



Research Article

Protective Role of Calf Circumference against Prediabetes and Prehypertension among Workers in Kano State, Nigeria

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ABSTRACT

Keywords:

Calf circumference,
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Calf circumference is an easy, cheap, and noninvasive method of assessing peripheral muscle and fat mass. It has been associated with cardiometabolic disease. This study aims to test the null hypothesis that, compared to the highest quartile/tertile, the lower quartiles/tertiles of calf circumference were not associated with a higher risk of prediabetes and prehypertension. In this cross-sectional study of students of the School of Continuing Education of Bayero University Kano, 58 prediabetic and 200 prehypertensive subjects were age-matched with an equal number of controls. Subjects were selected using a multi-stage sampling technique. Body height was measured using a portable stadiometer (Seca, Germany), and circumferences (waist, hip and calf) were measured using an inelastic measuring tape (MEDLINE, USA). Prediabetes was determined by measuring glycosylated haemoglobin levels using a fluorescence immunoassay system (Finccaretm, China) and blood pressure using a mercury sphygmomanometer (Accoson, England). Bayesian multilevel models of prediabetes and prehypertension odds ratios were fitted using the brms R package with calf circumference tertiles/quartiles as predictors, controlling for body mass index and waist-to-hip ratio. For the adjusted model, the odds ratios of prediabetes for the first and 3rd quartiles of calf circumference compared to the 4th were respectively found to be 1.15 [95% CrI: 0.35-3.91, Pnull = 0.4, evidence ratio in favor of alternative hypothesis = 1.5] and 1.48 [95% CrI: 0.52-4.05, Pnull = 0.23, evidence ratio in favour of alternative hypothesis = 3.4]. The odds ratios of prediabetes for the 2nd quartile of calf circumference compared to the fourth were 0.89 [95% CI: 0.36, 2.22, Pnull = 0.61, evidence ratio in favour of alternative hypothesis = 0.6]. The odds ratios of prehypertension for the 1st tertile of calf circumference compared to the 3rd were 1.76 [95% CI: 0.55, 5.87, Pnull = 0.18, evidence ratio in favour of alternative hypothesis = 4]. The odds ratios of prehypertension for the 2nd tertile of calf circumference compared to the fourth were 0.58 [95% CI: 0.2, 1.61, Pnull = 0.86, evidence ratio in favour of alternative hypothesis = 0.6]. In conclusion, calf circumference can be used as a cheap, easy, noninvasive prediabetes and prehypertension screening method. However, the non-linear relationship between calf circumference and the risk of prediabetes and prehypertension suggests a need for future studies to determine upper and lower cut-off values for calf circumference.

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INTRODUCTION

Prediabetes is a borderline glycemic status recognized as a toxic cardio-metabolic state similar to what is observed in established diabetes (Brannick *et al.*, 2016). It is a heterogeneous entity including Impaired Fasting Glucose (IFG) which is defined as Fasting Blood Sugar (FBS) in the range of 5.6 to 6.9mmol/L; Impaired Glucose Tolerance (IGT), defined as 2-hour blood sugar between 7.8 to 11.0mmol/L during glucose tolerance test (OGTT) and raised glycosylated hemoglobin (HbA1c) levels in the range 5.7 to 6.4% (American Diabetes Association, 2011). According to a recent meta-analysis, there are an estimated 15.8 million adult prediabetic individuals in Nigeria (Bashir *et al.*, 2021a).

Prehypertension (PHTN) is a borderline high-risk blood pressure status defined as systolic Blood Pressure (BP) of 120-139mmHg and/or diastolic BP of 80-89mmHg (National High Blood Pressure Education Program, 2004). There are estimated 41.1 million adult Nigerians with prehypertension according to a recent meta-analysis (Bashir *et al.*, 2021b).

Calf circumference is an easy, cheap and noninvasive method of assessing peripheral adiposity and skeletal muscle mass (Takamura *et al.*, 2017). It has been found to be negatively correlated with diabetes (Hussain *et al.*, 2009; Park *et al.*, 2012), cardiovascular disease (Debette *et al.*, 2008; Hsiang *et al.*, 2020; Liang *et al.*, 2020), and all-cause mortality (Abreo *et al.*, 2021; Li *et al.*, 2022). Its ease of measurement, compared to other measures of adiposity (such as body mass index and waist-to-hip ratio), makes it an attractive tool for screening cardiometabolic disease especially

in epidemiological settings. There is scarcity of studies in Nigeria investigating the relationship between calf circumference with cardiovascular disease and to the best of our knowledge there was no study conducted to investigate the relationship between calf circumference and borderline conditions of prediabetes and prehypertension. This study aims to test that null hypothesis that the risk of prediabetes and prehypertension associated with lower quartiles/tertiles of calf circumference was not higher compared to the highest quartile/tertile among selected workers in Kano State Nigeria. The alternative hypothesis states that that the risk of prediabetes and prehypertension associated with lower quartiles/tertiles of calf circumference was higher compared to the highest quartile/tertile among selected workers in Kano State Nigeria.

METHODOLOGY

Study Design

The study design was cross-sectional analytical study. The prediabetic and prehypertensive cases were age-matched with equal number of controls.

Study Area

The study was conducted in Bayero University Kano (BUK), a university located in the North-West Region of Kano State in Nigeria, a lower middle income (World Bank, 2021) Western African nation. Kano State shares boundary with Katsina in the northwest, Jigawa State in the northeast, Bauchi State in the southeast and Kaduna in the southwest. It has total land area of 21,276.9 Km² and a projected population of 12,150,811 by 2017 (Figure 1) (Abdulkadir *et al.*, 2018).

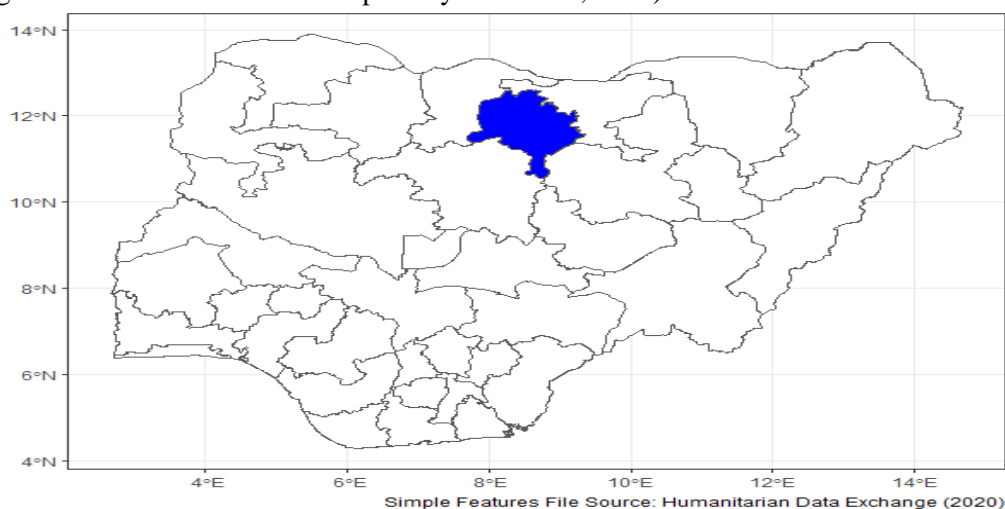


Figure 1: Map of Kano State in Nigeria

Study Population

The study population consists of the students of the School of Continuing Education (SCE) of Bayero University Kano. The university is leading tertiary institution in Nigeria founded in 1976 and about fifty thousand (50,000) students currently enrolled (MacArthur Foundation, 2024). SCE is a part-time program school meant mostly for workers with classes taking place mostly on weekends. There are 25 programs across five (5) departments and currently enrolls more than four thousand (4,000) students (Bayero University kano, 2024)

Sample Size Calculation

The minimum sample size of three hundred and forty five (345) was calculated using Epitools (EPITOOLS, 2021) online calculator assuming an estimated prehypertension prevalence of 34% based on a recent meta-

analysis (Bashir *et al.*, 2021b). 466 subjects were recruited into the study.

Sampling Methods

Figure 2 shows the process of the multi-stage sampling methodology employed in the study. The 25 programs in the school were assigned numbers 1 to 25 and then two programs were randomly selected using `runif()` random number generator function in R (R Core Team, 2021). Next, each of the four levels of the selected programs were assigned numbers and two levels were randomly selected from each of the selected programs using the same `runif()` random number generator function (R Core Team, 2021). The four selected levels had the sample size equally divided and systemic sampling (every other student in a serialized list) was employed to recruit the desired sample size

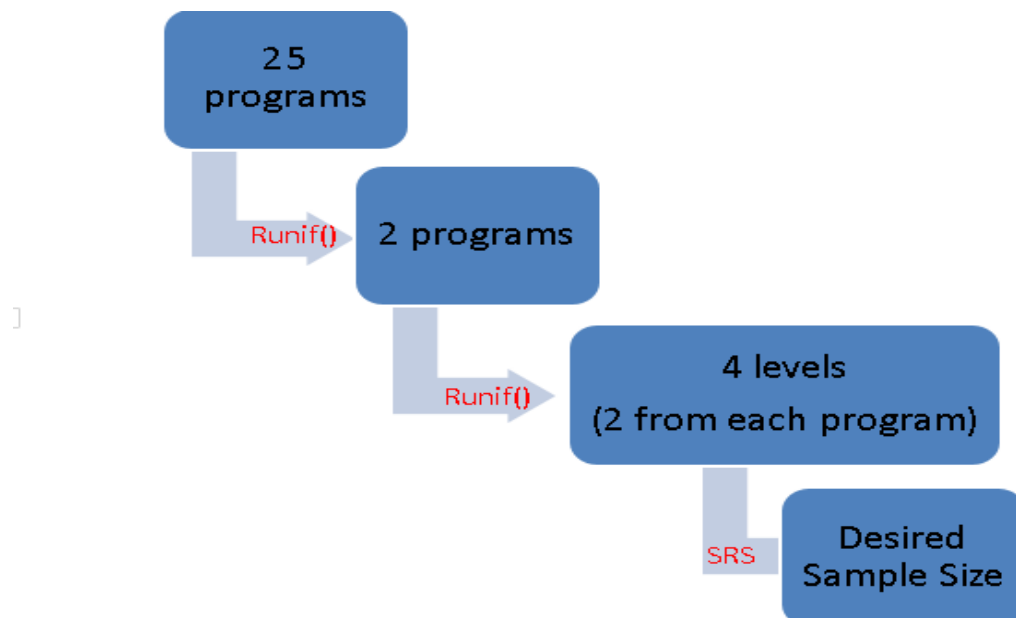


Figure 2: Multi-stage Sampling. `Runif()` = Random number generator function. SRS = Systematic Random Sampling

Inclusion Criteria

Inclusion Criteria were any student of the SCE BUK who

- i. is a worker
- ii. gave informed consent
- iii. is not diabetic or hypertensive
- iv. Does not have a cardiovascular endpoint event such as coronary heart disease or stroke.

Exclusion Criteria

Exclusion Criteria were any student who

- i. is not a worker
- ii. is pregnant

iii. refused participation in the study

iv. is diabetic, hypertensive or both

3.3.2 Ethical Considerations

Ethical clearance was sought from Bayero University Health Research Ethical Committee (NHREC/17/03/2018). Informed written consents was sought from the study participants

Anthropometric Measurements

Body weight was measured using an electronic weighing scale (Seca, Germany) with maximum reading of 150Kg and accuracy of 0.1Kg. With the scale reading zero, the subject

stood on the center of the scale without support and with the weight distributed evenly on both feet (Centers for Disease Control and Prevention, 2014). Height was measured using a portable stadiometer (Seca, Germany) with maximum of 200cm and accuracy of 0.1cm. With the subject standing with the feet together and the heels, buttocks and upper part of the back touching a wall and the head placed in the Frankfort plane (a position of the head whereby the lower edge of the eye socket is in the same horizontal plane as the notch superior to the tragus of the ear). When aligned, the Vertex was the highest point on the skull (Centers for Disease Control and Prevention, 2014).

The Body Mass Index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters). Normal BMI was defined as the range 18.50-24.99 Kg/m². Values at 25.0Kg/m² and above were defined as abnormal (WHO, 2000). There are 4 (four) categories of abnormal BMI; the preobesity and classes I-III of obesity. The ranges of the categories are, respectively, 25-29.99Kg/m², 30-34.99Kg/m², 35-39.99Kg/m² and values of 40Kg/m² or greater (WHO, 2000)..

Waist circumference was measured using an inelastic measuring tape (MEDLINE, 1-800-Medline, USA). With the subject assuming a relaxed standing position with the arms folded across the thorax, measurement was taken at the mid-point between the lower costal (10th rib) border and the iliac crest at the end of expiration. Hip circumference was measured using an inelastic measuring tape (MEDLINE, 1-800-Medline, USA). With the subject assuming a relaxed standing position with the arms folded across the thorax, the circumference was taken at the level of the greatest posterior protuberance of the buttocks which usually corresponds anteriorly to about the level of the symphysis pubis (Centers for Disease Control and Prevention, 2014). Central Obesity was defined as waist-to-hip ratio > 0.9 in males and > 0.85 in females (WHO, 2011).

Calf Circumference was measured using an inelastic measuring tape (MEDLINE, 1-800-Medline, USA). With the subject assuming a relaxed standing position with the arms hanging by the sides and feet separated with the weight evenly distributed, measurement was taken at the point of greatest circumference to the nearest 0.1cm. The point of maximum girth was established by moving

the tape in an up and down movement (Centers for Disease Control and Prevention, 2014).

Blood Pressure Measurement

Blood pressure (BP) was measured using a portable mercury sphygmomanometer (Accoson, England) calibrated in millimeters of mercury (mmHg) with minimum recording of 0mmHg and maximum of 320mmHg. The accuracy of the instrument is 2mmHg. Littman's stethoscope (Master Classic IITM, United States) was used to auscultate the Korotkoff sounds.

The subjects were allowed to relax, sitting in a chair (feet on floor, back supported) for >5 minutes. The subjects were advised to avoid caffeine, exercise and smoking for at least 30 min before measurement. Neither the subject nor the observer were allowed to talk during the measurement. All clothing covering the location of cuff placement were removed. Subject's arm was placed resting on a desk. The middle of the cuff was positioned on the patient's upper arm at the level of the right atrium (the midpoint of the sternum). Correct cuff size, such that the bladder encircles 80% of the arm, was used. Either the stethoscope diaphragm or bell were used for auscultatory readings. A palpated estimate of radial pulse obliteration pressure was used to estimate SBP. The cuff was inflated 20–30 mm Hg above this level for an auscultatory determination of the BP level. For auscultatory readings, the cuff pressure was deflated at the rate of 2 mm Hg per second and Korotkoff sounds listened for. Systolic BP and diastolic BP was recorded as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number (Whelton et al., 2018). An average of two readings was taken as the subject's blood pressure.

Glycosylated Hemoglobin (HbA1c) Measurement

HbA1c was measured a fluorescence immunoassay used along with Finecare™ FIA System (Model No.: FS-112, Guangzhou Wondfo Biotech Co. Ltd, China). This system had an accuracy (R²) of 0.9528 in correlation testing with the Bio-Rad Hemoglobin A1c Program, assay range of 4%-14.5%, linearity of > 0.99, good intra-lot precision (coefficient of variation <10%), good inter-lot precision (coefficient of variation of <10%) and an internal control within each test cartridge (Guangzhou Wondfo Biotech Co. Ltd, 2008).

Criteria for Defining Prediabetes and Prehypertension

Prediabetes was defined as HbA1c in the range 5.7% to 6.4% (American Diabetes Association, 2011). Prehypertension was defined as systolic BP of 120-139mmHg and/or diastolic BP of 80-89mmHg (National High Blood Pressure Education Program, 2004).

Statistical Analysis and Visualizations

The statistical analysis was carried out in R statistical environment (R Core Team, 2021). Data manipulations were done using tidyverse

R package (Wickham et al., 2019) and visualizations using ggplot2 (Wickham, 2016) and tidybayes R packages (Gabry & Mahr, 2021). Bayesian hierarchical logistic models were fitted using brms R package (Bürkner, 2017). The odds ratios of prediabetes and prehypertension were used as response variables of the models whereas calf circumference tertiles/quartiles, body mass index and waist-to-hip ratio categories were used as predictor/confounding variables. The null hypothesis tested was:

Null Hypothesis (H_0):

The risk of prehypertension and prediabetes associated with lower quartiles or tertiles of calf circumference is not higher than the risk of highest quartile or tertile.

Alternative Hypothesis (H_1):

The risk of prehypertension and prediabetes associated with lower quartiles or tertiles of calf circumference is higher than the risk of highest quartile or tertile.

Four models fitted to test the hypotheses were as follows:

- i. Model 1: unadjusted model for either quartiles or tertiles calf circumference
- ii. Model 2: adjusted for body mass index categories
- iii. Model 3: adjusted for waist-to-hip ratio and
- iv. Model 4: adjusted for both body mass index and waist-to-hip ratio

Age as confounding variable was controlled at the level of the study design as all prediabetes and prehypertensive cases were age-matched with equal number of controls during the selection of subjects.

There hierarchical models have 2 levels with the first (population) level estimating the overall odds of prediabetes and prehypertension and the second (group) level formed by the gender variable.

The choice of Bayesian paradigm enabled us to make explicit statements about the probabilities of null and alternative hypotheses (Kruschke, 2014); these capabilities are not available using p-values of the frequentist paradigm (Wasserstein, 2016). Accordingly, three statistics reported by the hypothesis tests conducted were:

- i. Probability of null hypothesis with the level of significance set at 0.05; probabilities greater than 0.05 indicate an unacceptably high probability of the null hypothesis.
- ii. Evidence ratio in favor of alternative hypothesis. This measures the ratio of probability of the alternative hypothesis to that of null hypothesis. An evidence ratio of 1

means the alternative and null hypothesis have equal probabilities, a value greater than 1 means the alternative hypothesis has a bigger probability and a value of less than 1 means the null hypothesis is more probable than alternative hypothesis.

95% Credibility interval (95% CrI). The set of values falling within this interval has 95% probability.

RESULTS

Characteristics of the Study Subjects

One hundred and sixteen (116) subjects were recruited into the prediabetes arm of the study with 58 prediabetes cases and 58 age-matched controls. The prediabetes cases consisted of 34 males (mean age = 42 years, ± 8.6) and 24

females (mean age = 36 years, ± 8.3). The

prediabetes control group consisted of 28 males (mean age = 42 years, ± 7.6) and 30

females (mean age = 36 years, ± 9.4). 400

subjects were recruited into the prehypertension arm of the study with 200 prehypertension cases and 200 age-matched controls. The prehypertension cases consisted of 125 males (mean age = 38 years, ± 7.8) and

75 females (mean age = 35 years, ± 8.6). The

prehypertension control consisted of 118 males

(mean age = 39 years, \pm 7.0) and 82 females(mean age = 32 years, \pm 8.6).**Table 1:** Characteristic of the Study Subjects

Parameter	Gender	Mean(\pm SD)			
		Prediabetes (116)		Prehypertension (400)	
		Cases (58)	Controls (58)	Cases (200)	Controls (200)
Age	Females	35.5(\pm 8.3)	36(\pm 9.4)	34.9(\pm 8.6)	32.9(\pm 8.6)
	Males	42.1(\pm 8.6)	42(\pm 7.6)	38.1(\pm 7.8)	39.4(\pm 7.0)
BMI	Females	28.2(\pm 6.8)	31.5(\pm 8.6)	29.4(\pm 7.1)	27.6(\pm 7.9)
	Males	27.5(\pm 5.8)	26.7(\pm 6.2)	26.3(\pm 4.9)	24.6(\pm 4.8)
WHR	Females	0.86(\pm 0.08)	0.83(\pm 0.07)	0.86(\pm 0.07)	0.82(\pm 0.08)
	Males	0.91(\pm 0.08)	0.90(\pm 0.05)	0.91(\pm 0.06)	0.88(\pm 0.06)
CC	Females	34.5(\pm 4.6)	36.6(\pm 5.8)	35.0(\pm 5.3)	34.5(\pm 5.0)
	Males	35.6(\pm 3.5)	34.6(\pm 3.4)	34.2(\pm 3.6)	34.0(\pm 3.1)
HbA1c	Females	6.3(\pm 0.47)	5.1(\pm 0.45)	-	-
	Males	6.5(\pm 0.60)	4.9(\pm 0.46)	-	-
SBP	Females	123.7(\pm 21.3)	126.3(\pm 19.0)	126.8(\pm 10.8)	107.2(\pm 10.4)
	Males	135.6(\pm 21.5)	126.8(\pm 15.6)	130.3(\pm 7.9)	107.7(\pm 9.3)
DBP	Females	82.3(\pm 8.6)	82.8(\pm 11.7)	88.2(\pm 4.6)	71.7(\pm 6.6)
	Males	86.5(\pm 13.1)	85.1(\pm 9.3)	85.8(\pm 6.4)	72.5(\pm 6.4)

SD = standard deviation, BMI = body mass index, WHR = waist-to-hip ratio, HbA1c = glycosylated hemoglobin, SBP = systolic blood pressure, DBP = diastolic blood pressure, CC = calf circumference

The Overall Risk of Prediabetes Associated with Lower Quartiles of Calf Circumference Compared to the Fourth

For both the unadjusted model (Model 1) and after adjusting for BMI (Model 2), WHR (Model 3) and both BMI and WHR (Model 4), compared to the highest quartile, the risk of prediabetes appeared to be lower in the second quartile and higher in the first and third quartiles (Figure 3). In particular the odds ratio associated with second quartile varied from 0.93 [95% CrI: 0.43- 2.11] for Model 1 to 0.89 [95% CrI: 0.36, 2.22] for Model 4. This implied that belonging to the second quartile was protective against prediabetes compared to the 4th quartile. The opposite was true for 1st and 3rd quartiles. Belonging the two quartile groups was respectively associated with prediabetes odds ratios of 1.24 [95% CrI: 0.48-3.2] and 1.49 [95% CrI: 0.58-3.78] for model 1 and 1.15 [95% CrI: 0.35-3.91] and 1.48 [95% CrI: 0.52-4.05] for Model 4. This implied that

the 1st and 3rd quartiles were associated with higher prediabetes risk compared to the 4th quartile (Figure 3).

The null hypothesis testing results revealed an interesting pattern shown in Figure 4. For all the 4 models, the probability of the null hypothesis is too high to allow for its rejection (>0.05 significance level). However, the probability was consistently higher for the second quartile across all the four models (Figure 4 plot B). The evidence ratio plot (Figure 4A) revealed for the 2nd quartile, the probability of alternative hypothesis was lower than that of the null hypothesis providing a compelling evidence in support of the null hypothesis for the quartile i.e. belonging to the 2nd quartile was associated with lower risk of prediabetes as compared to the 4th quartile. The evidence ratios for the 1st and 4th quartiles were in the favor of alternative hypothesis i.e. belonging to these lower quartiles was

associated with higher prediabetes risk as compared to the highest quartile.

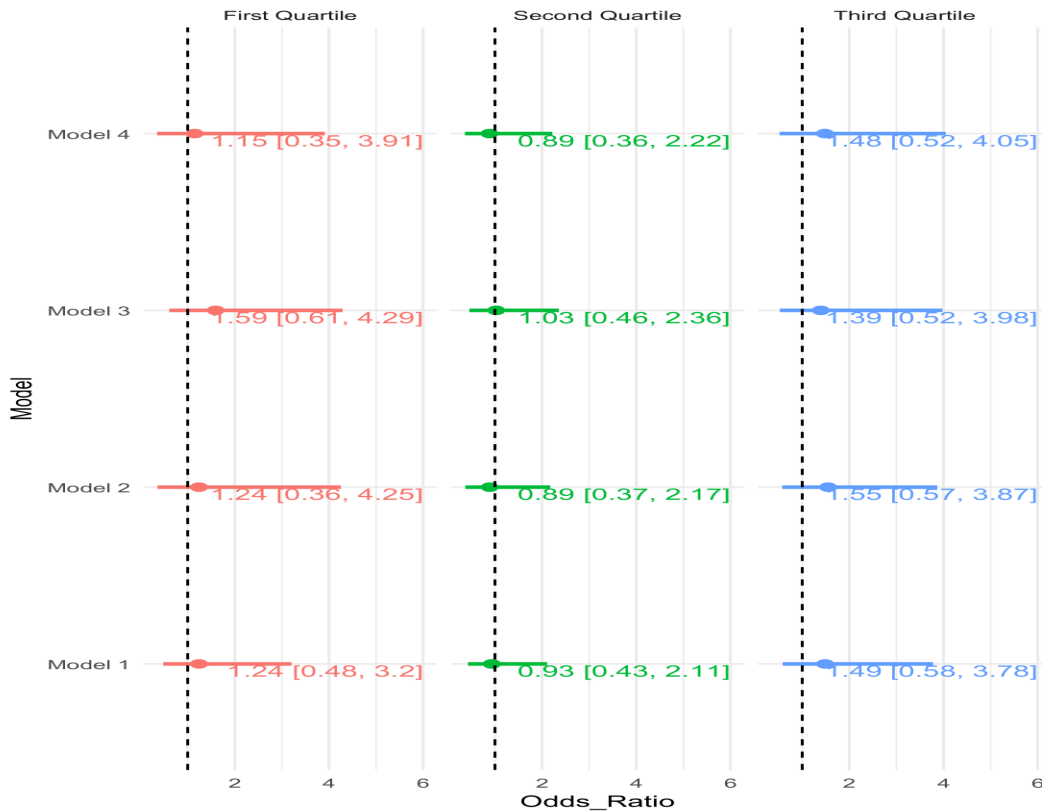


Figure 3: The Overall Risk of Prediabetes Associated with Lower Quartiles of Calf Circumference Compared to the Fourth. Dashed lines represent odds ratio of Fourth Quartiles = 1. Model 1 = unadjusted model, Model 2 = controlled for body mass index, Model 3 = controlled for waist-to-hip ratio, Model 4 = controlled for both body mass index and waist-to-hip ratio. Values in brackets are 95% Credible Intervals

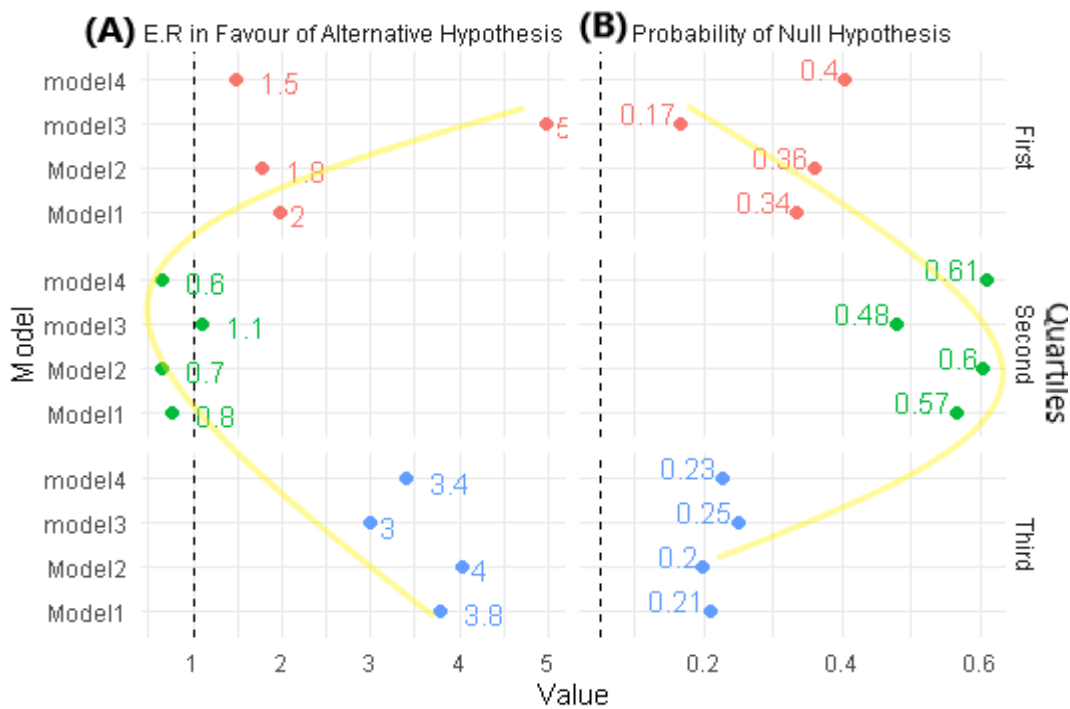


Figure 4: Overall Evidence Ratio of the Alternative Hypothesis and Probability of Null Hypothesis for Prediabetes Risk of Calf Circumference. E.R = evidence ratio. Dashed lines represent null value of 1 for the evidence ratio plot (A) and 0.05 significance level for the probability plot (B). Yellow curve added to reveal a pattern.

The Sex-specific Risk of Prediabetes Associated with Lower Quartiles of Calf Circumference Compared to the Fourth

The analysis of risk of prediabetes associated with quartiles of calf circumference in the 2 sexes reproduced the pattern observed in the overall analysis; the second quartile has lower risk whereas 1st and 3rd quartiles has higher risk of prediabetes compared to the highest quartile (Figure 5).

As was the case for the overall risk analysis, the probability of null hypothesis was higher

for 2nd quartile compared to the 1st and 3rd quartiles (Figure 6). However, the evidence ratio supports the 2nd quartile null hypothesis among the males only. In this gender, Model 4 revealed that probability of the 2nd quartile null hypothesis was as high as 0.75 with the null hypothesis being 3 times more likely (E.R = 0.3) than alternative hypothesis (Figure 6A). Among females, even though the 2nd quartile null hypothesis probability was high, the evidence ratio was in favor of the alternative hypothesis.

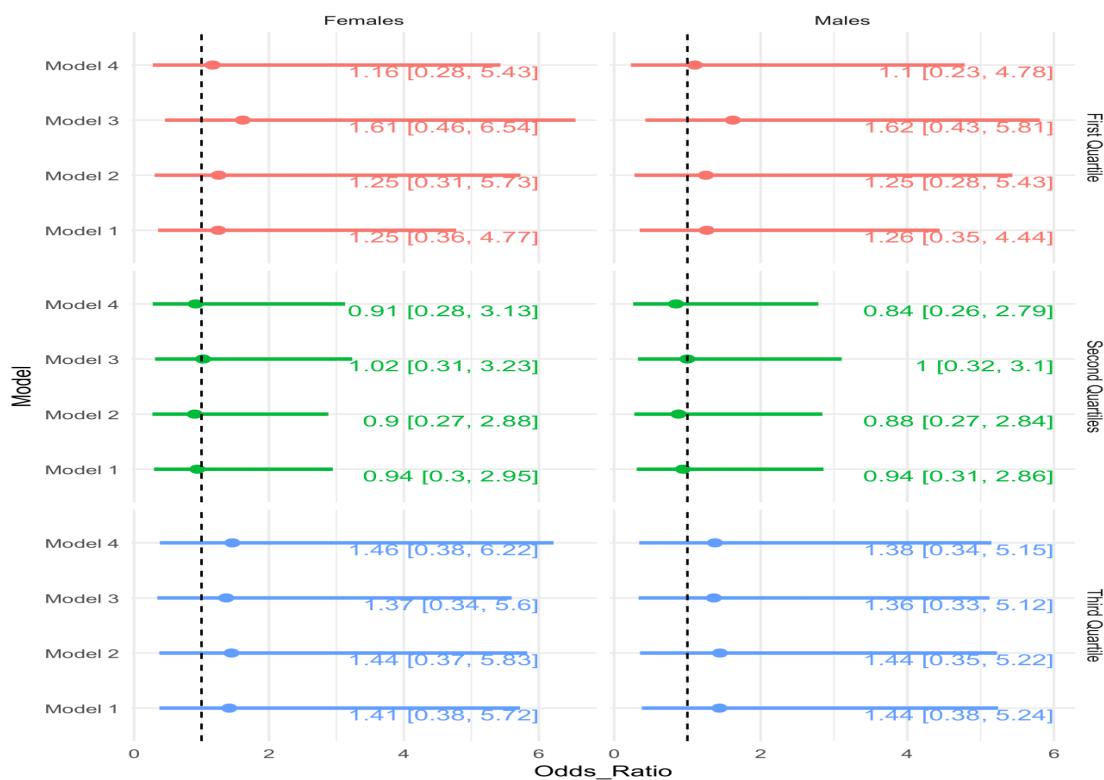


Figure 5: The Sex-specific Risk of Prediabetes Associated with Lower Quartiles of Calf Circumference Compared to the Fourth. Dashed lines represent odds ratio of Fourth Quartiles = 1. Model 1 = unadjusted model, Model 2 = controlled for body mass index, Model 3 = controlled for waist-to-hip ratio, Model 4 = controlled for both body mass index and waist-to-hip ratio. Values in brackets are 95% Credible Intervals

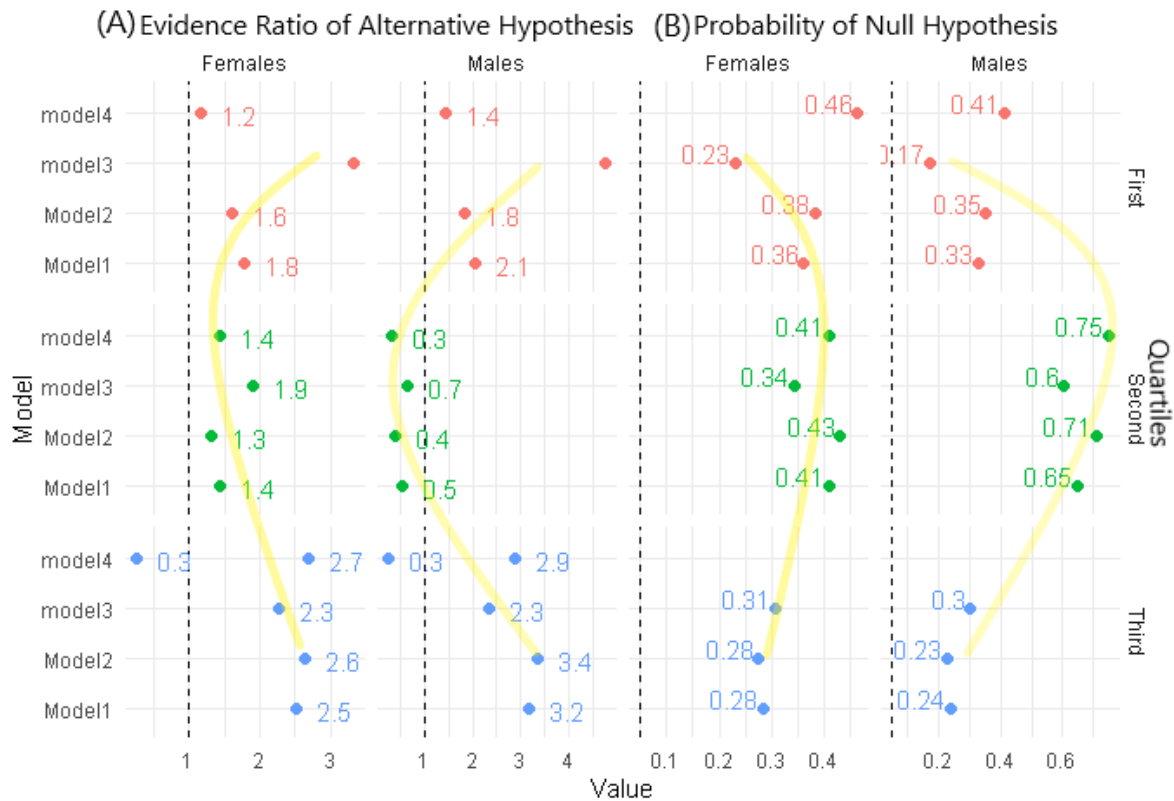


Figure 6: Sex-specific Evidence Ratio of the Alternative Hypothesis and Probability of Null Hypothesis for Prediabetes Risk of Calf Circumference. E.R = evidence ratio. Dashed lines represent null value of 1 for the evidence ratio plot (A) and 0.05 significance level for the probability plot (B). Yellow curve added to reveal a pattern

The Overall Risk of Prehypertension Associated with Lower Tertiles of Calf Circumference Compared to the Third

In the unadjusted model of the risk of prehypertension (Model 1), both 1st and 2nd tertiles of calf circumference were found to have lower odds of compared to the highest tertile (Figure 7). The null hypothesis of 1st tertile has probability of 0.93 with an alternative hypothesis evidence ratio of 0.1 i.e the null hypothesis was 10 times more probable than the alternative hypothesis (Figure 8). The corresponding null hypothesis

and evidence ratio of the unadjusted model for the 1st tertile were 0.36 and 0.6 (Figure 8). The adjusted models (Models 2-4) revealed a pattern similar to what was observed regarding the prediabetes risk; the 2nd tertile remained as the tertile with the lowest risk of prehypertension with the null hypothesis having a probability as high as 0.9 in Model 3 and being 10 times more probable than alternative hypothesis (Figures 7 & 8). The 1st tertile, on the other hand, had a null hypothesis with a probability as low as 0.18 and the alternative hypothesis being 4 times more likely than the null hypothesis (Figures 7 & 8).

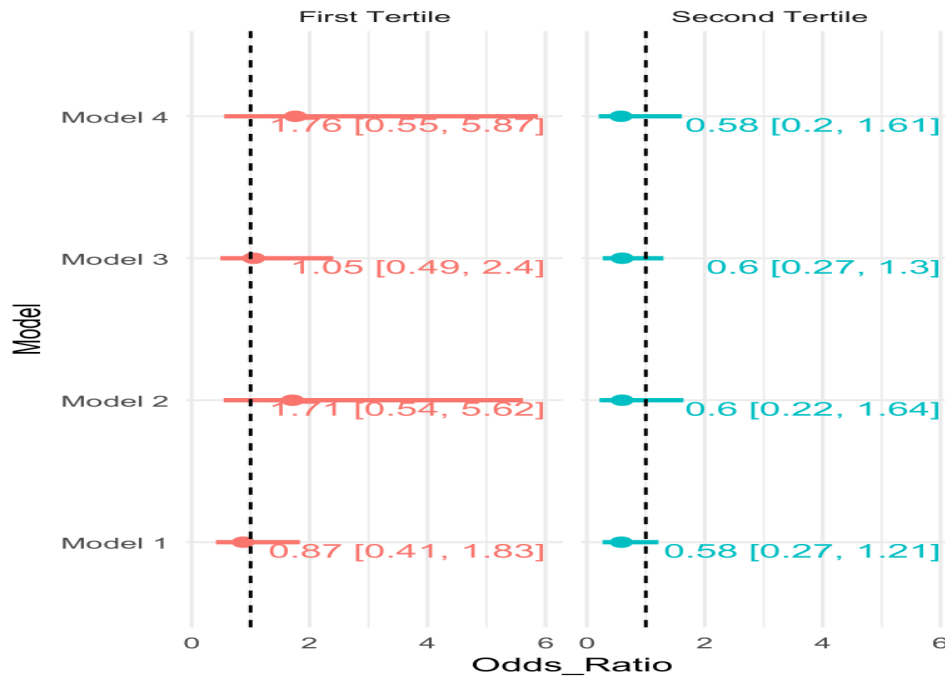


Figure 7: The Overall Risk of Prehypertension Associated with Lower Tertiles of Calf Circumference Compared to the Third. Dashed lines represent odds ratio of Third Tertiles = 1. Model 1 = unadjusted model, Model 2 = controlled for body mass index, Model 3 = controlled for waist-to-hip ratio, Model 4 = controlled for both body mass index and waist-to-hip ratio. Values in brackets are 95% Credible Intervals

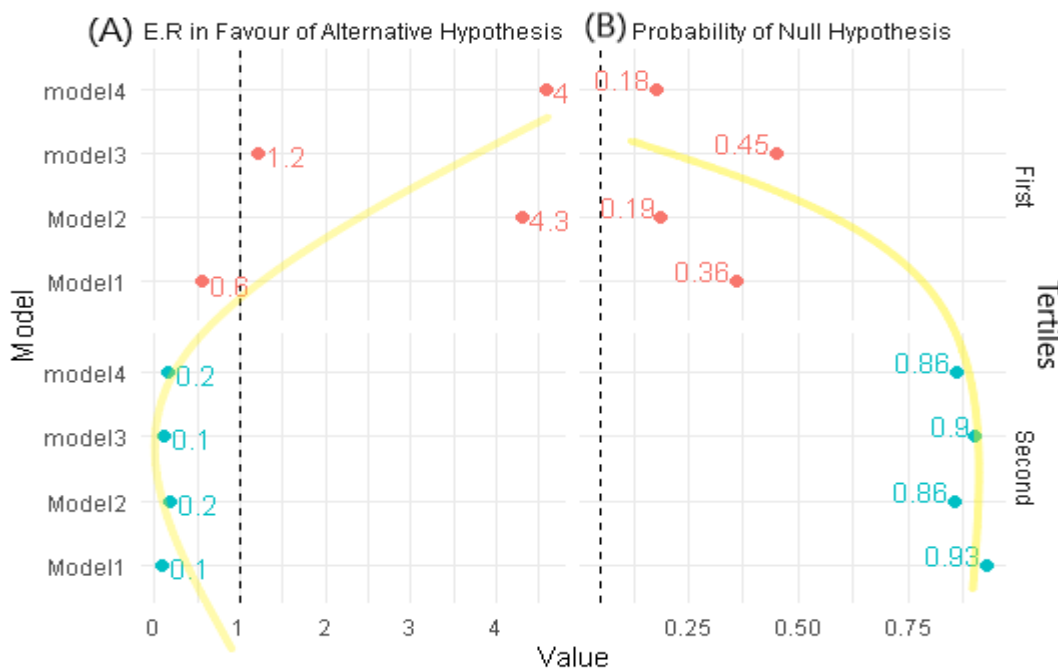


Figure 8: Overall Evidence Ratio of the Alternative Hypothesis and Probability of Null Hypothesis for Prehypertension Risk of Calf Circumference. E.R = evidence ratio. Dashed lines represent null value of 1 for the evidence ratio plot (A) and 0.05 significance level for the probability plot (B). Yellow curve added to reveal a pattern

The Sex-specific Risk of Prehypertension Associated with Lower Tertiles of Calf Circumference Compared to the Third

The analysis of the risk of prehypertension by sex revealed the same pattern observed during an overall analysis; the unadjusted model showing high probability for the null hypothesis and low evidence ratio in support of

alternative hypothesis for both lower tertiles of calf circumference (Figure 9 & 10). The adjusted models showed drastically reduced probability of null hypothesis for the 1st tertile in both sexes (0.17 and 0.16 for males and females in Model 4) and higher evidence ratio (5 for both sexes in Model 4) in support of alternative hypothesis (Figures 9 & 10).

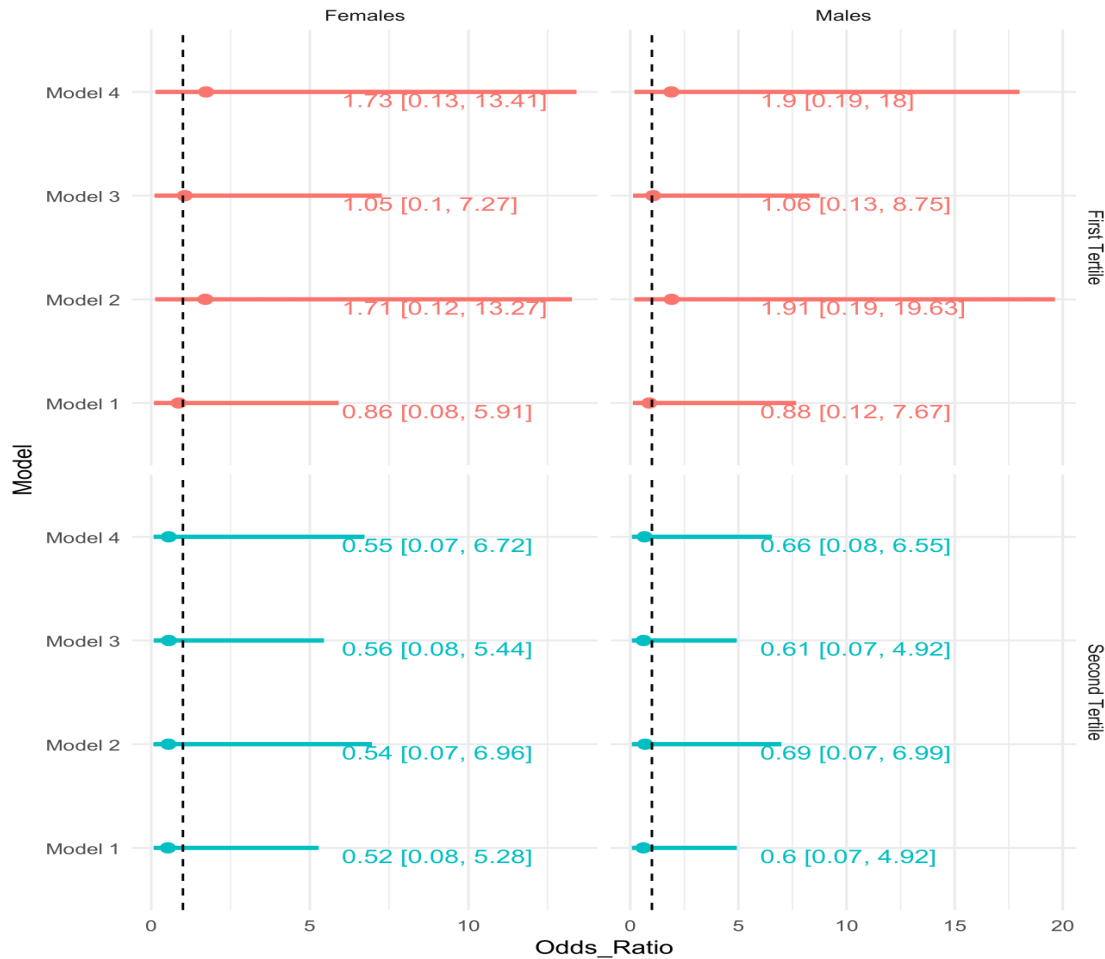


Figure 9: The Sex-specific Overall Risk of Prehypertension Associated with Lower Tertiles of Calf Circumference Compared to the Third. Dashed lines represent odds ratio of Third Tertiles = 1. Model 1 = unadjusted model, Model 2 = controlled for body mass index, Model 3 = controlled for waist-to-hip ratio, Model 4 = controlled for both body mass index and waist-to-hip ratio. Values in brackets are 95% Credible Intervals

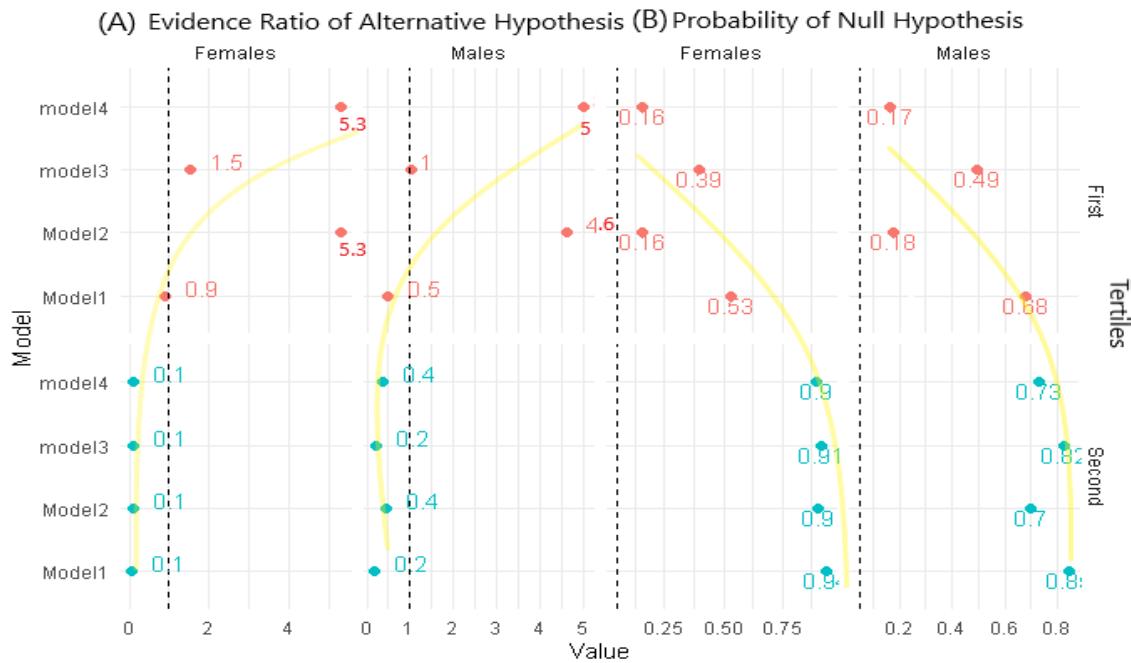


Figure 10: Sex-specific Evidence Ratio of the Alternative Hypothesis and Probability of Null Hypothesis for Prehypertension Risk of Calf Circumference. E.R = evidence ratio. Dashed lines represent null value of 1 for the evidence ratio plot (A) and 0.05 significance level for the probability plot (B). Yellow curve added to reveal a pattern

DISCUSSION

Across all the models tested (unadjusted and adjusted), the 1st and 3rd quartiles of calf circumference were found to have higher risk of prediabetes compared to the highest quartile just as the 1st tertile was found to have higher risk of prehypertension than the highest tertile. In both cases, the probability of the null hypothesis was too high to enable its rejection based on the chosen significance level (0.05). However, the alternative hypothesis was found to be consistently more probable across all the models for both prehypertension and prediabetes. This association of lower calf circumference with higher risk of prediabetes and prehypertension was similar to what was found among middle aged and elderly women in China (Bian et al., 2023) and in the analysis of data from the National Health and Nutrition Examination Survey (NHANES) sample from 1999 to 2006 (Jiajun et al., 2024)

The apparent protective role of calf circumference reported in this and previous studies might be due to the fact it measures peripheral subcutaneous fat (Schoettl et al., 2018) which was known to be protective against cardiovascular diseases. In particular, peripheral adiposity was found to have independent negative correlation with both

atherogenic metabolic risk factors and aortic calcification in elderly women (Tankó et al., 2003), with stiffness of brachial and carotid arteries in young men and women (Ferreira et al., 2004), with coronary atherosclerosis in both men and women (Hara et al., 2004), with insulin resistance and hypertriglyceridemia in post-menopausal women (Van Pelt et al., 2002) and with blood pressure and dyslipidemia in women (Williams et al., 1997). The biological plausibility of this finding resides in the biological properties of subcutaneous fat which include higher storage capacity thus making it more resistant to lipotoxicity and ‘lipid overflow’ phenomenon (Schoettl et al., 2018).

The current study revealed a second nadir for prediabetes risk in the 2nd quartile and for prehypertension risk in the 2nd tertile. This second nadir was consistent across all models tested and in both sexes. This suggested a non-linear relationship between calf circumference and the risk of prehypertension and prediabetes; the risk was lowest in the highest quartile/tertile and the 2nd quartile/tertile. This non-linear relationship between quartiles of calf circumference and risk of prediabetes differs from what was reported among type 2 diabetic South Korean (Park et al., 2012) and

Taiwanese elderly subjects (Hsiang et al., 2020). The disparity in the findings can be explained by the differences in the mean ages between current study and most other studies investigating cardiometabolic risk of calf circumference. While the mean age of the current study subject was 42 years most other studies were on elderly subjects ≥ 65 years. In the latter group of studies, a low calf circumference means either of two things:

- i. A low calf muscle mass which correlates strongly with low lean mass and sarcopenia (Kawakami et al., 2015) and
- ii. An age-related redistribution of body fat from the periphery to the central/visceral sites (Conte et al., 2019).

Both factors above signify higher cardiometabolic risk. However, in a much younger population both sarcopenia and age-related fat redistribution are comparably uncommon and low calf circumference is more likely to indicate a low peripheral and total body fat. To the extent that low calf circumference indicates low (protective) peripheral fat, it will predispose to cardiometabolic disease and to the extent that it indicates low total body fat, it will be protective against cardiometabolic disease. This might explain the non-linear relationship found in the current study. The practical implication for this observation is that cut off values for calf circumference should be set lower in the younger populations.

CONCLUSIONS AND RECOMMENDATIONS

This study found a non-linear relationship between calf circumference and risk of prediabetes and prehypertension; the risk being highest in the 1st tertile/quartile and lowest in the 2nd and 4th tertiles/quartiles contrary to what was reported in elderly populations where lower tertiles/quartiles were consistently associated with higher cardiometabolic risk compared to the highest tertile/quartile. This suggests a need for a lower cut off value for calf circumference in younger populations.

This study has a number of strengths which include the use of Bayesian paradigm allowing us to make explicit statements about the probabilities of null and alternative hypotheses. This allowed a more intuitive interpretation of the findings compared to the

frequentist traditions. Additionally, the control of age at the level of the study design enabled us to avoid controlling for age at the level of analysis removing the risk of poor representation of some age groups in either the cases or control groups.

The study has a number of limitations as well. The probabilities of null hypotheses tested were too high and above the significance level of 0.05 for all the odds ratios reported even though this could have been remedied by a larger sample size. Secondly, the study subjects were not representative of the general population thereby limiting us from generalizing the findings.

It is recommended that future studies, preferably longitudinal and using larger sample sizes and involving a more representative sample of the general population, should be conducted to confirm the findings indicated in the present study. Such a confirmation will enable integrating calf circumference as a cheap, easy and non-invasive screening tools into cost-effective public health measures and programs to prevent prediabetes and prehypertension and thus progression to diabetes and hypertension. This will go a long way in reducing the burden of cardiovascular diseases in the country.

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