular risk factors [1]. The co-existence of HPT and DM is associated with a four-fold increase in mortality [2]. In individuals with DM and HPT, microvascular and macrovascular complications are significantly more common than in those without HPT [3]. Early detection with improved blood pressure control, glucose and cholesterol levels and body weight in people with type 2 diabetes mellitus (T2DM) can potentially reduce the risk of diabetes-related complications and increase life expectancy [3].

Obesity is an independent risk factor for cardiovascular disease [4][5]. Obesity also promotes insulin resistance and metabolic syndrome whose other components besides hyperglycemia are HPT, dyslipidemia, proinflammatory and a prothrombotic state [6]. The development of HPT in patients living with diabetes (PLWD) not only makes treatment strategy more complex and increases healthcare costs but also heightens the risk for macrovascular and microvascular complications considerably [7].

Weight loss is considered a key measure in the management of T2DM [8]. The World Health Organization (WHO) has estimated that globally there are more than 650 million people with obesity (BMI ≥30 kg/m2) [9]. Globally, studies have found that patients with excess visceral adiposity, irrespective of their BMI, had increased cardiovascular risk [10][11]. In LMICs, high BMI remained the leading risk factor for T2DM-related deaths [12]. Patients with T2DM tend to be more obese than general cohorts [8], therefore anthropometric indices and thresholds in general cohorts may not be comparable to PLWD. Due to genetic and environmental factors, the body mass composition of African individuals differs from western individuals and Asians [5]. This becomes even more relevant as the prevalence of HPT and obesity in Sub-Saharan Africa among T2DM is unprecedentedly high and continues to rise [13]. For example, environmental factors influencing obesity in low socioeconomic areas include intake of cheap, energy-dense, processed foods [14]. In South Africa (SA), many PLWD with comorbidities such as HPT are overweight or obese [15]. In addition, their non-diabetic family members were more likely to have abnormal BMI and abdominal obesity [15].

There are various anthropometric indices to describe obesity [16]. Although BMI is widely utilised [9], the use of WC or WTHR is an alternative, acceptable method of measuring obesity [17][18]. Detecting obesity and identifying patients high at risk of HPT through use of anthropometry could be an important tool in clinical setting. Although the diagnosis of HPT is dependent on the use of a reliable sphygmomanometer, it's use can be challenging. These include human error, lack of protocol use, need for calibrated blood pressure monitors and multiple follow-ups are required for the diagnosis [19]. A recent study in 2021 showed in a general cohort of people that WTHR and WC measured were not inferior to BMI as a predictor of HPT. It was suggested that due to the low cost, simplicity of measurement and better ability to predict HPT, it may become a more usable metric in health facilities of LMICs [18]. However, it is important to consider that WC is sex, age, region and ethnic specific [21] [22]. This should be further investigated in African specific populations. We postulate that all indicators of obesity may not be equal predictors of HPT in PLWD.

The thesis included two components: (1) a scoping review entitled "Scoping review: associations between anthropometric indices and hypertension in patients living with diabetes in low-middle income countries in Sub-Saharan Africa" which focused on the current evidence on this topic and (2) a cross-sectional study at a diabetes clinic Harry Gwala Regional Hospital (formerly known as Edendale Regional Hospital) in Pietermaritzburg, South Africa entitled "Waist circumference, waist-to height ratio, or body mass index: Are they all equal as predictors of hypertension in patients living with diabetes mellitus?". The results of this and other studies can help the government make informed decisions on the most effective anthropometric strategy to identify patients at high risk of HPT.

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CHAPTER 2:

Scoping Review: Associations between Anthropometric Indices and Hypertension in Patients Living with Diabetes in Low-Middle Income Countries in Sub-Saharan Africa

This chapter focuses on a scoping review to describes the association between anthropometry and HPT in PLWD in LMICs in SSA.

This review found a positive association between HPT and anthropometry in most studies. BMI is a widely used anthropometric index and had a positive association with HPT in PLWD. Limited data was available comparing the different anthropometric indices.

Scoping Review: Associations between Anthropometric Indices and Hypertension in Patients Living with Diabetes in Low-Middle Income Countries in Sub-Saharan Africa

Kylie Divashnee Konar, Somasundram Pillay

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Abstract

Background

Hypertension (HPT) in low and middle-income countries (LMICs) remains a leading preventable factor for death and disability. Approximately 20-60% of patients living with diabetes (PLWD) have HPT which doubles the mortality risk and accelerates the progression of complications. Obesity is a well-known preventable risk factor for HPT. Despite this, countries in Sub-Saharan Africa (SSA) faces an increasing challenge of obesity. Current evidence on anthropometric indices as a predictor for HPT in PLWD remain unclear.

Methods

A scoping review was performed to determine the association between anthropometry and HPT in PLWD in LMICs in SSA, by using PubMed, Google, Scopus and Cochrane between 2011-2021. A total of 4590 records were identified. The associations between body mass index (BMI), waist circumference (WC) or waist-to-height ratio (WTHR) in PLWD and HPT in LMICs in SSA were assessed.

Results

We analyzed 21 studies with 11 057 patients included in this review. BMI was the most common anthropometric index used with more than 80% of studies suggesting a positive association with HPT. Varying associations between other anthropometric indices and HPT were found.

Conclusions

Our scoping review highlighted a positive association between HPT and anthropometry in most studies. Limited data was available comparing the different anthropometric indices. We found that additional studies are warranted to evaluate anthropometric indices in PLWD.

Keywords: Diabetes, waist-height ratio, waist circumference, body mass index, adults, hypertension and low-to-middle income countries, Sub-Saharan Africa

Background

Globally around 422 million people have diabetes mellitus (DM) with the majority living in low-and middle-income countries (LMICs) [1][2]. Most countries in Sub-Saharan Africa (SSA) are LMICs except for the Seychelles [3]. It is predicted that the number of adults with type 2 diabetes (T2DM) will increase faster (69% increase) in LMIC than in high-income countries (20%) by 2030 [4]. There is an added burden on healthcare to provide effective management [5]. The most common comorbidities among patients with T2DM in SSA were hypertension (HPT), hyperlipidaemia and obesity [6].

HPT, DM, dyslipidemia, obesity and smoking are well documented modifiable risk factors for cardiovascular disease (CVD) [7]. HPT in LMICs remains largely undiagnosed and uncontrolled despite being a leading factor in preventable death and disability [8]. Between 20-60% of individuals with T2DM will have concomitant HPT, and the co-morbidity varies with age, ethnicity, and body mass index [9]. HPT doubles the risk of all-cause mortality and stroke, triples the risk of coronary artery disease and accelerates the progression of diabetic nephropathy, retinopathy and neuropathy [9].

Obesity was shown to be an independent risk factor for dyslipidemia and cardiovascular diseases and weight loss is considered a key measure in the management of T2DM [10]. A 2022 review article found that weight loss of >15% can have a disease-modifying effect in people with T2DM, an outcome that may be superior to some blood glucose-lowering pharmacotherapy [11]. Management of obesity in SSA is particularly challenging as people in some African countries prefer being overweight or obese [12]. They often perceived obesity as a marker of wealth [12]. A cross-sectional study in 2016, found that South Africa (SA) had a statistically significant higher prevalence of obesity (54 %) compared to the other sites in SSA [13].

Genetics plays a role in fat distribution. Asians have more visceral fat as compared to Africans and Europeans [14]. Therefore, Asians tend to be more susceptible to T2DM even with lower BMIs when compared with Europeans [14]. Environmental determinants such as unhealthy diets, physical inactivity, and tobacco and alcohol consumption were found to affect HPT [7]. These factors increased the risk of insulin resistance [15]. Healthcare professionals have been shown to misclassify individuals based on phenotypic appearance, therefore a standard measurement to obesity is preferred [16]. Fat accumulation can be described by various indices including: waist circumference (WC), Body mass index (BMI), waist-to-height ratio (WTHR)

and waist-to-hip ratio (WHPR) [17] [2]. BMI is a commonly used index of weight-for-height to classify obesity in adults [2].

In addition to screening for obesity, identification of cardiovascular risk factors such as HPT has been documented in various studies with no consensus regarding the best anthropometric predictor for HPT. Most studies have described anthropometry in general cohorts rather than in PLWD. For example, a study found BMI in men and WC in women were the best predictors of HPT in a general cohort [18]. Studies that focused on anthropometric indices as predictors of cardiovascular risk factors in PLWD also lack consensus. A 2019 study in Pakistan found that HPT was strongly associated with all the parameters of obesity (WC, WHPR, and BMI) [19], while in 2020 a study in Cameroon found that BMI was a non-significant risk factor for HPT in PLWD [20].

The use of WC requires ethnic and sex-specific cut-off values in PLWD. For example, African women were found to have a high prevalence of obesity and the WC cut-off point recommended for the diagnosis of the metabolic syndrome (80.0 cm) should be increased to 91.5 cm [21]. In 2020, Xing et al. described in a diabetic cohort that WC was not an adequate predictor of major cardiovascular adverse events in women as compared to men [22].

WTHR values of 0.5 or above may indicate increased cardiovascular disease risk across sub-populations [23]. WTHR has been described to be cheaper, lacks the need for a scale and calibration with easier boundaries that may be used from consumer-friendly charts as compared to BMI [23]. WTHR does however require a stadiometer and tape measure [23]. A 2022 study in China found that WTHR has a stronger association with cardio-cerebrovascular events in PLWD [24]. In a prospective study, WTHR was a more accurate tool for predicting HPT as compared to WHPR and BMI in PLWD [25].

Current evidence on anthropometric indices as a predictor for HPT remain unclear in PLWD. The purpose of this scoping review was to determine the associations between various anthropometric indices as a predictor for HPT in PLWD in LMICs in the context of SSA.

METHODS

Study Design

We performed a scoping review of literature using a systematic approach outlined by the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines [26]. The scoping review approach was used to cover the scope of literature and identify key characteristics or factors related to the topic.

Search strategy

The search was conducted using the following databases: PubMed, Scopus and Cochrane. Keywords used in the search included diabetes, waist-height ratio, waist circumference, body mass index, adults, hypertension, low-middle income countries and Sub-Saharan Africa countries.

A brief google search was also performed to find articles related to the topic. Broader search terms were included: 'BMI', 'waist-to-height ratio', 'waist circumference', 'hypertension' 'diabetes', 'LMIC' and 'Sub-Saharan Africa'. From the results, articles were identified by title and read in full for possible associations. Articles that were found on other search engines were not read in the google search. An additional 15 articles met the inclusion criteria for screening.

Only published journal articles were included in the study.

PubMed Search String

Waist-height ratio OR waist circumference OR body mass index OR obesity OR overweight OR anthropometry OR BMI OR WC OR WTHR AND
In diabetes OR diabetes Mellitus OR Insulin-dependent diabetes mellitus OR non-insulin-dependent diabetes mellitus OR NIDDM OR IDDM OR Type 2 diabetes mellitus OR Type 1 diabetes mellitus OR DM AND
Hypertension OR high blood pressure OR systolic hypertension OR diastolic hypertension AND
In adults AND
Low-middle income countries OR low-income country OR middle-income country * as noted by the World Bank (6) AND
Sub-Saharan Africa OR Africa, Sub-Saharan

Study selection and inclusion criteria

Studies that were included in the review if they:

(1) were in cohorts of PLWD

(2) in non-pregnant adults (defined as 18 years or older);

(3) stated an association between anthropometric indices and hypertension

(4) were either cross-sectional, retrospective or prospective;

(5) were in countries that were defined as lower middle-income in economies are those with a Gross National Income (GNI) per capita between $1,036 and $4,045 as listed by The World Bank in 2021 in SSA [3];

(6) and were published between 2011 and 2021.

We excluded articles that did not meet all six of the above criteria.

<u>The following definitions were utilised in the study:</u>

The definition of HPT was systolic blood pressure ≥140mmHg or diastolic blood pressure ≥90mmHg [27], unless otherwise stated. Studies were utilised even if alternative cut-off values were used in local guidelines, provided that a diagnosis of HPT was made. BMI was defined as underweight (<18.5kg/m^2), normal (18.5-24.9kg/m^2), overweight (25-29.9kg/m^2), obese (≥30kg/m^2) [unless otherwise stated e.g. Asian criteria]. Abnormal WTHR, WHPR and WC were defined as stated by each study.

Data extraction and synthesis

All references were captured by each search engine and uploaded to Zotero. Duplicates were identified and subsequently removed. The eligibility of the articles was assessed by the primary reviewer in two steps, the first step included a review of all titles and abstracts relevant to the research question. In the second step, relevant full texts were read to assess their eligibility for the review. The primary reviewer extracted all data from all eligible articles by using a standard data collection tool which including the following: author name, year of publication, country, region, study type, sex, participant's characteristics, type of diabetes, associations between hypertension and WC, WTHR and BMI. The secondary reviewer reviewed all the extractions. Finally, the next steps included recording the data appropriately using a table in Microsoft Word, summarizing and reporting of results. The results were reported using the PRISMA guidelines.

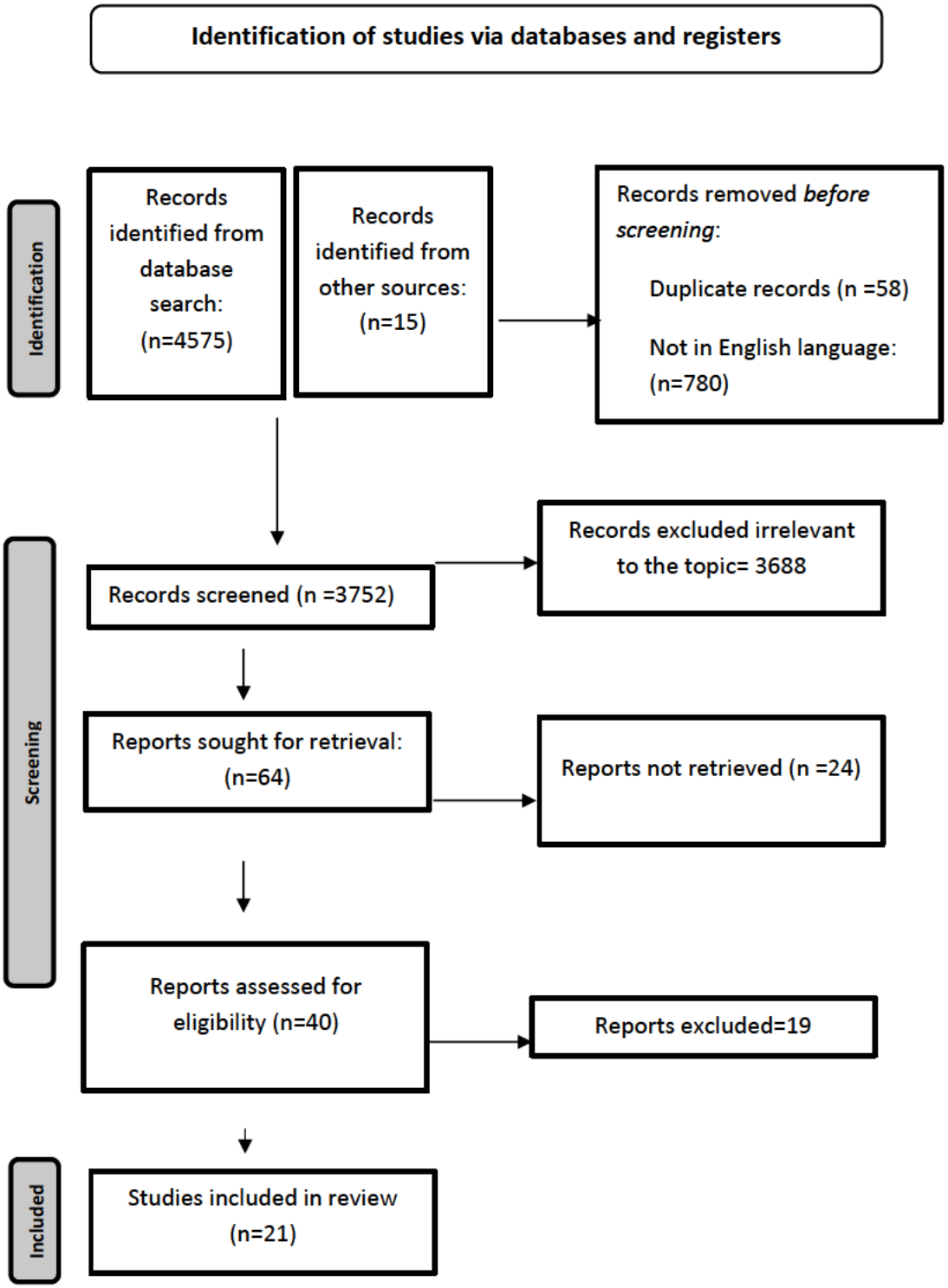

Figure 1: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews*

*Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: 71. doi: 10.1136/bmj.n71. PMID: 33782057; PMCID: PMC8005924.

RESULTS

Table 1: Summary of studies in the scoping review

No.	Author name and year of publication	Country	No of PLWD	% HPT	Type of anthropometric index used	Cut-off points for anthropometric index	Association between HPT and anthropometry			
							BMI (kg/m^2)	**WC (cm)**	**WTHR**	**WHPR**
1.	Mwitha et al. 2019 [28]	Botswana	500	80.8%	BMI. WC. WHPR	BMI* WHPR≥0.85 women ≥0.9 men WC - NR	0	NR		0
2.	Kemche et al. 2020 [20]	Cameroon	109	86.2% # ***	BMI WC WHPR	BMI * WC (NR) WHPR (NR)	0	+		+
3.	Abdissa et al. 2020 [29]	Ethiopia	366	37.4%	BMI	BMI*	+			
4.	Akalu et al. 2020 [30]	Ethiopia	378	59.5% #	BMI	BMI*	+			
5.	Azeez et al. 2021 [31]	Ethiopia	67	NR #	WHPR. BMI WTHR, WC	WHPR >0.9 in men and >0.85 in women. BMI* ≥30.0 kg/m2 WTHR >0.5 WC >94CM men, 80cm women	+SBP +DBP	+DBP	NR	NR
6.	Migora et al. 2021 [32]	Ethiopia	540	29.0%	BMI	BMI*	+			
7.	Tsegaw et al. 2021 [33]	Ethiopia	739	50.2%	BMI	BMI*	+			
8.	Ephraim et al. 2016 [34]	Ghana	107	37.4% #	BMI	BMI*	0			
9.	Chinedu et al. 2015 [35]	Nigeria	244	57.4%	BMI	BMI*	+			
10.	Enikuomehin et al. 2020 [36]	Nigeria	400	NR # **	BMI WHPR WC	BMI* WHPR >0.9 in men and >0.85 in women was defined as central obesity WC ≥94 cm in men and ≥80cm in women.	+ Women	NR		NR

No.	Author name and year of publication	Country	No of PLWD	% HPT	Type of anthropometric index used	Cut-off points for anthropometric index	Association between HPT and anthropometry			
							BMI (kg/m2)	**WC (cm)**	**WTHR**	**WHPR**
11.	Gezawa et al. 2019 [37]	Nigeria	220	46.8% #	BMI WHPR WC WTHR	BMI* WC≥102 cm in men and ≥88 cm in women WHPR≥0.90 in men and ≥0.85 in women WTHR≥0.5 in both sex	+SBP +DBP	+SBP +DBP	+SBP +DBP	+SBP
12.	Ogundele et al. 2015 [38]	Nigeria	150	79.0% ****	BMI	BMI*	+			
13.	Unadike et al. 2011 [39]	Nigeria	450	54.2%	BMI WHPR	BMI (Categories not stated) WHPR (Categories not stated)	+			NR
14.	Adeniyi et al. 2016 [40]	South Africa	265	81.0%	BMI	BMI*	+			
15.	Kalk et al. 2011 [41]	South Africa	203	NR **	WC	Men WC >90cm		+		
16.	Abdelbagi et al. 2021 [42]	Sudan	1973	45.6%	BMI	BMI*	+			
17.	Ali et al. 2017 [43]	Sudan	1337	39.7%	BMI WC	BMI* WC (>94 and >80cm for men and women respectively)	+ women	+ women		
18.	Mwitha et al. 2012 44]	Tanzania	150	54.7%	BMI	BMI*	+			
19.	Namusisi et al. 2011 [45]	Uganda	1383	37.5%	BMI	BMI*	+ women			
20.	Muddu et al. 2018 [46]	Uganda	201	61.9%	BMI WHPR	BMI* WHPR (NR)	+			0
21.	Tino et al. 2020 [47]	Uganda	1275	69.6%	BMI	BMI*	+			

Key for Table 1

* BMI was defined as underweight<18.5kg/m2. normal 18.5-24.9kg/m2; overweight 25-29.9kg/m2; obese≥30 kg/m2

** Definition of HPT: BP≥130/85mmHg

*** Definition of HPT: BP≥130/80mmHg

****No definition of HPT recorded

#: Appropriate cuff technique stated in study.

NR: No record

0: No association between anthropometry and HPT

+ Positive association between overweight/obese or increased WC or increased WTHR or increased WHPR and HPT

- Negative association between overweight/obese or increased WC or increased WTHR or increased WHPR and HPT

Demographics of the different studies

There were 21 studies that met our inclusion criteria (Table 1). A total of 11 057 patients were studied across 9 countries in the various regions across SSA. (Table 2)

Table 2: Summary of origin of studies utilised in study

Country	Number of studies
Ethiopia	5
Nigeria	5
Uganda	3
South Africa	2
Sudan	2
Botswana	1
Cameroon	1
Ghana	1
Tanzania	1

Relationships between anthropometry and HPT

There were varying associations found between HPT and anthropometry. Seventeen (17) studies (81%) found that HPT was positively associated with anthropometry in all categories that were commented on from the study. Two (2) studies found no association [28][34], while 2 studies found a mixed associations between anthropometric indices [20][46] e.g. WHPR offered no association while BMI was positively associated with HPT [46]. No studies found an inverse relationship between anthropometry and HPT. (Table 1)

Anthropometric sub-analysis

The most common anthropometric index used was BMI. It was positively associated with HPT in 17 studies while 3 studies found no association with HPT. Twelve studies (57.14%) commented solely on BMI as their anthropometric index. There was a positive association in all studies that recorded the association between WC and HPT. Only 1 study reported a positive association between WTHR and HPT. Mixed findings were found between studies that reported on WHPR. (Table 1)

Hypertension:

The HPT prevalence in PLWD ranged from 29.0% to 86.2% throughout the various studies. Six (6) studies recorded that the appropriate cuff technique was used, while the other studies did not comment on this. (Table 1)

DISCUSSION

Our scoping review found that most studies utilised BMI as their anthropometric index of choice. Most studies in the review, regardless of demographics, found that anthropometry is positively associated with HPT. These findings concur with reports in PLWD in other LMICs [19] [48] [49].

Variation in body habitus and the need for local guidelines is important to consider. In 5 studies that found WC to be positively associated with HPT, we found various cut-off points for WC being utilised. In males, Azeez et al. [31] found a positive association between HPT and WC of >94cm, while Kalk et al. [41] and Gezawa et al. [37] found this association at >90cm and ≥102cm respectively. In females, both Azeez et al. [31] and Ali et al. [43] found a positive association at a WC≥80cm, while Gezawa et al. [37] used a higher cut-off of ≥88cm. In SSA, Crowther et al. [21] found that current WC for females is not appropriate for the diagnosis of metabolic syndrome (including HPT) and should be increased from 80cm to 91.5cm. The study highlights the inappropriate use of guidelines derived from non-African study cohorts for the diagnosis of diseases within Africa. This highlights that variation in body habitus according to sex, ethnicity and region should be considered when assessing anthropometry.

Research shows that comorbid diseases, such as T2DM and HPT, occur at lower BMI levels in Asian populations than in the white populations [50]. Asian obesity criteria utilise different cut-off values to define BMI. For example, in China (LMIC), Chen et al. defines obesity as BMI≥28kg/m^2 and overweight as BMI of 24-28kg/m^2 [51]. This contrasts the standard definition of overweight/obesity with the standard 'overweight' classification now being defined as 'obese'. Although there are fewer Asian people in Africa, this example illustrates the importance of interpreting anthropometry with local protocols considering demographics or ethnicity.

Central obesity as compared to BMI has been associated with increased cardiovascular risk and mortality in PLWD [52]. We focused on three indices in this review (BMI, WC and WTHR),

however some studies mentioned WHPR which was important to note. In terms of WHPR, there were few studies noted with no consensus between studies found regarding its ability to predict HPT in PLWD. Despite using the same cut-off values for WHPR, Mwitha et al. 2019 [44] and Gezawa et al. [37] found conflicting associations with regards to HPT. In another LMIC, Chaudhary et al. [19] found a positive association with a WHPR of > 0.9 and > 0.8 in men and women. This shows its potential value of being utilised in PLWD; however, further studies are needed for comparison.

WTHR has been proposed as a superior screening tool than both WC and BMI for adult cardiometabolic risk factors [23]. The reason proposed by Ashwell et al. is due to it being a sensitive test utilising the same values among different ethic groups [23]. In our study, there were limited associations of WTHR with only one study examining this association in PLWD. Globally, however, other studies conducted in LMIC (Iran and China) outside of SSA have also determined that WTHR is the preferred index for anthropometry in PLWD [24] [25]. This serves to highlight that not all anthropometric indices are equal and more attention ought to be given to determine the best anthropometric index in cohorts of PLWD. This is worthwhile to determine as obesity is a key modifiable risk factor. In our scoping review only one study commented on the association of WTHR on HPT in the context of DM [37], while most studies utilised BMI as their choice of anthropometry. In terms of WHPR and WC, varying results were also present with some find positive association vs negative association vs no association.

LIMITATIONS

Our results may be susceptible to the bias related to the search being restricted to three electronic databases and journals written in the English language only. However, PubMed is one of the largest medical search engines available. Grey literature was not included, only published journals. Journal articles that were not retrievable due to lack of access were excluded. The author was a single reviewer in the manuscript selection stage; however, screening and extraction included a second reviewer. Due to variation in studies, there were different cut-off values for anthropometry in different locations. The ethnic and cultural impact on anthropometry can be further explored. The studies focus on HPT prevalence rather than incidence.

CONCLUSION

Our scoping review highlighted a positive association between HPT and anthropometry in most studies. Limited data was available comparing the different anthropometric indices. We found that additional studies are warranted to evaluate anthropometric indices in PLWD.

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CHAPTER 3:

WAIST CIRCUMFERENCE, WAIST-TO HEIGHT RATIO, OR BODY MASS INDEX: ARE THEY ALL EQUAL AS PREDICTORS OF HYPERTENSION IN PATIENTS LIVING WITH DIABETES MELLITUS?

THE RESEARCH ARTICLE

This chapter focuses on original cross-sectional study research describing the associations between three anthropometric indices and HPT in patients visiting the Harry Gwala Regional Hospital (formerly known as Edendale Regional Hospital) diabetes clinic situated in Pietermaritzburg, KwaZulu-Natal.

Waist circumference, waist-to height ratio, or body mass index: are they all equal as predictors of hypertension in patients living with diabetes mellitus?

Kylie Divashnee Konar, Somasundram Pillay

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ABSTRACT

Background: Obesity is a well-documented risk factor for hypertension (HPT) with increasing evidence to suggest visceral adiposity as a greater risk factor for cardiovascular disease (CVD) than body mass index (BMI). Current evidence on anthropometric indices as a predictor for HPT remain unclear in patients living with diabetes mellitus (PLWD).

Objectives: To determine the association between HPT and anthropometry indices [BMI, waist circumference (WC) and waist-to-height ratio (WTHR)] in PLWD.

Methods: A cross-sectional study analysed data captured from standardised clinic sheets from the DM clinic at the Harry Gwala Regional Hospital, Pietermaritzburg, South Africa, from 1 January 2019 to 31 December 2019. Data was analysed using Statistical Package for Social Sciences (SPSS). Chi-square test was used to calculate associations where a p-value of < 0.05 was considered statistically significant. Logistic regression was performed using HPT as a dependant variable and coded anthropometric indices (categorical) as independent variables.

Results:

Data from 957 PLWD was used for the study, majority having type 2 diabetes mellitus (T2DM) [811; 86.2%]. We found that over three-quarters (77%) of PLWD had HPT. About 55% of the population was obese. Women with DM and HPT were significantly more obese, older and had a longer duration of DM as compared to men. More than 85% of hypertensive PLWD that were overweight or obese, had an increased WC and abnormal WTHR. All anthropometry was found to be significantly associated with HPT. Overall, WTHR had the highest adjusted odds for predicting HPT in PLWD (AOR 4.81 [95% CI 2.05-11.31, $p<0.001$]). Approximately 15% of the study cohort was HIV-infected. However, in our multivariate analysis, HIV status did not play a significant role in the association of anthropometry and HPT.

Conclusion: Our study found that all anthropometric indices were significantly associated with HPT. WTHR had the highest odds in the association of HPT in PLWD. Although anthropometry may not replace a sphygmomanometer in any clinical setting, we found that it may help identify patients at high risk of developing HPT. In addition, the use of anthropometry can help detect patients that are overweight or obese for flag them for further monitoring. We advocate for more research on local guidance of anthropometric thresholds in PLWD.

Keywords: diabetes mellitus, waist circumference (WC), waist-to-height ratio (WTHR), body mass index (BMI), hypertension, HIV, cardiovascular disease

Background

T2DM is associated with a life expectancy loss of 6 years as compared to people without T2DM at the age of 50 [1]. Better control of blood pressure, glucose and cholesterol levels and body weight in people with T2DM can potentially reduce the risk of diabetes-related complications and increase life expectancy [2]. Patients with T2DM are generally more obese as compared to patients without T2DM [3]. Weight loss is considered an important management goal in T2DM [4]. Anthropometry is a commonly used tool to detect obesity; however, its uses can be multifaceted including predicting cardiovascular risk factors such as HPT [5]. A study in Iran showed in a general cohort that BMI in men and WC in women were the best predictors of incident HPT [6]. Currently, there is no consensus on anthropometric index of choice to predict HPT in PLWD.

Obesity can be described by various anthropometric indices some of which include waist circumference (WC), body mass index (BMI) and waist-to-height ratio (WTHR) [7]. BMI is a standard index of weight-for-height used to classify obesity in adults [8]. Patients with T2DM tend to be more obese, therefore predictions of cardiovascular risk from general cohorts may not be comparable with PLWD [9]. There is increasing evidence suggests that visceral adiposity is a greater risk for CVD than BMI [10]. Detecting obesity and cardiovascular risk factors through the use of anthropometry adds to its importance as its rightful purpose of identifying metabolic syndrome. Considering low-to-middle-income countries (LMICs), the use of WC or WTHR is an alternative, acceptable method of measuring obesity [11, 12]. A simple tape measure and stadiometer could provide vital information that can risk stratify people.

The diagnosis of HPT is dependent on the use of a reliable sphygmomanometer which doesn't come without its challenges. A 2021 study in Uganda found blood pressure (BP) machines are often not available, not calibrated and difficult to access. It is also affected by cuff size, anxiety and substances. For example, white coat hypertension is elevated BP in office settings that may unnecessarily lead to false diagnoses of HPT [13]. This is further supported by a 2020 review of "Human Errors in Automated Office Blood Pressure Measurement". The review identified that failure to follow standard BP measuring protocols is a barrier to using automated BP machines [14]. Multiple readings are recommended for the diagnosis of HPT and patients may be lost to follow-up [14]. This could be difficult in some countries where attendance to follow-up is already low. A study in Pakistan found attendance at follow-up visits was low among

patients with HPT which may have contributed to poor treatment outcomes in patients [15]. Considering this, an additional tool, may aid detection of HPT and add value to the uses of anthropometry.

The purpose of this cross-sectional study was to determine if anthropometric indices viz. WC, WTHR, or BMI were equal predictors of HPT in PLWD.

METHODS

Study Design

A cross-sectional study was performed using data collected from patients who attended a specialised diabetes clinic at the Harry Gwala Regional Hospital (formerly Edendale Regional Hospital) Pietermaritzburg, KwaZulu- Natal. The study sample included all patients who attended the clinic during the period of 1 January 2019 to 31 December 2019. Data of all first visit patients to the Edendale Diabetes Clinic that met inclusion criteria during the study period were utilised for the study.

Patients were not invited to participate; rather the datasheets utilised were standardised practice in the Edendale Diabetes Clinic for every patient. Database class approval at this clinic was authorised by both Harry Gwala Regional Hospital (formerly Edendale Regional Hospital) and the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BREC BCA194/15). All patient details were taken anonymously to protect patients and maintain confidentiality. The data for this study included all patients 18 years or older.

Patient demographics, family history of DM, glycated haemoglobin (HbA1c %), HIV status, type of DM (Type 1 or 2), total cholesterol (TC)(mmol/l), triglyceride level (mmol/l), high density lipoprotein (HDL)(mmol/l), low density lipoprotein (LDL) (mmol/l), blood pressure (mmHg), eGFR (estimated Glomerular Filtration Rate) (ml/min) and social factors (diet adherence, exercise) were recorded. The presence of microvascular complications of DM (nephropathy, peripheral neuropathy, proliferative and non-proliferative retinopathy) and macrovascular complications of DM (stroke or cerebrovascular accident (CVA), ischaemic heart disease (IHD), myocardial infarction (MI) were also recorded.

Weight, height, WC, WTHR and BMI were calculated by trained healthcare workers following standardised protocols, as set by the World Health Organization (WHO) [8]. To perform height, weight and BMI calculations, the Adam® Equipment MDW-300L scale was used. The patient's WC was taken at the end of normal expiration with a measuring tape at a point midway between the lower ribcage and the superior iliac crest in the midaxillary line. BMI was calculated as weight in kilograms divided by the square of height in meters. WTHR was calculated as WC (cm) divided by height (cm).

The values were categorised according to standardised guidelines. BMI (kg/m^2) was calculated and defined as underweight <18.5kg/m^2, normal weight 18.5-24.9kg/m^2, overweight as >25kg/m^2, 30-34.9kg/m^2 (Class 1 obesity), 35-39.9kg/m^2 (Class 2 obesity), ≥40kg/m^2 (Class 3 obesity) [8]. Abnormal WC was classified as >94cm for men and >80cm for women [16]. According to a systemic review, the mean boundary values for WTHR covering all cardiometabolic outcomes from studies in 14 different countries and including Caucasian, Asian, and Central American people were 0.5 for both men and women, hence was used in this study as a cut-off point for both men and women [17].

Good glycaemic control was defined as a HbA1c value <7% [16]. The Bio-Rad D-10 machine (Bio-Rad Laboratories, Hercules, CA, USA) was used for analysing the HbA1c values at the laboratory. Both the laboratory and the machines are NGSP (National Glycohemoglobin Standardization Program) accredited to maintain standardisation of HbA1c results. Blood pressure (BP) and pulse were recorded using a Mindray® VS-800 machine. BP was recorded, as described in the 2014 South African hypertension guidelines. HPT is defined as persistent elevated blood pressure ≥140/90mmHg [18]. BP was taken while the patient was in a sitting position, from the right arm after the patient rested for at least 5 minutes before measurement. Two readings using an appropriate standard adult cuff were taken at a 5 min interval, and the average of the two readings was reported. All patients that were known to be hypertensive irrespective of current blood pressure reading were included in the study. All patients classified as having HPT in the study were either on anti-hypertensive medication or not. No incident cases of HPT were recorded. Raised TC was defined as ≥4.5mmol/l, triglycerides ≥1.7mmol/l, LDL ≥1.8mmol/l. [16] Reduced HDL was recorded as <1mmol/l for men and <1.2mmol/l for women [16]. Abnormal eGFR <60ml/min was considered as chronic kidney disease (CKD) [19]. We followed basic recommendations that were made which constituted "following diet"

in our study. This included a minimum of 5 portions of fruit and vegetable a day and avoidance of sugars and processed foods. Calorie intake was not calculated [16]. Patients that performed at least 150 minutes of aerobic exercise a week were considered to be 'following exercise' [16] Peripheral sensory neuropathy was diagnosed both from a history of painful feet, paraesthesia and using monofilament testing [16].

This study was approved by the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BREC) 3287/2021.

Statistical analysis

Statistical analysis was conducted with continuous data using Kruskal Wallis test or independent samples test with ANOVA corrections, while categorical data relationships were determined using either chi-square or Fisher's exact tests. Z proportion tests were also used for cross-tabulations. A p-value <0.05 was used as indicator of significance. Data were analysed by Statistical Package for Social Science (SPSS) version 25 for Windows (IBM Corp, Armonk, NY, USA). We used standardised reporting of non-parametric data as median ± interquartile range (IQR). Logistic regression was done to determine odds ratios using HPT as a dependant variable and coded anthropometric indices (categorical) as independent variables. Adjustment variables were determined using bivariate analysis. Only significant variables were chosen as adjustment factors.

RESULTS

(A) Participant characteristics

In our study of patients attending Edendale DM clinic, we found women with DM were significantly older than men (p<0.001). Women had a longer duration of DM as compared to men (p<0.001). More PLWD had T2DM than T1DM (85.89% vs 13.79%, respectively). Approximately eighty-five percent (85.12%) of PLWD had poor glycaemic control (HbA1C >7%). More than 77% of PLWD were hypertensive. The proportion of hypertensive patients did not differ significantly between men and women (p=0.272). The most common diabetic complications identified in this study population was chronic kidney disease (34.38%) and peripheral neuropathy (39.08%).

There were 146 PLWD who were HIV-infected (PLWDHIV) in the study population, of which more than 80% were on ART.

(B) Table 1: Characteristics of study population

	Women n=664 (%)	Men n=293 (%)	Overall [a] N=957 (%)	**P value**
Age (years)*	57 (48-65)	50 (36-61)	56 (44-64)	**<0.001[b]**
Duration of DM (years)*[a] (n=954)	9 (4-17)	6 (2-13)	8 (3-15)	**<0.001[b]**
T1DM[a] (n=954)	65 (9.79)	67(22.87)	132 (13.79) [a]	**0.022[c]**
T2DM[a] (n=954)	596 (89.76)	226 (77.13)	822 (85.89) [a]	0.328[c]
HIV-infected	96 (14.46)	50 (17.06)	146 (15.26)	0.643[c]
On ART [d]	81 (84.38) [d]	48 (96.00) [d]	129 (88.36) [d]	0.387[c]
Adherence to dietary recommendations [a] (n=951)	558 (84.04)	249 (84.98)	807 (84.33) [a]	0.942[c]
Adherence to exercise recommendations [a] (n=951)	495 (74.55)	227 (77.47)	722 (75.44) [a]	0.813[c]
HPT	545 (82.08)	201 (68.60)	746 (77.95)	0.272[c]
HbA1c[a] >7%	539 (81.17)	222 (75.77)	761 (79.52) [a]	0.666[c]
BMI Categories [a] (n=875)				
BMI <18.5 kg/m2	5 (0.75)	10 (3.41)	15 (1.57) [a]	0.192[c]
BMI 18.5-24.9 kg/m2	56 (8.43)	80 (27.30)	136 (14.21) [a]	**0.002[c]**
BMI 25-29.9 kg/m2	107(16.11)	85(29.01)	192 (20.06) [a]	**0.055[c]**
BMI >30 kg/m2	437(65.81)	95(32.42)	532 (55.59) [a]	**<0.001[c]**

	Women n=664 (%)	Men n=293 (%)	Overall [a] N=957 (%)	**P value**
WTHR [a] ≥0.5 (n=868)	572 (86.14)	189 (64.51)	761 (79.52) [a]	0.078[c]
Elevated WC [a] (Men>94cm, Women>80cm) (n=862)	574 (86.45)	142(48.46)	716 (74.82) [a]	**0.001[c]**
TC [a] ≥ 4.5mmol/l (n=880)	328 (49.40)	108 (36.86)	436 (45.56) [a]	0.177[c]
Triglycerides [a]>1.7 mmol/l (n=875)	271 (40.81)	107 (36.52)	378 (39.50) [a]	0.626[c]
LDL [a] >1.8mmol/l (n=874)	296 (44.58)	124 (42.32)	420 (43.89) [a]	0.808[c]
HDL [a]<1.2 in women or <1.0 in men, mmol/l (n=862)	239 (35.99)	76 (25.94)	315 (32.92) [a]	0.202[c]
Diabetic complications				
CVA	21 (3.16)	11(3.75)	32 (3.34)	0.822[c]
MI	3 (0.45)	3(1.02)	6 (0.63)	0.638[c]
Angina	7 (1.05)	4(1.37)	11 (1.15)	0.837[c]
CKD (eGFR<60)	251 (37.80)	78 (26.62)	329 (34.38)	0.164[c]
Proliferative Retinopathy	19 (2.86)	4 (1.37)	23 (2.40)	0.469[c]
Non-Proliferative Retinopathy	66(9.94)	18(6.14)	84 (8.78)	0.343[c]
Peripheral Neuropathy	286 (43.07)	88 (30.03)	374 (39.08)	0.127[c]

Key for Table 1

*Median (IQR)

[a] Some information missing from sub-categories (% new n)

b Calculated using the median values through the Independent samples ANOVA test

[c] Percentage values between men vs women compared via Chi-Squared Test

[d] Percentage totals of HIV-infected patients only

Keywords: ART Anti-retroviral therapy **BMI** Body Mass Index **CVA** Cerebrovascular accident (Stroke) **CKD** Chronic Kidney Disease **DM** Diabetes Mellitus **HBA1C** Glycated Haemoglobin **HDL** High density lipoprotein **HIV** Human Immunodeficiency Virus **HPT** Hypertension **IHD** Ischaemic heart disease (angina) **IQR** Interquartil**e** r**an**ge **LDL** Low density lipoprotein **MI** Myocardial infarction **T1DM** Type 1 Diabetes Mellitus **T2DM** Type 2 Diabetes Mellitus **TC** Total Cholesterol **WC** Waist circumference **WTHR** Waist-to-height ratio

(C) Anthropometry

Approximately 55% of the study population were obese by BMI classification [Table 1]. There was significant association between sex and BMI (p<0.001). More than 74% of PLWD had abnormal WC, while more than 79% had an abnormal WTHR [Table1]. More than 85% of hypertensive PLWD were overweight/obese, had an increased WC and abnormal WTHR [Table 2].

(D) Sex

Women with DM and HPT were significantly more obese than men (P=0.001), whereas with men the association was found in those with normal weight (P=0.004) and being overweight (P=0.010). A greater proportion of hypertensive women had an increased WC (p=0.006) and WTHR (p=0.384) as compared to men. By contrast, men with normal WC and WTHR were found to be significantly associated with HPT as compared to women (P<0.001) [Table 2].

(E) HIV

A greater proportion of HIV-uninfected patients with HPT had obesity, increased WC and abnormal WTHR; however, associations were found to be non-significant. Only HIV-infected patients with normal WC were significantly associated with HPT as compared to HIV-uninfected patients (p=0.010) [Table 3].

Table 2 Association between Anthropometric indices and Sex in Hypertensive Patients living with Diabetes

	Men with HPT* (n=201)	Women with HPT* (n=545)	Total number of patients with HPT* (n=746)	P value
BMI (kg/m^2)				
	n=182 (%)	n=491 (%)	n=673 (%)	**<0.001[a]**
<18.5	3 (1.65)	3 (0.61)	6 (0.89)	P=0.490[b]
18.5-24.9	42 (23.08)	35 (7.13)	77 (11.44)	**P=0.004[b]**
25-29.9	65 (35.71)	83 (16.90)	148 (21.99)	**P=0.010[b]**
≥30	72 (39.56)	370 (75.36)	442 (65.68)	**P=0.001[b]**
WC (cm)				
	n=181 (%)	n=481 (%)	n=662 (%)	**<0.001[a]**
Normal**	68 (37.36)	5 (1.02)	73 (10.85)	**P<0.001[b]**
Increased***	113 (62.09)	476 (96.95)	589 (87.52)	**P=0.006[b]**
WTHR				
	n=177 (%)	n=451(%)	n=628 (%)	**<0.001[a]**
<0.5	32 (17.58)	4 (0.82)	36 (5.35)	**P<0.001[b]**
≥0.5	145 (79.67)	447 (91.04)	592 (87.96)	P=0.384[b]

Key for Table 2

* Some information missing from sub-categories

**Normal: <80cm Women OR <94cm Men

***Increased: ≥80cm Women OR ≥94cm Men

[a] Overall P-value comparison between hypertensive men vs women for each anthropometric index via Chi-Squared Test

[b] Percentage values between men and women compared via Chi-Squared Test

Keywords: **BMI** Body Mass Index **HPT** Hypertension **WC** Waist circumference **WTHR** Waist-to-height ratio

Table 3 Comparison between Hypertension and Anthropometric indices in HIV-infected and HIV-uninfected patients

	HIV-infected with HPT* (n=104)	HIV-uninfected with HPT* (n=569)	P value
BMI (kg/m^2)			
	n=104 (%)	n=569 (%)	**0.001[a]**
<18.5	3 (2.88)	3 (0.53)	0.203[b]
18.5-24.9	13 (12.50)	64 (11.25)	0.798[b]
25-29.9	34 (32.69)	114 (20.04)	0.081[b]
>30	54 (51.92)	388 (68.19)	0.138[b]
WC (cm)			
	n=103 (%)	n=559 (%)	**<0.001[a]**
Normal**	24 (23.30)	49 (8.77)	**0.010[b]**
Increased***	79 (76.70)	510 (91.23)	0.262[b]
WTHR			
	n=103 (%)	n=555 (%)	**0.039[a]**
<0.5	10 (9.71)	26(4.68)	0.185[b]
≥0.5	93 (90.29)	529 (95.32)	0.712[b]

Key for Table 3

* Some information missing from sub-categories

**Normal: <80cm Women; <94cm Men

*** Increased: ≥80cm Women /≥94cm Men

[a] Overall P-value comparison between HIV-infected vs -uninfected patients for each anthropometric index via Chi-Squared Test

b Percentage values between men and women compared via Chi-Squared Test

Keywords: **BMI** Body Mass Index HIV Human Immunodeficiency Virus **HPT** Hypertension **WC** Waist circumference **WTHR** Waist-to-height ratio

Binary Logistic Regression

Binary Logistic Regression (BLR) was performed on the data with HPT as the dependent variable and each of BMI, WC and WTHR as independent variables [Table 4].

(A) Overall analysis

Table 4: Overall Bivariate and Multivariate analysis

	Bivariate Analysis				**Multivariate Analysis**		
Variable	**Unadjusted OR**	**CI**	**Pearson Chi-Square Value**	**p-value**	**Adjusted OR**	**CI**	**p-value**
BMI	3.60	2.49 - 5.23	49.50	< **0.001**	2.97	1.53-5.79	**0.001**
WC	4.63	3.18 - 6.76	79.69	< **0.001**	3.67	1.66-8.14	**0.001**
WTHR	7.58	4.83 - 11.91	95.82	< **0.001**	4.81	2.05-11.31	<**0.001**

A Chi-square test of independence was done for the bivariate analysis. Each of the independent conditions were significantly related to HPT ($p<0.001$) [Table 4]. All anthropometric indices were significantly associated with HPT in the bivariate and multivariate analysis. Overall, WTHR had the highest odds for predicting HPT in PLWD ($p<0.001$). All adjustment variables that were significant in the bivariate analysis were included in the model. We adjusted for the following variables: Sex, CVA (Stroke), Peripheral Neuropathy (PN), HIV Status, total cholesterol, triglycerides, HDL, LDL, GFR, exercise and HbA1c. All anthropometric indices studied on was found to be significant in the multivariate analysis. No significant difference in overall multivariate analysis was found for HIV status ($p=0.995$).

(B1) Anthropometry in Women

All anthropometric indices were found to be significant in women in the multivariate regression. Abnormal WTHR was found to have the highest odds in predicting HPT in women ($p<0.001$) [Table 5].

Table 5: Bivariate and Multivariate analysis of women only

	Bivariate Analysis				Multivariate Analysis		
Variable	**Unadjusted OR**	**CI**	**Pearson Chi-Square Value**	**p-value**	**Adjusted OR**	**CI**	**p-value**
BMI	3.01	1.71 - 5.30	15.78	< **0.001**	2.91	1.33-6.38	**0.008**
WC	14.57	5.18 - 41.03	42.10	< **0.001**	17.98	4.00-80.86	**0.001**
WTHR	22.60	7.48 - 68.26	58.48	< **0.001**	22.30	5.06-98.31	**0.001**

(B2) Anthropometry in Men

In men, all anthropometric indices were significantly associated with HPT in men [Table 6]. Men with an abnormal WTHR were 3.83 times more likely to be hypertensive than with normal WTHR (p=0.002).

Table 6: Bivariate and multivariate analysis of men only

	Bivariate Analysis				Multivariate Analysis		
Variable	**Unadjusted OR**	**CI**	**Pearson Chi-Square Value**	**p-value**	**Adjusted OR**	**CI**	**p-value**
BMI	3.17	1.86 - 5.45	18.62	< **0.001**	3.23	1.54-6.77	**0.002**
WC	3.32	1.94 - 5.69	19.97	< **0.001**	2.39	1.18-4.82	**0.015**
WTHR	4.42	2.51 - 7.82	28.18	< **0.001**	3.83	1.59-7.18	**0.002**

DISCUSSION

We found that over three-quarter (77%) of PLWD had HPT while 55% of the population was obese by BMI classification. Women with DM and HPT were significantly more obese, older and had a longer duration of DM as compared to men. We found more than 85% of hypertensive PLWD that were overweight/obese, had an increased WC and abnormal WTHR. All anthropometry was found to be significantly associated with HPT. Overall, WTHR had the highest odds for HPT in PLWD.

In South Africa, a recent 2021 study conducted by Goetjes et al. found that men were 11.32% less likely to be obese than women [20]. Our study concurred with the findings of men being less obese than women but found greater differences between sexes. Previous studies in America and Europe have also documented a higher BMI among women [21,22].Our study found a higher prevalence of obesity than a recent Ethiopian study conducted in 2022 (55.9% vs 18.8%, respectively) [23]. Similarly, to our study, women were more obese than men [23]. The Ethiopian study also had a lower prevalence of HPT in their DM cohort as compared to our study (40% vs 77%) [23]. We postulate that our findings could reflect the effects of longer duration of DM on the population, and a greater proportion of women with higher levels of obesity. In South Africa, rapid urbanisation characterised by the adoption of unhealthy energy-dense diets and physical inactivity have contributed to the steadily increasing obesity epidemic, with 69% of women and 39% of men being classified as overweight or obese [24]. A systematic review and meta-analysis in 2016 found that African women are affected more by DM than African men. This may be as a result of women taking the position of unpaid caregiver roles for affected family members, which results in less attention being given to their own health e.g., taking care of their own health [25, 26].

Among patients with T2DM, blood pressure lowering was associated with decreased mortality [27]. Globally, there is more CVD in men compared to women in patients of all ages without DM [28]. However, these CVD event rates are shown to be similar among those women and men living with diabetes [29]. Therefore, predicting cardiovascular risk in PLWD varies from general cohorts. Healthcare professionals have been shown to misclassify individuals based on phenotypic appearance, hence a missed opportunity for management [30]. Among PLWD who are either overweight or obese, modest and sustained weight loss has been shown to improve glycaemic control, blood pressure, and lipids [31]. Anthropometry does offer a potential add on benefit to assess the risk of HPT in PLWD. Despite not being able to replace the standard

blood pressure measurement, it does provide us with an association for HPT in high-risk populations such as PLWD when no sphygmomanometers are available or problematic [14].

BMI is the most widely accepted anthropometric index and is universally accepted [32]. In our study we found that BMI was positively associated with HPT, but had a lower adjusted odds ratio (AOR) than the other two anthropometric indices for predicting HPT. Although BMI is the most widely utilised index, it may not offer the most relevant association in this current cohort of patients. A 2021 prospective study conducted by Moosaie et al. also determined that BMI was sub-optimal in predicting HPT in PLWD [33]. Although BMI is relatively easy to perform, the other anthropometric indices also can be done with ease [11,12].

Our study found that WTHR>0.5 provided the highest odds ratio associated with HPT. Similar results have been found in studies from Asia which support that WTHR>0.5 is a better associated with HPT as compared to other indices [34,35,36]. A recent prospective study in a diabetic cohort found WTHR and BMI were significantly associated with an increased incidence of HPT [33]. A recommendation to help clinicians would be to "keep one's waist-line half of one's height. However, the use of WTHR could be region specific. Some earlier studies had suggested that using a cut-off point of 0.5 for WTHR may not be suitable for African blacks and the one-size fits all approach needs to be reviewed [37,38].

WC is an easy to use, inexpensive measure of obesity [39]. Women have a higher proportion of total subcutaneous fat distribution compared to men [40]. This leads to the potential risk of misclassification of obesity. There is need to validate the WC≥94 cm for men and ≥80 cm for women observed in this present study for other Sub-Saharan African populations. Most studies in South Africa have demonstrated the need for different WC thresholds in local populations [41,42,43].

Interestingly in this study, there were 146 PLWDHIV in the study population. Both DM and Human Immunodeficiency Virus (HIV) infection are independently associated with an increased risk of atherosclerosis. [44, 45] In Africa, BMI was significantly associated with HPT in HIV-infected patients in Tanzania [46] and Cameroon [47]. However, in our multivariate analysis, HIV status did not play a significant role in the association of anthropometry and HPT. We postulate that smaller sample size may have impacted its effect.

We have shown a positive association between HPT and all anthropometric indices. All indicators were not equal as WTHR had the highest odds associated with HPT in PLWD. We

advocate that more research on local guidance for anthropometric thresholds in PLWD. The diagnosis of HPT should be performed with a sphygmomanometer as intended; however, anthropometry can be an additional tool to alert the clinician on weight management and the risk of HPT in PLWD.

STUDY LIMITATIONS

- As this was a cross-sectional study no causal relationships could be determined; rather, associations were defined.
- We had less than 10% of data that was missing for some variables which we found to be acceptable with minimal consequent bias.
- Waist-to-hip ratio data was not recorded.

CONCLUSION

Our study found that all anthropometric indices are significantly associated with HPT. WTHR had the highest odds in the prediction of HPT in PLWD. Although anthropometry may not replace a sphygmomanometer in our clinical setting, we recommend that it can be an additional tool to identify HPT in PLWD. At the same time, flag patients that are overweight or obese for further monitoring. We advocate for more research on local guidance of anthropometric thresholds in PLWD.

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CHAPTER 4: CONCLUSION

It is known that PLWD are more obese than general cohorts [1]. Obesity is a well-known preventable risk factor for HPT [2]. Despite this, LMICs face an increasing trend of people being obese or overweight [3]. In addition to identifying obesity, studies have shown that anthropometry has been used to predict HPT in general cohorts [4], however studies in DM cohorts are limited.

This thesis by publication included two components addressing two primary aims: (1) a scoping review on the current evidence on this topic and (2) a cross-sectional study to describe the associations between HPT and anthropometric indices. Our scoping review highlighted a positive association between HPT and anthropometry in most studies. Limited data was available comparing the different anthropometric indices. We found that additional studies are warranted to evaluate which anthropometric index would be better in PLWD. We addressed this gap in research in our cross-sectional study which could offer more insight in PLWD within the context of LMICs in SSA.

Our research article found that all anthropometry was found to be significantly associated with HPT. Overall, WTHR had the highest odds for predicting HPT in PLWD (AOR 4.81 [95% CI 2.05-11.31, $p<0.001$]). This finding was not found in any previous diabetic cohort in SSA. This study unique to its setting, included 146 PLWDHIV. Although HIV status did not play a significant role in the association of anthropometry and HPT, however more research can be done to explore this association.

The number of people with T2DM is expected to increase faster (69% increase) in LMIC than in high-income countries (20%) by 2030 [5]. There is an added pressure on healthcare to provide effective healthcare strategies [6]. Considering this, an additional tool to identify a known cardiovascular risk factor like HPT, can be useful in LMICs. Although anthropometry may not replace a sphygmomanometer in any clinical setting, we found that it may help identify patients at high risk of developing HPT. In addition, the use of anthropometry can help detect patients that are overweight or obese for flag them for further monitoring. We advocate that future prospective studies investigate on local guidance on anthropometric thresholds in PLWD.

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APPENDIX 1: THE STUDY PROTOCOL

University of KwaZulu-Natal

College of Health Sciences

School of Clinical Medicine

Waist circumference, waist-to height ratio,

or body mass index: Which is the better predictor of cardiovascular risk in patients living with diabetes mellitus in low-to-middle-income countries?

PROTOCOL IN COMPLETION OF MMEDSCI

Principal investigator: Kylie Divashnee Konar

Student number: 214504785

Cell: 0659562424

E-mail: divashnee@hotmail.com

Supervisor: Professor Somasundram Pillay
Email: drspillay@iafrica.com

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EXECUTIVE SUMMARY

Diabetes Mellitus (DM) is a chronic, metabolic illness diagnosed by elevated levels of blood glucose. Globally about 422 million people have DM with the majority living in low-and middle-income countries (LMICs). By 2030, the number of adults with type 2 diabetes (T2DM) is expected to increase faster in LMIC (69% increase) than in high-income countries (20%).

It is known that T2DM is associated with increased cardiovascular morbidity and mortality. The challenge in LMICs is to establish effective and affordable interventions to prevent the development T2DM and its complications.

Obesity is a well-documented risk factor for CVD, with increasing evidence to suggest visceral adiposity as a greater risk for CVD than body mass. Current evidence on anthropometric indices as a predictor for cardiovascular risk remain unclear in patients living with diabetes (PLWD). Most studies have described these indices in non-diabetic patients which is not amenable to the PLWD profile. This scoping review, complemented by a retrospective study that will be conducted in a diabetes clinic in Pietermaritzburg, Kwa-Zulu Natal in South Africa, a LMIC and a place endemic to HIV and diabetes. The results of this study can help the government to implement cost-effective strategies to improve current diabetes care in patients in LMIC.

1. BACKGROUND AND LITERATURE REVIEW

1.1 Defining the Clinical Problem

Diabetes Mellitus (DM) is a chronic, metabolic illness diagnosed by elevated levels of blood glucose. Globally about 422 million people have DM with the majority living in low-and middle-income countries (LMICs). By 2030, the number of adults with type 2 diabetes (T2DM) is expected to increase faster in LMIC (69% increase) than in high-income countries (20%)

It is known that T2DM is associated with increased cardiovascular morbidity and mortality. Obesity was shown to be an independent risk factor for dyslipidemia and cardiovascular diseases and weight loss is considered a key measure to the management of T2DM. Obesity is a well-documented risk factor for CVD, with increasing evidence to suggest visceral adiposity as a greater risk for CVD than body mass. Current evidence on anthropometric indices as a predictor for cardiovascular risk remain unclear in PLWD. Most studies have described these indices in non-diabetic patients which is not amenable to the PLWD profile.

This scoping review, complemented by a retrospective study that will be conducted in a diabetes clinic in Pietermaritzburg, Kwa-Zulu Natal in South Africa, a LMIC and a place endemic to HIV and diabetes. The results of this study can help the government to implement cost-effective strategies to improve current diabetes care in patients in LMIC.

1.2 The literature review

Cardiovascular disease (CVD) is the leading cause of death worldwide. Patients with T2DM have a two- to four-fold increase in risk of incident coronary heart disease, ischemic stroke and mortality. HPT, DM, dyslipidaemia, obesity are well documented modifiable risk factors for CVD.

Obesity is an independent risk factor for CVD. Patients with T2DM tend to be more obese and have more cardiovascular risk factors when compared with patients without T2DM.

Fat accumulation can be described by four indices: waist circumference (WC), Body mass index (BMI), waist-to-height ratio (WTHR), and waist-to-hip ratio (WHPR). BMI is a commonly used index of weight-for-height that is commonly used to classify obesity in adults. Globally, studies have found that patients with excess visceral adiposity, irrespective of their BMI, had increased cardiovascular risk. In

LMICs, the relationship between BMI and CVD display vast heterogenicity as a result of genetic and biological factors. Despite its limitations, BMI has been adopted as a simple tool to categorise patients into risk groups.

Both DM and Human Immunodeficiency Virus (HIV) infection are independently associated with an increased risk of atherosclerosis. Whether HIV infection is associated with increased DM risk, relative to uninfected controls, has been debated. Among large cohort studies, some have found an association of HIV with a higher risk of DM while others have reported a similar or even lower risk compared to those who are uninfected. It is proposed that the combined effects of chronic inflammation milleu caused by the HIV and the associated metabolic effects of antiretroviral (ART) can increase cardiovascular risk.

When compared with BMI, studies have shown that WC is a more effective measure of body fat distribution. However, WC remain uncertain in certain populations. In 2020, Xing et al described that WC was not a sufficient predictor of major cardiovascular adverse events in female T2DM patients as compared to male counterparts. Patients with T2DM tend to be more obese, hence research from non-diabetic populations may not compare well in patients with T2DM.

WTHR values of 0.5 or above may indicate increased cardiovascular disease risk across sub-populations. WTHR has been described to be cheaper, lacks the need for a scale and calibration with easier boundaries that may be used from consumer-friendly charts as compared to BMI.

Obesity is a well-documented risk factor for CVD, with increasing evidence to suggest visceral adiposity as a greater risk for CVD than body mass. Current evidence on anthropometric indices as a predictor for cardiovascular risk remain unclear in PLWD. Most studies have described these indices in non-diabetic patients which is not amenable to the PLWD profile. The scoping review will be complemented by a retrospective study that will be conducted in a diabetes clinic in Pietermaritzburg, Kwa-Zulu Natal in South Africa, a LMIC and a place endemic to HIV and diabetes. The results of this study can help the government to implement cost-effective strategies to improve current diabetes care in patients in LMIC.

1.3 The Research Question (or hypothesis)

The following question has been hypothesised:

- What is the association between waist circumference (WC), waist-to height ratio (WTHR), body mass index (BMI) and cardiovascular risk factors in patients living with diabetes mellitus (PLWD) in LMIC?
- What is the association between WC, WTHR, BMI and cardiovascular risk factors in patients living with diabetes mellitus and HIV (PLWHD) IN LMIC?

2. AIMS AND OBJECTIVES

Aim:

- To perform a scoping review of what is currently known on WC, WTHR, BMI as predictors of cardiovascular risk in PLWD in LMICs.
- To identify any significant associations in PLWD between WC, WTHR, BMI and the following variables:
    - Glycaemic control (HbA1c and random blood glucose)
    - Dyslipidaemia (Total Cholesterol, Triglyceride, HDL and LDL- Cholesterol)
    - Blood pressure (mmHg)
    - HIV (Human Immunodeficiency) status
    - Demographics (Sex/Family History of Diabetes)
    - Type of DM (Type 1 and Type 2 DM)
    - Kidney function (Glomerular Filtration Rate-GFR)
    - Thyroid function (TSH)
    - Electrolytes (Calcium, Magnesium, Phosphate)
    - Social factors (diet adherence, exercise and home glucose monitoring)
    - Microvascular complications of DM (nephropathy, neuropathy, retinopathy)
    - Macrovascular complications of DM (Stroke, IHD, MI)
- If any, to postulate why these associations occur.
- To identify if these associations also occur in PLWHD.
- To postulate if these associations are similar or different to results of studies conducted in other parts of the world in comparison to LMICs.

Objectives:

To achieve the above aims, the following steps will be followed:

- Conduct a scoping review of relevant literature using electronic search engines of what is currently known on the association between WC, WTHR and BMI and cardiovascular risk in PLWD.

- Capture clinical and biochemical variables from the Harry Gwala Regional Hospital diabetes datasheet for all patients consulted between 1 January 2019 to 31 December 2019.
- Use this data to describe any associations that may exist between WC, WTHR, BMI and these variables.
    - Mean HbA1c (%)
    - Mean Random Blood Glucose (mmol/l)
    - HIV status (positive or negative)
    - CD4 count (cells/mm^3)
    - Duration of HIV diagnosis (years)
    - Duration of antiretrovirals (ARVs) in years
    - Names of ARVs
    - Family History of Diabetes Mellitus
        - Maternal
        - Paternal
        - Grandmother
        - Grandfather
        - Brother
        - Sister
    - Sex (male/female)
    - BMI (mass/$height^2$)
    - Type of DM (Type 1 or Type 2)
    - Duration of DM (years)
    - Mean Total Cholesterol (mmol/l)
    - Mean Triglyceride (mmol/l)
    - Mean HDL (mmol/l)
    - Mean LDL (mmol/l)
    - Mean systolic blood pressure (mmHg)
    - Mean systolic diastolic blood pressure (mmHg)
    - GFR (ml/minute/1.73m^2)
    - Creatinine (mmol/L)
    - Urine dipstick
    - TSH (mIU/L)
    - Calcium (mmol/L)
    - Magnesium (mmol/L)
    - Phosphate (mmol/L)
    - Diet control (yes or no)

- Exercise (yes or no)
- Home Glucose Monitoring (yes or no)
- Sensory-neuro examination (intact or not)
- Glaucoma (yes or no)
- Cataract (yes or no)
- Non-proliferative retinopathy (yes or no)
- Proliferative retinopathy (yes or no)
- Cerebral Vascular Event (yes or no)
- Ischemic Heart Disease (yes or no)
- Myocardial Infarction (yes or no)

3. METHODS

3.1 PART 1: SCOPING REVIEW

3.1.1 Study Design

A scoping review of literature using a systematic approach outlined by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) will be conducted.

3.1.2. Search strategy

The search will be conducted using the following databases: PubMed, Scopus and Cochrane. Keywords used in the search included waist circumference, waist-to-height ratio, body mass index, diabetes, cardiovascular risk, and low-middle-income countries.

Table 1: PubMed Search String

Waist circumference OR waist length OR waist-to-height ratio OR body mass index OR obesity OR overweight OR WC OR BMI OR WTHR
Diabetes OR Diabetes Mellitus OR Insulin-dependent diabetes mellitus OR non-insulin-dependent diabetes mellitus OR NIDDM OR IDDM OR Type 2 diabetes mellitus OR Type 1 diabetes mellitus OR DM OR HIV-infected and diabetes OR HIV-positive and diabetes
In adults

Cardiovascular risk OR cardiovascular risk factors OR smoking OR smoker OR non-smoker OR Hypertension OR high blood pressure OR systolic hypertension OR diastolic hypertension OR dyslipidaemia OR increased lipids OR hyperlipidaemia
Low-middle income countries OR LMIC OR low-income country OR middle-income country

3.1.3. Study selection and inclusion criteria

Studies will be included in the review if they: (1) reported on PLWD (2) and in adults; (3) and relationship between BMI, WC or WTHR; (4) and cardiovascular risk; (5) and reported in observational and experimental methods with primary data within randomised controlled trials (RCTs), cross-sectional or cohort (prospective and retrospective) designs; (6) in countries that will be defined as lower middle-income economies are those with a Gross National Income (GNI) per capita between $1,036 and $4,045 as listed by The World Bank in 2021.

Eligible studies will include only published journal articles. We excluded articles that did not meet all six criteria from the review. Studies that reported on pregnant and breastfeeding women, children younger than ten years old were excluded from the review.

3.1.4. Data collection and extraction

All references captured by each search engine will be uploaded to Zotero and duplicates will be identified and removed. The eligibility of the articles will be assessed by the primary reviewer in two steps, the first step included all titles and abstracts relevant to the research question. In the second step, relevant full texts will read to assess their eligibility for the review. The primary reviewer will extract all data from all eligible articles by using a standard data collection tool which including the following: author name, year of publication, country, region, study type, sex, participant's characteristics, type of diabetes, associations between cardiovascular risk and WC, WHTR and BMI.

The secondary reviewer will review all the extractions. Finally, the next steps include recording the data appropriately using a table on Microsoft Word, summarizing and reporting of results. The results were reported using the PRISMA guidelines for scoping reviews.

3.2 PART 2: RETROSPECTIVE STUDY

3.2.1 Study design

A retrospective, quantitative, observational, analytical cohort study will be performed.

3.2.2 Setting

This study will be conducted at the diabetes clinic at Harry Gwala Regional Hospital (HGR) which is a regional hospital based in Pietermaritzburg, Kwa-Zulu Natal (KZN).

3.2.3 Participant selection and sampling strategy

Inclusion criteria

- Data for all patients 18 years or older who attended the diabetes clinic at HGR between 1 January 2019 to 31 December 2019 will be used in the study.

Exclusion criteria

- Patients under 18 years of age
- Incomplete or missing information on datasheets.

The HGR diabetes clinic uses a comprehensive diabetes datasheet for all patients consulted in this clinic. This datasheet has been approved by the University of KwaZulu-Natal Biomedical Ethics and Research Committee BREC – BCA Number 194/15. The data will be accessed from this datasheet and captured on an excel document.

3.2.4 Measurements

All data will be captured from the Harry Gwala Regional diabetes datasheet. Any datasheets with missing information will be omitted from the analysis.

3.2.5. Data Collection and statistical analysis

The data will be collected and inserted into an excel datasheet by using patients' identifiers to maintain confidentiality. Continuous variables will be documented as mean values ± standard deviations (SD). Numbers (n) and percentages (%) will be expressed for categorical variables. Numerical data will be compared using Anova, whilst categorical data relationships will be determined using either Chi-square or Fisher's Exact tests. A p-value < 0.05 will be used as indicator of significance. Data will be analysed

by Statistical Package for Social Science (SPSS) version 25 for windows (SPSS Inc., Chicago, IL, USA).

When analysing data, the following parameters to assess good cardiovascular risk will be used:

Dyslipidaemia

- Total cholesterol <4.5mmol/l
- Low density lipoprotein (LDL) cholesterol <1.8 mmol/l
- High density lipoprotein (HDL) cholesterol > 1 mmol/l (men) and >1.2 mmol/l (women)
- Triglycerides <1.7 mmol/l

Smoking

- Non-smoker

Obesity

- Waist circumference (WC) <94cm (men); <80cm (women)
- Body mass index (BMI) <25kg/m^2
- Waist-height ratio (WTHR) <0.5

Hypertension

- Systolic blood pressure < 140mmHg
- Diastolic blood pressure <90mmHg

Thereafter, within each group, the HIV status will be investigated to determine if there is a statistically significant relationship between HIV status (positive or negative) on WC, WHR, BMI and cardiovascular risk.

3.2.6 Sample size, statistical power and variable selection

Data of all patients who meet inclusion criteria will be captured for the study time period 1 January 2019 till 31 December 2019.

4. ETHICAL CONSIDERATIONS

This study will follow all ethical standards of research without direct contact with human or animal subjects**.**

4.1 Community participation

Gatekeeper permission will be required from HGR and the Department of Health to use data from their diabetes clinic (see below for Gatekeeper permission)

4.2 Social Value

Anthropometry is a cheap cost-effective method to predict cardiovascular risk and is a sustainable tool to be used in low-middle income countries. A local study can contribute to the existing knowledge of cardiovascular risk in diabetes in a South African context which can help improve local policies and diabetes care programmes.

4.3 Scientific validity

The datasheets will be analysed, and it will be subjected to statistical analysis aligned to the aims of the study.

4.4 Fair selection of participants

All patients who meet the inclusion criteria will be included in the study.

4.5. Risk/benefit balance

Biologically, there will be no risk of harm to any patients that will result from this study.

Psychologically, no intimidation, anxiety or fear will be experienced by patients as this is a retrospective study.

Socially, patient identifiers will be used when capturing data thereby maintaining confidentiality of patients' details.

4.6 Independent ethic review

Ethics approval will be obtained from BREC prior to conducting the study.

4.7 Informed consent

No informed consent will be required as the data required will be retrospective and taken from datasheets

4.8 Ongoing respect for participants

Data will be processed without using the patients' name or details which can identify them to protect their confidentiality.

5. METHODOLOGICAL CHALLENGES AND STUDY LIMITATIONS

Electronic search engines for scoping review: the scoping review will be limited to three search engines, however PubMed containing the most significant number of medical journals. Missing data or information from journals will be excluded from the review.

Managing missing data from datasheets: Not all sheets will have all data filled in. Due to this, those which are incompletely filled will be excluded from the study.

Adequate sample size: The study will use the datasheet, approved by BREC, which is used for all patients who attended the HGR diabetes clinic. It will sample a 12-month period which should offer an adequate representation and sample size of the population.

Retrospective study: findings are associations, not causation, however, will still be relevant in this setting.

6. FEASIBILITY

6.1. Time lines and project management

Tasks	**Time period**
Topic and literature review	08 June 2021 – 18 June 2021
Protocol	18 June 2021-25 July 2021
Scoping review	26 June- 20 July 2021
BREC approval	25 July – 25 August 2021
Permission from HGR	15 August – 15 September 2021
Data capturing	21 September -28 October 2021
Statistical analysis	28 November– 15 December 2021
Results and Discussion	15 – 30 December 2021

6.2. Study team, contributors and authorship.

Name	**Department**	**Contribution**	**Author acknowledgement**
KD Konar	2nd year Intern, Mahatma Gandhi Memorial Hospital, KZN	Literature Review and Protocol BREC approval Permission from HGR Results and Discussion	Author
Professor S Pillay	Department of Internal Medicine at King Edward Hospital (KEH), Clinical Lecturer NRM SCM UKZN	Literature Review and Protocol BREC approval Permission from HGR Results and Discussion	Supervisor

6.3. Participating Centres

Diabetes clinic, HGR

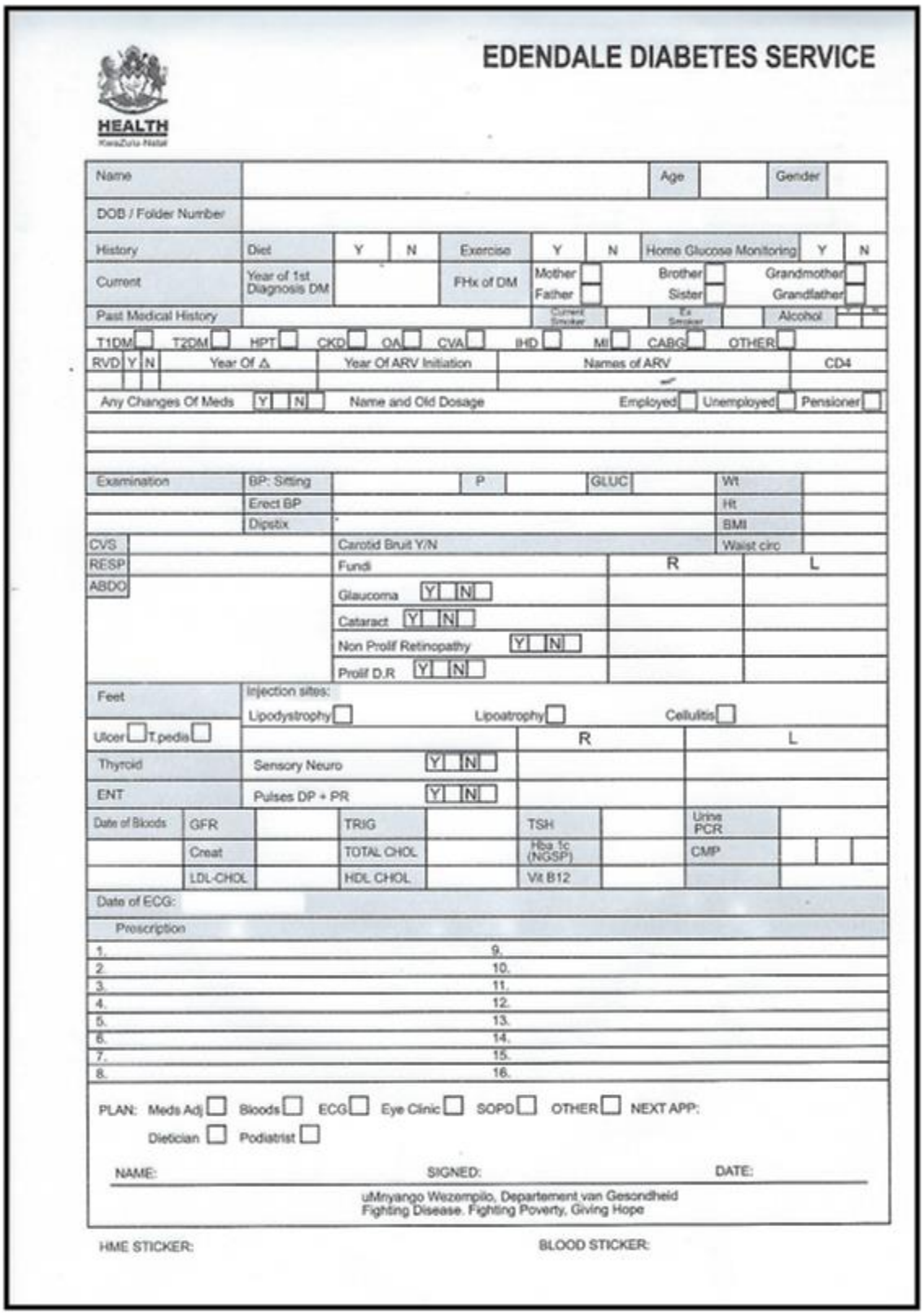
6.4. Study Funding and Progress

ITEM DESCRIPTION	**COST**
Registration fee	R4000
Data capturer	R5000
Statistician	R5000
Stationery (pens, paper, printing costs)	R200
Transport costs	R500
Publication costs if published	R10 000
TOTAL COST	**R24700**

7. STUDY SIGNIFICANCE

Cardiovascular disease is a significant contributor to morbidity and mortality in PLWD, obesity being a major risk factor. Anthrometric are a cheap tool to predict cardiovascular risk, however many studies internationally focus on traditional risk factors in non-diabetic patients, with limited studies in PLWD and especially in LMICs. Furthermore, there is a gap in research addressing cardiovascular risk factors in HIV-infected PLWD. This study will offer insight into glycaemic control and aid in the prediction of cardiovascular disease in these patients. This will contribute meaningfully to cost-effective strategies that could be used in diabetes care interventions locally and internationally.

APPENDIX 2: DATASHEET



HEALTH
KwaZulu-Natal

EDENDALE DIABETES SERVICE

Name							Age		Gender		
DOB / Folder Number											
History	Diet	Y	N	Exercise	Y	N	Home Glucose Monitoring			Y	N
Current	Year of 1st Diagnosis DM			FHx of DM	Mother Father		Brother Sister		Grandmother Grandfather		
Past Medical History					Current Smoker		Ex Smoker		Alcohol		

T1DM ☐ T2DM ☐ HPT ☐ CKD ☐ OA ☐ CVA ☐ IHD ☐ MI ☐ CABG ☐ OTHER ☐

RVD	Y	N	Year Of Δ	Year Of ARV Initiation	Names of ARV	CD4

Any Changes Of Meds Y ☐ N ☐ Name and Old Dosage Employed ☐ Unemployed ☐ Pensioner ☐

Examination	BP: Sitting		P		GLUC		Wt	
	Erect BP						Ht	
	Dipstix						BMI	
CVS		Carotid Bruit Y/N					Waist circ	
RESP		Fundi				R		L
ABDO		Glaucoma Y ☐ N ☐						
		Cataract Y ☐ N ☐						
		Non Prolif Retinopathy Y ☐ N ☐						
		Prolif D.R Y ☐ N ☐						

Feet	Injection sites: Lipodystrophy ☐ Lipoatrophy ☐ Cellulitis ☐		
Ulcer ☐ T.pedis ☐		R	L
Thyroid	Sensory Neuro Y ☐ N ☐		
ENT	Pulses DP + PR Y ☐ N ☐		

Date of Bloods	GFR		TRIG		TSH		Urine PCR		
	Creat		TOTAL CHOL		Hba 1c (NGSP)		CMP		
	LDL-CHOL		HDL CHOL		Vit B12				

Date of ECG:

Prescription

1.	9.
2.	10.
3.	11.
4.	12.
5.	13.
6.	14.
7.	15.
8.	16.

PLAN: Meds Adj ☐ Bloods ☐ ECG ☐ Eye Clinic ☐ SOPD ☐ OTHER ☐ NEXT APP:
Dietician ☐ Podiatrist ☐

NAME: SIGNED: DATE:

uMnyango Wezempilo, Departement van Gesondheid
Fighting Disease. Fighting Poverty, Giving Hope

HME STICKER: BLOOD STICKER:

APPENDIX 3: BIOMEDICAL RESEARCH AND ETHICS COMMITTEE (BREC) APPROVAL LETTER

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

15 December 2021

Dr Kylie Divashnee Konar (214504785)
School of Clinical Medicine
Medical School

Dear Dr Konar,

Protocol reference number: BREC/00003287/2021
Project title: Waist circumference (WC), waist-to height ratio (WTHR), or body mass index (BMI): Which is the better predictor of cardiovascular risk in patients living with diabetes mellitus (PLWD) in low-to-middle-income countries (LMIC)?
Degree: MMedSc

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application.

The conditions have been met and the study is given full ethics approval and may begin as from 15 December 2021. Please ensure that any outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is subject to national and UKZN lockdown regulations, see (http://research.ukzn.ac.za/Libraries/BREC/BREC_Amended_Lockdown_Level_1_Guidelines.sflb.ashx). Based on feedback from some sites, we urge PIs to show sensitivity and exercise appropriate consideration at sites where personnel and service users appear stressed or overloaded.

This approval is valid for one year from 15 December 2021. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2020) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on 08 February 2022.

Yours sincerely,

[redacted]

Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee
Chair: Professor D R Wassenaar
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

APPENDIX 4: KWA-ZULU NATAL DEPARTMENT OF HEALTH APPROVAL LETTER

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email: [redacted]
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

NHRD Ref: KZ_202111_031

Dear Dr KD Konar
(UKZN)

Approval of research

1. The research proposal titled **'Waist circumference (WC), waist-to height ratio (WTHR), or body mass index (BMI): Which is the better predictor of cardiovascular risk in patients living with diabetes mellitus (PLWD) in low-to-middle-income countries (LMIC)?'** was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at Harry Gwala Regional Hospital.

2. You are requested to take note of the following:
   a. *All research conducted in KwaZulu-Natal must comply with government regulations relating to Covid-19. These include but are not limited to: regulations concerning social distancing, the wearing of personal protective equipment, and limitations on meetings and social gatherings.*
   b. *Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.*
   c. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   d. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za*
   e. *Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.*

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

[redacted]
Dr E Lutge
Chairperson, Health Research Committee
Date: 10/12/2021

Fighting Disease, Fighting Poverty, Giving Hope

APPENDIX 5: HARRY GWALA REGIONAL HOSPITAL (GATEKEEPER) APPROVAL LETTER

KWAZULU-NATAL PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

DIRECTORATE:

Harry Gwala Regional Hospital, Private Bag X565
Pietermaritzburg, 3201
Tel: 033 3954042 Fax: 033 3954187

MEDICAL SERVICES

Enquiries: Miss NF Mbele
Telephone: (033) 395 4042
26 November 2021

Dr Konar
Mahatma Gandhi Hospital
Durban
4000

Dear Dr Konar

RE: WAIST CIRCUMFERENCE (WC), WAIST-TO HEIGHT RATIO (WTHR), OR BODY MASS INDEX (BMI): WHICH IS THE BETTER PREDICTOR OF CARDIOVASCULAR RISK IN PATIENTS LIVING WITH DIABETES MELLITUS (PLWD) IN LOW-TO-MIDDLE-INCOME COUNTRIES (LMIC)?

Your request dated 27 September 2021 is acknowledge and refers.

I have pleasure in informing you that the permission has been granted by Harry Gwala Regional Hospital to conduct research.

Please note the following:

1. Please ensure that you adhere to all policies, procedures, protocols and guidelines of the department of health with regards to this research.
2. The hospital will not provide any resources for this research.
3. You will be expected to provide feedback on your findings to HGRH.
4. You will also be expected to notify the Medical Manager's office prior start date of the research.

[redacted]

Dr E K Mthembu
Senior Medical Manager
Harry Gwala Regional Hospital

GROWING KWAZULU-NATAL TOGETHER