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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.

Designs: Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in 2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socio-economic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses.

Results: The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high HDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, most prevalent in participants above 45 years of age. Low-HDL-C was most prevalent among participants ≥18 to < 45 years old, while high LDL-C was more prevalent above 45 years. BMI, WC and BF% were associated with hypertension (OR=2.41 (1.33, 4.47); OR=3.68 (1.81, 7.52); OR=2.51 (1.40, 4.51), respectively). High WC or high BF% was associated with higher chances of high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). Considering obesity indices within one regression model, only high WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). **Conclusion**: High BMI, WC and BF% were strongly

associated with hypertension, individuals with high WC were twice more likely to have hypertension. Overweight/obesity and cardio-metabolic risk factors were highly prevalent in the present study population which calls for early and effective screening strategies for this population.

Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa

Strengths and limitations of this study

- This is the first study to report the associations between obesity indices with cardio-metabolic risk factors in Zanzibar.
- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate, thus minimise risk of selection bias
- The cross-sectional design hindered us from concluding the impact of changes in obesity indices on risk factors
- Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage which might have underestimated adiposity in children.

Introduction

Worldwide, cardiovascular diseases (CVDs) are the leading cause of death in individuals above 45 years of age [1] at least three quarters of the world's deaths from CVDs occur in low-and-middle-income countries (LMIC) [2] and CVDs are emerging as notable public health problem in sub-Saharan Africa [3]. These countries are undergoing epidemiological transition from communicable to non-communiable diseases (NCDs), which has been closely linked to increased urbanization and rural-urban migration which leads to unhealthy behaviours including poor dietary habits and sedentary lifestyles [3 4]. Most LMIC are dealing with a double burden of coexistance of underweight children and overweight/obese adults [5], thus making it particulary difficult for policy makers to address the diverse population needs. Obesity is one of the global public health problems that is associated with CVDs [6]. Data from mainland Tanzania showed increasing prevalence of overweight and obesity in urban, peri-urban and rural areas [7]. According to the International Diabetes Federation (IDF) about 12 million people are estimated to have type 2 diabetes mellitus in Africa [8], where the prevalence ranged from 1% in rural Uganda to 12 % in urban Kenya [9 10]. Overweight and obesity have been identified to be modifiable risk factors for cardio-metabolic and other chronic diseases [11] including hypertension [12], diabetes [13] and dyslipidemia [14]. Previous research [15 16] reported that both total body fat and adipose tissue distribution were associated with cardio-metabolic risk. Previous studies from sub-Saharan African countries described high prevalences of obesity and cardio-metabolic risk factors in adults in rural and urban areas [11]. Also associations between cardio-metabolic risk factors and socio-economic status (SES), urbanisation and lifestyle patterns in adults were found to be low [3]. However, there is still a dearth of pupulation-based studies in sub-Saharan Africa investigating these associations with multiple cardio-metabolic risk factors and different obesity indices including body fat percent, e.g. in both Tanzania mainland and Zanzibar Island.

Thus, based on cross-sectional data of 470 individuals between 5-95 years recruited in 2013 in Unguja Island, Zanzibar, this study first describes the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups (≥5 to <18 years, ≥18 to < 45 years and above 45 years), and secondly investigates the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, Glycated HbA1c, fasting plasma glucose and HOMA-IR) considering either three obesity indices independently as well as BMI, WC, and BF% combined reflecting different aspects of body composition.

Subjects and Methods

Study population and design

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selecetd and all household members were invited for the examination. 1,443 family members were willing to participate and completed anthropometric and blood pressure measurements, interviewer-administered questionnaires, collection of morning spot urine and venous blood; detailed subgroup examinations were descibed below. The complete description of the study design and methods has been described in detail elsewhere [17]. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave a written consent and parents/guardians gave a written consent on behalf of their children.

Patient and Public Involvement

Patients were not involved in this study.

Questionnaires and anthropometric measurements

Questionnaires were developed in English, translated into Swahili, and then back-translated to controll for translation errors. Parents reported age and sex of their children and of themselves. Age was grouped into three categories ≥5 to <18 years, ≥18 to <45 years and 45 years and above. In addition, their highest educational level according to the International Standard Classification of Education (ISCED) [18] was used as a proxy indicator for socio-

economic status (SES) of the family and categorized into low education (no education and primary school) and high education (secondary school and above). For assessing area of residence of the participants, information on region, district and Shehia (the smallest administrative unit in Zanzibar) were recorded and two categories for area of residence were developed (urban and rural). For quality data collection, this study used proven examination methods and laboratory standards [19 20]. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures [21 22]. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using (SECA 213 stadiometer. UK) and waist circumference (WC) was measured using an inelastic measuring tape (SECA 201) midway between the lowest rib and the iliac creast, all measurements were taken over light clothing and on standing position and were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study have been described elsewhere [17].

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m^2 and then transformed to age-and sex-specific z-score and percentiles as well as categories for overweight (BMI between >75th and <95th percentile) and obesity (BMI >95th percentile) according to the WHO centile curves [23 24]. For adults, overweight/obesity was defined as BMI ≥25kg/m^2 as recommended by WHO [25]. Considering waist circumference (WC), high abdominal obesity was defined as (WC ≥90th percentile) for children below 10 years [26], WC ≥90th percentile for adolescents below 16 years and WC >94 cm for men and > 80 cm for women for participants above 16 years as recommended by IDF [27]. Body fat percentage (BF%) was categorized as high according to the ≥85th percentile with regard to boys and girls below 18 years as recommended by McCarthy et al. [28]. For adults above 18 years, high

BF% was categorised as ≥20 for men and ≥32 for women [29]. The cut-offs and references are listed in Table 1 below.

Cardio-metabolic risk factors

Fasting blood samples were collected from all eligible participants over 5 years of age by venepuncture [30], detailed procedures about the collection, processing and storage of blood samples are described elsewhere [17]. Anthropometric measurements and collection of venous blood was carried out in fasting status and processed according to international standards [20]. Not being in fasting status was recorded using anthropometry documentation sheet. Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study popluation. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Trigylcerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)) and blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG) were defined according to the IDEFICS Study [26 31] and Glycated hemoglobin (HbA1c) was defined according to Rodoo et al. [32] for children under 17 years. For children, adolescence and adults from 10 years and above, hypertension was defined according to age-sex-specific cut-offs as recommended [33] we used this cut-off for children between 10 and 18 years only and for adult above 18 years hypertension was defined as recommended [34]. Blood lipids (TC and LDL-C) were defined according to National Cholesterol Education Program (NCEP) [35] and TG, HDL-C and FPG

were defined according to International Diabetes Federation (IDF) [27] . HbA1c for adults above 17 years was defined according to Stern et al. [36] and insulin resistance was estimated as HOMA-IR according to reference value of HOMA-IR as recommended by Shashaj et al. [37]. In the present study, 75th percentile cut-off was used for children and adolescents from 10 till 17 years and for participants above 17 years, HOMA-IR was defined according to von Eyben et al [38]. HOMA-IR was calculated from glucose (mmol/l)) and insulin (μU/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)[39].

Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children: ≤10y	BMI ≥75th percentile [1]	TC ≥90th percentile [2]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [2]	TG ≥90th percentile [2]	HOMA-IR ≥ 95th percentile [2]
	BF %≥85th percentile [3]	HDL-C ≤ 10th percentile [2]	FPG ≥ 95th percentile [2]
	SBP≥90th centile or DBP ≥90th centile [2]	LDL ≥90th percentile [2]	
Adolescents: >10 to <16 y	BMI ≥ 75th percentile [1]	TC ≥5.2 mmol/L [6]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [4]	TG ≥1.7mmol/L [4]	HOMA-IR ≥75th percentile [9]
	BF %≥85th percentile [3]	HDL-C < 1.03 [4]	FPG ≥ 5.6mmol/L [4]
	SBP≥140mmHg or DBP≥90mmHg [11]	LDL ≥3.4mmol/L [6]	
Adults: ≥16y	BMI ≥ 25 kg/m[1]	TC ≥5.2 mmol/l [6]	HbA1c ≥ 6.1% [5]
	WC ≥ 94 cm male, ≥80cm female [4]	TG ≥1.7mmol/L,[4]	HOMA-IR >4.65 or HOMA-IR >3.60 and BMI >27.5 kg/m[2] [7]
	BF % ≥ 20 male and ≥32 female [8]	HDL-C < 1.03 male,< 1.29 female [4]	FPG ≥ 5.6mmol/L[4]
	SBP≥140mmHg or DBP≥90mmHg [12]	LDL ≥3.4mmol/L [6]	

1 WHO
2 IDEFICS Study
3 McCarthy, H.D., et al. (2006)

4 IDF
5 Stern, S.E., et al (2003) for adults above 17 years
6 NCEP
7 von Eyben, F.E., et al (2005)
8 Gallagher, D., et al (200)
9 Shashaj et al. (2015)for children and adolescence under 17 years
10 Rodoo P et al. (2013)
11, 12 National Institute of Health 3rd and 7th report respectively

Inclusion criteria for study sample

Out of 1,443 individuals who participated in this study, 1,314 fullfilled the inclusion criteria (age, sex, weight, height) for the oeverall study analysis. Of the 1,314 participants, 1,234 provided complete waist circumference and body fat percent measurements. Among those, 557 provided complete blood samples for the cardio-metabolic risk analysis and out of those only 505 were on fasting status. Top 1% was excluded for cardio-metabolic risk and obesity indices variables with high extreme values, thus remaining with a complete sample size of 470 participants included in the analysis.

Statistical analysis

Descriptive analyses were conducted to calcuate mean standard deviation (SD) and range (minimum, maximum) for continuous variables as well as distribution of the categorical data in N and percentages (%). Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure in Zanzibar, we conducted sensitivity analysis modeling either shehias or households within shehias as a random intercept in the models. Since results of the models showed only marginal differences, we only considered household as a random intercept in our analyses. First, logistic regression models were calculated separately for each obesity indicator (BMI, WC and BF%) as exposure variables against each of the risk factors

(hypertension, TC, TG, HDL-C, LDL-C, HbA1C, FPG and HOMA-IR) as dependent variables. Since BMI, WC and BF% are interrelated, their predictive power on cardio-metabolic risk factors was investigated in a regression model considering all obesity indices against each of the risk factors. All models were adjusted for potential confounders such as gender, age, education level (ISCED) and area of residence, while with regard to hypertension, utilization of medication was also included in the analysis. Statistical analyses were performed using SAS 9.3 (SAS Institute. Cary. NC. U SA) and particularly mixed logistic regression models were conducted based on the GLIMMIX procedure.

Results

Characteristics of study population

General characteristics of the study sample (N=470) are described in Table 2. Mean age was 29 (±18) years with the highest proportion of participants from the age group (≥18 to <45 years). The overall mean BMI was 22 (± 5.2)kg/m^2, WC was 75 (± 16) cm and BF% was 22 (± 11) %, the mean BMI 26 (± 5.7)kg/m^2 for participants above 45 years was slightly higher than normal indicating overweight. Mean diastolic blood pressure was on normal range for all the age groups, a higher mean value of systolic blood pressure 150 (± 280)mmHg was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR) which showed no specific trend.

Table 2: characteristics of study population (n=470) in terms of means and standard deviation (SD) and range.

	≥5 to <18 years (n=165)		≥18 to <45 years (n=195)		45+years (n=110)		Total (n=470)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53
DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

Distribution of obesity and cardio-metabolic risk in the study population by age groups

Table 3 shows the distribution of obesity markers and cardio-metabolic risks by age-group. Of the 470 participants, more than half were women 52.6% (n=247). The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively and increased with age, where the highest proportions were observed in participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups: the prevelance of hypertension, total cholesterol, LDL-C and HbA1c increased with age except for trigylcerides and HOMA-IR which decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%), raised LDL-C (21.3%) and HbA1c levels (19.1%). Hypertension, LDL-C and HbA1c were more prevalent in participants above 45 years, and low HDL-C was most prevalent among ≥18 to <45 year olds.

Table 3: Distribution of obesity and cardio-metabolic risk in the study population by age group, n=470.

	≥5 to <18 years		**≥18 to <45 years**		**45+ years**		**Total**	
	n	(%)	n	(%)	n	(%)	n	(%)
All	165	(100)	195	(100)	110	(100)	470	(100)
Gender								
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
High [a]	0	(0)	54	(27.7)	63	(57.3)	117	(24.9)
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0)
High [b]	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1)
Hypertension								
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5)
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1)
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5)
Dyslipidaemia [c]								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9)
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11)
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3)
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68)
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5)
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4)
LDL-cholesterol								
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7)
High	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3)
Diabetes Markers [d]								
HbA1C								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)

[a] High WC was defined as WC ≥90th percentile for children under 10y [26]. Adolescents between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off [27]

[b] High BF% for adults (overweight/obese)≥ 20 for men and ≥32 for women according to (NIH/WHO) BMI guidelines [29] and ≥85th percentile for children [28]

[c] High dyslipidemia for adults; was defined as total serum cholesterol (≥6.2mmol/l) and LDL-cholesterol (≥3.4mmol/l) [35] low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in

women high and hypertriglyceridemia (≥1.7 mmol/l) [27] and for children according to IDEFICS study [26]

[d] High diabetes risk markers; high HbA1C (>6.1%) [38], high fasting plasma glucose (≥5.6 mmol/l) [27] and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [36] and for children high HbA1c (≥97.5th percentile), high fasting plasma glucose ≥95th percentile and HOMA-IR ≥95th percentile.

Association between obesity indices and cardio-metabolic risk factors

Results of the mixed logistic regression models are presented in Table 4. Obesity indices (BMI, WC and BF %) were found to be associated with one or more risk factors. Participants having high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52)) or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive. Having high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) were associated with higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C, elevated glucose and HOMA-IR. Due to a very small sample in HOMA-IR, the results were omitted. Looking at goodness of fit of the the models, the AIC values showed that models including WC as an obesity index tend to have a slightly stronger predictive power compared to models including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and medication (for hypertension only) (n=470)

Obesity indices	High BMI			High WC			High BF%		
Risk factors	OR	(95% CI)	AIC	OR	(95% CI)	AIC	OR	(95% CI)	AIC

Hypertension	**2.41**	**1.33**	**4.47**	**504.86**	**3.68**	**1.81**	**7.52**	**499.79**	**2.51**	**1.40**	**4.51**	**503.46**
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Trigycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	**2.52**	**1.24**	**5.13**	**452.23**	**1.91**	**1.02**	**3.58**	**454.77**
High HbA1c	**2.08**	**1.15**	**3.79**	**442.70**	**3.01**	**1.51**	**6.03**	**438.53**	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC again was associated with a higher chance of hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)).

Table 5: Associations between obesity indices (independent) and cardio-metabolic risk factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

	Combined Obesity Indices									**AIC total**
Obesity indices	**BMI**			**WC**			**BF%**			
Risk Factors	**OR**	**(95% CI)**		**OR**	**(95% CI)**		**OR**	**(95% CI)**		
Hypertension	1.19	0.48	2.95	**2.62**	**1.1**	**6.06**	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	**2.62**	**1.1**	**6.15**	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6

Discussion

This study is the first population–based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) with multiple cardio-metabolic risk factors in a representative Zanzibari population, aged between 5-95 years. This study population, like in many other LMICs is undergoing a coesxistance of a double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age, this has also been reported in demographic health surveys from seven sub-Saharan African countries [40]. In the adult population, the prevalence of overweight/obesity was lower than the prevalence reported for example in Ghana [11] but higher than that reported in Nigeria [3] and Benin [41]. In parralel, more than 50% of the children in this study were underweight, which is higher than the reported prevalence in other sub-Sharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon) [42].

Dyslipidemia is a risk for variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particulary in terms of low HDL-C [43 44]. Despite the relatively normal levels of total cholesterol and trigylcerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C afffects a large proportion of adults above 18 years,this is in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C [45]; other studies in sub-Saharan Africa reported even a higher prevalence of 43.1% in Nigeria [3] and 80% in Botswana [46], mostly affecting individuals between 35-54 years.

In the present study, high proportion of participants with high HbA1c (14.1%) and elevated fasting glucose (18%) are children below 18 years; since diabetes in children in LMICs has not been given much attention, there is a high chance of having more children with sub-

clinical complications due to delayed or missed diagnosis and lack of frequent monitoring. The high proportions in this study could be due to the fact that majority of the diabetic participants are not aware of their status and are not monitored or treated. However, when using WHO diabetes diagnostic criteria [47], i.e. HbA1c cut-off ≥6.5% and FPG ≥7.0mmol/l, the prevalence of diabetes in participants above 18 years reduced to 8.14% and 3.05%, respectively (data not shown). The most intriguing result is the risk for diabetes and/or diabetic in children below 18 years when screened by elevated fasting glucose levels ≥5.6mmol/l, as recommended by IDF [27]. In this study, the prevalence is higher than that of adults above 18 years but less than adults above 45 years. This could be due to both a) misreporting (children did not report having eaten prior to the blood drawing) and b) a true high risk within this age group. However, when using WHO [47] diabetes diagnostic criteria (FPG ≥7mmol/l) for the same age group, the prevalence reduced to 0.61% (data not shown). This indicates, that majority of the children are at risk for diabetes and that the cut-off for HbA1c ≥6.1% as well as elevated FPG≥5.6 mmol/l seem to be better screening tools in identyfing those at risk earlier.

Our study showed that there is an association between BMI, WC and BF% with major cardio-metabolic risk factors in the study population. These findings are in agreement with other studies who also reported the association between hypertension/pre-hypertension, BMI and WC [48] as well as BF% [11]. This study also observed a strong association between WC and LDL-C levels, similar association has also beenreported in a comperative cross-sectional study in Ghana by Obirikorang [11]. In the separate models, strong associations were observed between BMI and WC with HbA1c levels, which could be explained by the interrelation of the two indices, since abdominal fat accumulation is increased in proportion to BMI [49] and BMI is one of the main risk factors for diabetes and pre-diabetes [50 51]. However, considering

the association of all three obesity indices, only the strong associations of WC with HbA1c levels and hypertension remained.

This study has some limititations that should be considered. First, we were only able to investigate the association between obesity indices and risk factors using cross-sectional data, thus the impact of changes in obesity indices on risk factors could not be considered. Second, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage as many epidemiological studies and clinical trials. Still, BIA measurements compared to skinfold measurements may underestimate adiposity in children [52] Third, even though participants who reported food or beverage intake prior to blood drawing were excluded during the data cleaning process, we can not entirely exclude misreporting of "fasting status".

The main strengths of the present study are; the random selection of the study participants, and the standardised assessment of anthropometrical and laboratory measurements. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group rather than applying the fixed cut-offs used in the adult population. There is little information on the association of multiple obesity indices with multiple cardio-metabolic risk factors in this population, hence this study to our knowledge is the first to report such associations in the Island of Unguja in Zanzibar.

Conclusion

This study adds up to the literature that obesity is associated with higher risks for having hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. For similar epidemiological studies incuding children, adolescents, adults and elderly, we suggest to set diabetes and/or pre-diabetes cut-offs of HbA1c at ≥6.1% and/or elevated fasting glucose at ≥5.6mmol/l. The study also suggests, when feasible, using BF% and WC besides BMI in screening and health monitoring for dyslipedemia and hypertension. We further conclude, there is a need for effective interventions to create awareness and a need for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island using local multidiscipinary approaches in the local language, Swahili. Addidionally, health surveillance initiatives, targeting in particular the age group ≥18 to <45 years will help to monitor prevention activities in future.

List of Abbreviations

BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
HbA1c	Glycated Haemoglobin
HDL-C	High Density-Lipoprotein Cholesterol
HOMA-IR	homeostasis model assessment of insulin resistance
IDEFICS	Identification and prevention of Dietary-and lifestyle-induced health EFects In Children and infantS
IDF	International Diabetes Federation
ISCED	International Standard Classification of Education
LDL-C	Low Density-Lipoprotein Cholesterol
LMICs	Low-middle-Income Countries
NCDs	Non-Communicable Diseases
WC	Waist Circumference
WHO	World Health Organization

Declarations

Ethics Approval and Consent to participate

Ethical approval was obtained from the Ethics Committees of the University of Bremen in Germany with a reference number 06-3 and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee in Zanzibar, Tanzania with a reference number ZAMREC/0001/AUGUST/013. Written informed consents were taken from all participants and parents/guardians gave a written informed consent for their children. The consent forms were approved by the Institutional Ethics Committee.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

The authors' responsibilities were as follows: AH and SK were responsible for study design. AH and MAN conducted data collection and developed study hypothesis. MAN and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN wrote the manuscript and had primary responsibility for final content. MN,CB,SK,MS,KB and AH critically revised the manuscript and gave final consent.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available since a follow-up study is planned.

Consent for publication

All participants agreed and signed that; the data collected during the survey can be stored and used for future analysis.

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.

Designs: Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in 2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socio-economic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

Results: The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants ≥18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). **Conclusion**: High BMI, WC

and BF% were strongly associated with hypertension, with individuals with high WC being twice more likely to have hypertension; this calls for early and effective screening strategies for this study population.

Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa

Strengths and limitations of this study

- This is the first study to report the associations between obesity indices and cardio-metabolic risk factors in Zanzibar.
- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate, thus minimising risk of selection bias.
- The cross-sectional design prevents us from drawing conclusions regarding the impact of changes in obesity indices on risk factors.
- Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which might have underestimated adiposity in children.

Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death[1], they are also emerging as a notable public health problem in sub-Saharan African countries [2]. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles [2 3]. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus [4], with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya [5 6]. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases [7] including hypertension [8], diabetes [9] and dyslipidemia [10]. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors[11].

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardio-metabolic risk in clinical and research settings[12-14] due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population[13 15]. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status [16], which is linked to metabolic risk, e.g. in South African youth[17]. However, BMI does not distinguish well between lean mass and fat mass[18]. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The

correlation on the other hand varies significantly across ethnicities [19 20]. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies[21]. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings [22 23].

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations [2 7 18]. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas [24]. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups (≥5 to <18 years, ≥18 to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

Subjects and Methods

Study population and design

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere [25]. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of minors in writing.

Patient and Public Involvement

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting.

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study.

This observational epidemiological study examined participants in their home environment and did not enrol clinical patients.

Questionnaires and anthropometric measurements

Questionnaires were developed in English, translated into Swahili, and then back-translated to control for translation errors. Information was collected during an interviewer administered personal interview conducted by trained survey staff. Parents reported their age and sex, as well as of their children. Age was grouped into three categories ≥5 to <18 years, ≥18 to <45 years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) [26] was used as a proxy indicator for socio-economic status (SES) of the family. It was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented

in the questionnaire. Regarding medication for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoprotenemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards [27 28]. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures [29 30]. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing and were standing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere [25].

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m^2 and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between >75th and <95th percentile) and obesity (BMI >95th percentile) were built according to the WHO centile curves [31 32]. For adults, overweight/obesity was defined as BMI ≥25kg/m^2 as recommended by WHO [33]. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight (≤ 75th percentile for children and adolescents and < 25kg/m^2 for adults) and 2) overweight/obesity (>75th percentile and ≥25kg/m^2). Regarding waist circumference (WC), high abdominal obesity was defined as WC ≥90th percentile for children below 10 years [34];WC ≥90th percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF [35]. As recommended by

McCarthy et al. [36], for boys and girls below 18 years, high body fat percentage (BF%) was set at ≥85th percentile. For adults above 18 years, high BF% was defined as ≥20 % for men and ≥32 % for women [37]. The cut-offs and references are listed in Table 1.

Cardio-metabolic risk factors

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture [38]. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. All blood samples collected at the field were kept at 4°C and the processing was performed immediately at the laboratory in Zanzibar, according to international standards[28]. EDTA Blood was centrifuged for 10 minutes at 2500g and then separated into 3 aliquots; plasma, red blood cells (RBC) and white blood cells (WBC), which were then stored at -80 °C. Detailed procedures about the collection, processing and storage of blood samples are described elsewhere [25].

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of

Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study [34 39]. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. [40] for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as recommended [41]; for adolescents and adults above 16 years hypertension was defined as recommended [42]. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP) [11] and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) [35]. HbA1c for participants above 17 years was defined according to Stern et al. [43] and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. [44]. In the present study, the 75th percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al [45]. HOMA-IR was calculated from glucose (mmol/l)) and insulin (µU/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)[46].

Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children: ≤10y	BMI ≥75th percentile [1]	TC ≥90th percentile [2]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [2]	TG ≥90th percentile [2]	HOMA-IR ≥ 95th percentile [2]
	BF %≥85th percentile [3]	HDL-C ≤ 10th percentile [2]	FPG ≥ 95th percentile [2]
	SBP≥90th centile or DBP ≥90th centile [2]	LDL ≥90th percentile [2]	
Adolescents: >10 to <16 y	BMI ≥ 75th percentile [1]	TC ≥5.2 mmol/L [6]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [4]	TG ≥1.7mmol/L [4]	HOMA-IR ≥75th percentile [9]
	BF %≥85th percentile [3]	HDL-C < 1.03 [4]	FPG ≥ 5.6mmol/L [4]
	SBP≥140mmHg or	LDL ≥3.4mmol/L [6]	

	DBP≥90mmHg [11]		
Adults: ≥16y	BMI ≥ 25 kg/m[1]	TC ≥5.2 mmol/l [6]	HbA1c ≥ 6.1% [5]
	WC ≥ 94 cm male, ≥80cm female [4]	TG ≥1.7mmol/L,[4]	HOMA-IR >4.65 or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [7]
	BF % ≥ 20 % male and ≥32 % female [8]	HDL-C < 1.03 male,< 1.29 female [4]	FPG ≥ 5.6mmol/L[4]
	SBP≥140mmHg or DBP≥90mmHg [12]	LDL ≥3.4mmol/L [6]	

1 WHO
2 IDEFICS Study
3 McCarthy, H.D., et al. (2006)
4 IDF
5 Stern, S.E., et al (2003) for adults above 17 years
6 NCEP
7 von Eyben, F.E., et al (2005)
8 Gallagher, D., et al (200)
9 Shashaj et al. (2015) for children and adolescents under 17 years
10 Rodoo P et al. (2013)
11, 12 National Institute of Health 3rd and 7th report respectively

Inclusion criteria for study sample

Of 1,443 individuals who participated in this study, 1,314 fulfilled the inclusion criteria (age, sex, weight, height) for the overall study analysis. Of the 1,314, 1,234 provided complete waist circumference and body fat percent measurements. Among these, 557 provided complete blood samples for the cardio-metabolic risk analysis and only 505 were on fasting status. To reduce bias when estimating mean and SD in the regression analysis, we excluded the top 1% of individuals with extremely high values for cardio-metabolic risk and obesity indices, leaving us with a complete sample of 470 participants for the analysis.

Statistical analysis

Descriptive analysis was conducted to calculate the mean standard deviation (SD) and range (minimum, maximum) for continuous variables, as well as the distribution of the categorical

data in N and percentages (%). As part of the regression analysis, we tested the necessary assumptions in terms of symmetry and normality using residual-plots and Q-Q-Plots. Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, their predictive power on cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at $\alpha = 0.05$.

Results

Distribution of obesity and cardio-metabolic risk and characteristics of the study population by age groups (n=470)

The mean age was 29 (±18) years, with the highest proportion being in the age group (≥18 to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m^2, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7) kg/m^2 for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure, 150 (± 280) mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend.

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had a higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with a higher education level were aged ≥18-<45 years (150/244 = 61%) (Table 3).

Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by age group (means and standard deviation (SD))

	≥5 to <18 years (n=165)		≥18 to <45 years (n=195)		45+years (n=110)		Total (n=470)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53

DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among ≥18 to <45 year olds.

Table 3: Characteristics of the study population (n=470) by age group (n/%)

	≥5 to <18 years		**≥18 to <45 years**		**45+ years**		**Total**	
	n	(%)	n	(%)	n	(%)	n	(%)
All	165	(100)	195	(100)	110	(100)	470	(100)
Gender								
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1)
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9)
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6)
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4)
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)
High [a]	0	(0)	54	(27.7)	63	(57.3)	117	(24.9)
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0)
High [b]	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1)
Hypertension								
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5)
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1)
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5)
Hypertension medication[c]								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02)
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0)
Dyslipidaemia [d]								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9)
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11)
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3)
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68)
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5)
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4)
LDL-cholesterol								
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7)
High	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Diabetes Markers [e]								
HbA1c								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)

[a] High WC was defined as WC ≥90th percentile for children under 10y [34]. Adolescents between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off [35]

[b] High BF% for adults (overweight/obese)≥ 20 for men and ≥32 for women according to (NIH/WHO) BMI guidelines [37] and ≥85th percentile for children [36]

[c] Missing information from 12 participants (n=458)

[d] High dyslipidemia for adults; was defined as total serum cholesterol (≥6.2mmol/l) and LDL-cholesterol (≥3.4mmol/l) [11] low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in women high and hypertriglyceridemia (≥1.7 mmol/l) [35] and for children according to IDEFICS study [34]

[e] High diabetes risk markers; high HbA1c (>6.1%) [45], high fasting plasma glucose (≥5.6 mmol/l) [35] and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [43] and for children high HbA1c (≥97.5th percentile), high fasting plasma glucose ≥95th percentile and HOMA-IR ≥95th percentile.

Association between obesity indices and cardio-metabolic risk factors

Obesity indices (BMI, WC and BF %) were observed to be associated with one or more risk factors. Participants with high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52)) or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive (Table 4). Having high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) was associated with higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C, elevated glucose and HOMA-IR. As the proportion of individuals with high HOMA-IR was

very small in our sample (1,28%/n=6), the results was not considered in the final regression analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion (AIC), which estimates the quality of each model relative to that of each of the other models, showed that models including WC as an obesity index tended to have a slightly stronger predictive power compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices	**High BMI**				**High WC**				**High BF%**			
Risk factors	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**
Hypertension	**2.41**	**1.33**	**4.47**	**504.86**	**3.68**	**1.81**	**7.52**	**499.79**	**2.51**	**1.40**	**4.51**	**503.46**
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	**2.52**	**1.24**	**5.13**	**452.23**	**1.91**	**1.02**	**3.58**	**454.77**
High HbA1c	**2.08**	**1.15**	**3.79**	**442.70**	**3.01**	**1.51**	**6.03**	**438.53**	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR (1,28%/n=6), the results are not shown was very small, it was not considered in the final regression analysis. in our sample.

Table 5: Associations between obesity indices (independent) and cardio-metabolic risk factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

	Combined Obesity Indices									AIC total
Obesity indices	**BMI**			**WC**			**BF%**			
Risk Factors	**OR**	**(95% CI)**		**OR**	**(95% CI)**		**OR**	**(95% CI)**		
Hypertension	1.19	0.48	2.95	**2.62**	**1.1**	**6.06**	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	**2.62**	**1.1**	**6.15**	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6

Discussion

This study is the first population–based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population was overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries [47]. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana [7], but higher than in Nigeria [2] and Benin [48]. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon) [49].

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C [50 51]. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years. As HDL-C plays a key role in reverse cholesterol transport, has anti-thrombotic, anti-inflammatory and anti-oxidant properties, as well as the ability to improve diabetic control and promote angiogenesis, it is referred to as cardioprotective[52]. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C [53]. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria [2] and 80% in Botswana [54], mostly affecting individuals between 35-54 years.

In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria [55], i.e. HbA1c cut-off ≥6.5% and FPG ≥7.0mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of ≥5.6mmol/l, as recommended by IDF [35]. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty[56] and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion[57]. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Taking this into account, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to

0.61% when we used the WHO [55] diabetes diagnostic criteria (FPG ≥7mmol/l) for the same age group (data not shown). This, in our opinion, indicates that the majority of the children are at risk for diabetes, and that the cut-off for HbA1c ≥6.1% as well as elevated FPG≥5.6 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC [58] as well as BF% [7]. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better predictor for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana [7].

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI [59] and BMI is one of the main risk factors for diabetes and pre-diabetes [60]. However, when all three obesity indices were considered combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus[61]. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time

consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari population.

This study has some limitations that should be considered. First, we were only able to investigate the association between obesity indices and risk factors using cross-sectional data, thus the impact of changes in obesity indices on risk factors could not be considered. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children [62]. Third, even though participants who reported food or beverage intake prior to blood drawing were excluded during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". According to our power calculation, our sample size of 1,314 individuals would have been enough to reach a statistical power. However, our study sample decreased to 470 due to the individual opt-out option for particular examinations as well as the exclusion of outliers and the requirement of completeness of variables of interest. We nevertheless believe that our findings provide important information for public health stakeholders, policy makers and researchers, despite the fact that some of the detected associations did not reach the significance threshold due to the small sample size.

The results of this research, the first study providing information on the prevalence and risk of NCDs with particular focus on identifying vulnerable age groups in Zanzibar, can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult population. There is little information on the association of

multiple obesity indices with multiple cardio-metabolic risk factors in this population; hence, our study provides an important contribution towards filling this gap.

Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at ≥6.1% and/or elevated fasting glucose at ≥5.6mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group ≥18 to <45 years. These can also be used to help monitor prevention activities.

List of Abbreviations

BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
HbA1c	Glycated Haemoglobin
HDL-C	High Density-Lipoprotein Cholesterol
HOMA-IR	homeostasis model assessment of insulin resistance
IDEFICS	Identification and prevention of Dietary-and lifestyle-induced health EFects In Children and infantS
IDF	International Diabetes Federation
ISCED	International Standard Classification of Education
LDL-C	Low Density-Lipoprotein Cholesterol
LMICs	Low-middle-Income Countries
NCDs	Non-Communicable Diseases
WC	Waist Circumference
WHO	World Health Organization

Declarations

Funding

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Competing interests

The authors declare that they have no competing interests.

Author's Contribution

The authors' responsibilities were as follows: AH and MN were responsible for study design. AH , MN and SK conducted data collection and developed study hypothesis. MAN and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN wrote the manuscript and had primary responsibility for final content. MN, CB, SK, MS ,KB and AH critically revised the manuscript and gave final consent.

STROBE checklist

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Cross-sectional study
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Completed in the abstract, please refer to *line 27-53*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This has been explained in the Introduction section .
Objectives	3	State specific objectives, including any prespecified

		hypotheses -To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. -To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper This has been presented in the abstract, please refer to *line 31-34*. **Key elements of study design** : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selected and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This has been described in the method section, please refer to *line 115-125*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants This has been described in the method section, refer to *line 116-124*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This has been defined in the method section, refer to *line 150-225* including **Table 1** *line 225-237* *Since clinical patients were not included, diagnostic criteria is not applicable*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). -Please refer to method section *line 161-225* Describe comparability of assessment methods if there is more than one group -*Not applicable*

Data sharing statement

The datasets generated and/or analysed during the current study are not publicly available since a follow-up study is planned.

Acknowledgement

This work was done as part of the Leibniz Graduate School SUTAS (Sustainable Use of Tropical Aquatic Systems; http://www.zmt-bremen.de/SUTAS.html). This study would not have been possible without the voluntary collaboration of the Zanzibari families who participated in the extensive examinations. We are grateful for the support from regional and local community leaders and municipalities. The authors gratefully acknowledge the assistance from all fieldworkers and the laboratory technicians.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Cross-sectional study
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Completed in the abstract, please refer to *line 27-53*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This has been explained in the Introducion section .
Objectives	3	State specific objectives, including any prespecified hypotheses -To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. -To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper This has been presented in the abstract , please refer to *line 31-34*. **Key elements of study design** : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selecetd and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This has been described in the method section, please refer to *line 115-125*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants This has been described in the method section, refere to *line 116-124*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This has been defined in the method section, refer to *line 150-225* including **Table 1** *line 225-237* *Since clinical patients were not included, diagnostic criteris is not applicable*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). -Please refer to method section *line 161-225* Describe comparability of assessment methods if there is more than one group

		-*Not applicable*
Bias	9	Describe any efforts to address potential sources of bias This was described in the inclusion criteria were outliers were deleted from the sample in order to reduce bias. Refer to *line 246*
Study size	10	Explain how the study size was arrived at This has been described in *line 119-122*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why -Quantitative variables were grouped into categories according to the given cut-offs, please refer to method sections *anthropometric measurements and cardiometabolic risk factors*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses -all the above points have been discussed in the statistical analysis , refer to *line 251-272*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed This has been described in *line 242-246*
		(b) Give reasons for non-participation at each stage This has been described in *line 242-246*
		(c) Consider use of a flow diagram -Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Please refer to *line 277-304* and *Tables 2 and 3*
		(b) Indicate number of participants with missing data for each variable of interest -This was not described in the manuscript, the missing data for each variable of interest were deleted during data cleaning and before running the statistical analysis. Please refer to the inclusion criteria section for general overview, *line 242-248*
Outcome data	15*	Report numbers of outcome events or summary measures -Please refer to result sections table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period . *Not relevant* -Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses -This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives -This has been decribed in the discussion section, please refer to *line 348 onwards*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias -Limitations of the study have been described in *line 427-441*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence -Please refer to the conclusion section from *line 353 onwards*
Generalisability	21	Discuss the generalisability (external validity) of the study results -Based on the findings of the study,similar epidemiological surveys could be conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based -This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012-ZMT-4. *See line 483* -The present article is based on the "Access to Food and Nutritional Status of the Zanzibari population" study, *please refer to reference no.25*

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.

Designs: Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in 2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socio-economic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

Results: The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants ≥18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). **Conclusion**: High BMI, WC

and BF% were strongly associated with hypertension, with individuals with high WC being twice more likely to have hypertension; this calls for early and effective screening strategies for this study population.

Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa

Strengths and limitations of this study

- This is the first study to report the associations between obesity indices and cardio-metabolic risk factors in Zanzibar.
- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate, thus minimising risk of selection bias.
- The cross-sectional design prevents us from drawing conclusions regarding the impact of changes in obesity indices on risk factors.
- Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which might have underestimated adiposity in children.

Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death[1], they are also emerging as a notable public health problem in sub-Saharan African countries [2]. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles [2 3]. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus [4], with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya [5 6]. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases [7] including hypertension [8], diabetes [9] and dyslipidemia [10]. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors[11].

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardio-metabolic risk in clinical and research settings[12-14] due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population[13 15]. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status [16], which is linked to metabolic risk, e.g. in South African youth[17]. However, BMI does not distinguish well between lean mass and fat mass[18]. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The

correlation on the other hand varies significantly across ethnicities [19 20]. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies[21]. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings [22 23].

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations [2 7 18]. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas [24]. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups (≥5 to <18 years, ≥18 to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

Subjects and Methods

Study population and design

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere [25]. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of their children in writing.

Patient and Public Involvement

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting.

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study.

This observational epidemiological study examined participants in their home environment and did not enrol clinical patients.

Questionnaires and anthropometric measurements

Questionnaires were developed in English, translated into Swahili, and then back translated to control for translation errors. Trained field staff collected the survey information. Parents reported their age and sex, as well as that of their children. Age was grouped into three categories ≥5 to <18 years, ≥18 to <45 years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) [26] was used as a proxy indicator for socio-economic status (SES) of the family. Education was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented in the questionnaire. Regarding medication

for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoproteinemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards [27] [28]. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures [29] [30]. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere [25].

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m^2 and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between >75th and <95th percentile) and obesity (BMI >95th percentile) were built according to the WHO centile curves [31] [32]. For adults, overweight/obesity was defined as BMI ≥25kg/m^2 as recommended by WHO [33]. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight (≤ 75th percentile for children and adolescents and < 25kg/m^2 for adults) and 2) overweight/obesity (>75th percentile and ≥25kg/m^2). Regarding waist circumference (WC), high abdominal obesity was defined as WC ≥90th percentile for children below 10 years [34];WC ≥90th percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF [35]. As recommended by

McCarthy et al. [36], for boys and girls below 18 years, high body fat percentage (BF%) was set at ≥85th percentile. For adults above 18 years, high BF% was defined as ≥20 % for men and ≥32 % for women [37]. The cut-offs and references are listed in Table 1.

Cardio-metabolic risk factors

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture [38]. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. Collection, processing and storage of blood samples are described elsewhere [25].

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study [34 39]. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. [40] for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as

recommended [41]; for adolescents and adults above 16 years hypertension was defined as recommended [42]. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP) [11] and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) [35]. HbA1c for participants above 17 years was defined according to Stern et al. [43] and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. [44]. In the present study, the 75th percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al [45]. HOMA-IR was calculated from glucose (mmol/l)) and insulin (µU/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)[46].

Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children: ≤10y	BMI ≥75th percentile [1]	TC ≥90th percentile [2]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [2]	TG ≥90th percentile [2]	HOMA-IR ≥ 95th percentile [2]
	BF %≥85th percentile [3]	HDL-C ≤ 10th percentile [2]	FPG ≥ 95th percentile [2]
	SBP≥90th centile or DBP ≥90th centile [2]	LDL ≥90th percentile [2]	
Adolescents: >10 to <16 y	BMI ≥ 75th percentile [1]	TC ≥5.2 mmol/L [6]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [4]	TG ≥1.7mmol/L [4]	HOMA-IR ≥75th percentile [9]
	BF %≥85th percentile [3]	HDL-C < 1.03 [4]	FPG ≥ 5.6mmol/L [4]
	SBP≥140mmHg or DBP≥90mmHg [11]	LDL ≥3.4mmol/L [6]	
Adults: ≥16y	BMI ≥ 25 kg/m[1]	TC ≥5.2 mmol/l [6]	HbA1c ≥ 6.1% [5]
	WC ≥ 94 cm male, ≥80cm female [4]	TG ≥1.7mmol/L,[4]	HOMA-IR >4.65 or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [7]
	BF % ≥ 20 % male and	HDL-C < 1.03 male,< 1.29	FPG ≥ 5.6mmol/L[4]

	≥32 % female [8]	female [4]	
	SBP≥140mmHg or DBP≥90mmHg [12]	LDL ≥3.4mmol/L [6]	

1 WHO
2 IDEFICS Study
3 McCarthy, H.D., et al. (2006)
4 IDF
5 Stern, S.E., et al (2003) for adults above 17 years
6 NCEP
7 von Eyben, F.E., et al (2005)
8 Gallagher, D., et al (200)
9 Shashaj et al. (2015) for children and adolescents under 17 years
10 Rodoo P et al. (2013)
11, 12 National Institute of Health 3rd and 7th report respectively

Inclusion criteria for study sample

Of 1,443 individuals who participated in this study, 1,314 fulfilled the inclusion criteria (age, sex, weight, height) for the overall study analysis. Of the 1,314 participants, 1,234 provided complete waist circumference and body fat percent measurements. Among these, 557 provided complete blood samples for the cardio-metabolic risk analysis and only 505 were on fasting status. To reduce bias while estimating mean and SD in the regression analysis, we excluded the top 1% of individuals with extremely high values for cardio-metabolic risk and obesity indices, leaving us with a complete sample of 470 participants for the analysis.

Statistical analysis

Descriptive analysis was conducted to calculate the mean standard deviation (SD) and range (minimum, maximum) for continuous variables, as well as the distribution of the categorical data in N and percentages (%). As part of the regression analysis, we tested the necessary assumptions in terms of symmetry and normality using residual-plots and Q-Q-Plots. Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure

in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, the strongest relationship with cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at $\alpha = 0.05$.

Results

Distribution of obesity and cardio-metabolic risk and characteristics of the study population by age groups (n=470)

The mean age was 29 (±18) years, with the highest proportion being in the age group (≥18 to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m^2, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7) kg/m^2 for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure, 150 (± 280) mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend.

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with higher education level were aged ≥18-<45 years (150/244 = 61%) (Table 3).

Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by age group (means and standard deviation (SD))

	≥5 to <18 years (n=165)		≥18 to <45 years (n=195)		45+years (n=110)		Total (n=470)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53

DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only about 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among ≥18 to <45 year olds.

Table 3: Characteristics of the study population (n=470) by age group (n/%)

	≥5 to <18 years		**≥18 to <45 years**		**45+ years**		**Total**	
	n	(%)	n	(%)	n	(%)	n	(%)
All	165	(100)	195	(100)	110	(100)	470	(100)
Gender								
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1)
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9)
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6)
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4)
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)
High [a]	0	(0)	54	(27.7)	63	(57.3)	117	(24.9)
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0)
High [b]	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1)
Hypertension								
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5)
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1)
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5)
Hypertension medication[c]								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02)
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0)
Dyslipidaemia [d]								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9)
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11)
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3)
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68)
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5)
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4)
LDL-cholesterol								
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7)
High	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Diabetes Markers [e]								
HbA1c								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)

[a] High WC was defined as WC ≥90th percentile for children under 10y [34]. Adolescents between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off [35]

[b] High BF% for adults (overweight/obese)≥ 20 for men and ≥32 for women according to (NIH/WHO) BMI guidelines [37] and ≥85th percentile for children [36]

[c] Missing information from 12 participants (n=458)

[d] High dyslipidemia for adults; was defined as total serum cholesterol (≥6.2mmol/l) and LDL-cholesterol (≥3.4mmol/l) [11] low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in women high and hypertriglyceridemia (≥1.7 mmol/l) [35] and for children according to IDEFICS study [34]

[e] High diabetes risk markers; high HbA1c (>6.1%) [45], high fasting plasma glucose (≥5.6 mmol/l) [35] and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [43] and for children high HbA1c (≥97.5th percentile), high fasting plasma glucose ≥95th percentile and HOMA-IR ≥95th percentile.

Association between obesity indices and cardio-metabolic risk factors

Obesity indices (BMI, WC and BF %) were observed to be associated with one or more risk factors. Participants with high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52)) or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive (Table 4). Having high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) was associated with higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C, elevated glucose and HOMA-IR. As the proportion of individuals with high HOMA-IR was

very small in our sample (1,28%/n=6), the results was not considered in the final regression analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion (AIC), which estimates the quality of each model relative to that of each of the other models, showed that models including WC as an obesity index tended to have a slightly stronger relationship compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices	**High BMI**				**High WC**				**High BF%**			
Risk factors	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**
Hypertension	**2.41**	**1.33**	**4.47**	**504.86**	**3.68**	**1.81**	**7.52**	**499.79**	**2.51**	**1.40**	**4.51**	**503.46**
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	**2.52**	**1.24**	**5.13**	**452.23**	**1.91**	**1.02**	**3.58**	**454.77**
High HbA1c	**2.08**	**1.15**	**3.79**	**442.70**	**3.01**	**1.51**	**6.03**	**438.53**	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR levels was very small in our sample (1,28%/n=6), HOMA-IR was not considered in the final regression analysis.

344 Table 5: Associations between obesity indices (independent) and cardio-metabolic risk

345 factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

	Combined Obesity Indices									**AIC total**
Obesity indices	**BMI**			**WC**			**BF%**			
Risk Factors	**OR**	**(95% CI)**		**OR**	**(95% CI)**		**OR**	**(95% CI)**		
Hypertension	1.19	0.48	2.95	**2.62**	**1.1**	**6.06**	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	**2.62**	**1.1**	**6.15**	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6

Discussion

This study is the first population–based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries [47]. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana [7], but higher than in Nigeria [2] and Benin [48]. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon) [49].

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C [50 51]. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years.. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C [52]. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria [2] and 80% in Botswana [53], mostly affecting individuals between 35-54 years.

In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has

not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria [54], i.e. HbA1c cut-off ≥6.5% and FPG ≥7.0mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of ≥5.6mmol/l. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty[55] and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion[56]. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Considering this, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to 0.61% when we used the WHO [54] diabetes diagnostic criteria (FPG ≥7mmol/l) for the same age group (data not shown). This, in our opinion, indicates that the majority of the children are at risk for diabetes, and that the cut-off

for HbA1c ≥6.1% as well as elevated FPG≥5.6 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC [57] as well as BF% [7]. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better indicator for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana [7].

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI [58] and BMI is one of the main risk factors for diabetes and pre-diabetes [59]. However, when all three obesity indices were combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus[60]. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari population.

This study has some limitations that should be considered. First, this study investigated the association between obesity indices and cardio-metabolic risk factors using cross-sectional

data; thus we were not able to examine the impact of changes in obesity indices on risk factors. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children [61]. Third, even though we excluded participants who reported food or beverage intake prior to blood drawing during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". According to our power calculation, our sample size of 1,314 individuals would have been enough to reach a statistical power. However, our study sample decreased to 470 due to the individual opt-out option for particular examinations as well as the exclusion of outliers and the requirement of completeness of variables of interest. We nevertheless believe that our findings provide important information for public health stakeholders, policy makers and researchers, despite the fact that some of the detected associations did not reach the significance threshold due to the small sample size.

The results of this research can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult population. There is little information on the association of multiple obesity indices with multiple cardio-metabolic risk factors in this population; hence, our study provides an important contribution towards filling this gap.

Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at ≥6.1% and/or elevated fasting glucose at ≥5.6mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group ≥18 to <45 years. These can also be used to help monitor prevention activities.

Declarations

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Competing interests

The authors declare that they have no competing interests.

Author's Contribution

The authors' responsibilities were as follows: AH and MN were responsible for study design. AH , MN and SK conducted data collection and developed study hypothesis. MAN and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN wrote the manuscript and had primary responsibility for final content. MN, CB, SK, MS ,KB and AH critically revised the manuscript and gave final consent.

Data sharing statement

The datasets generated and/or analysed during the current study are not publicly available since a follow-up study is planned.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Cross-sectional study
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Completed in the abstract, please refer to *line 27-53*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This has been explained in the Introducion section .
Objectives	3	State specific objectives, including any prespecified hypotheses -To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. -To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper This has been presented in the abstract , please refer to *line 31-34*. **Key elements of study design** : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selecetd and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This has been described in the method section, please refer to *line 115-125*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants This has been described in the method section, refere to *line 116-124*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This has been defined in the method section, refer to *line 150-225* including **Table 1** *line 225-237* *Since clinical patients were not included, diagnostic criteris is not applicable*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). -Please refer to method section *line 161-225* Describe comparability of assessment methods if there is more than one group

		-*Not applicable*
Bias	9	Describe any efforts to address potential sources of bias This was described in the inclusion criteria were outliers were deleted from the sample in order to reduce bias. Refer to *line 246*
Study size	10	Explain how the study size was arrived at This has been described in *line 119-122*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why -Quantitative variables were grouped into categories according to the given cut-offs, please refer to method sections *anthropometric measurements and cardiometabolic risk factors*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses -all the above points have been discussed in the statistical analysis , refer to *line 251-272*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed This has been described in *line 242-246*
		(b) Give reasons for non-participation at each stage This has been described in *line 242-246*
		(c) Consider use of a flow diagram -Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Please refer to *line 277-304* and *Tables 2 and 3*
		(b) Indicate number of participants with missing data for each variable of interest -This was not described in the manuscript, the missing data for each variable of interest were deleted during data cleaning and before running the statistical analysis. Please refer to the inclusion criteria section for general overview, *line 242-248*
Outcome data	15*	Report numbers of outcome events or summary measures -Please refer to result sections table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period . *Not relevant* -Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses -This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives -This has been decribed in the discussion section, please refer to *line 348 onwards*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias -Limitations of the study have been described in *line 427-441*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence -Please refer to the conclusion section from *line 353 onwards*
Generalisability	21	Discuss the generalisability (external validity) of the study results -Based on the findings of the study,similar epidemiological surveys could be conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based -This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012-ZMT-4. *See line 483* -The present article is based on the "Access to Food and Nutritional Status of the Zanzibari population" study, *please refer to reference no.25*

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.

Designs: Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in 2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socio-economic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

Results: The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants ≥18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). **Conclusion**: High BMI, WC

and BF% were strongly associated with hypertension, with individuals with high WC being twice more likely to have hypertension; this calls for early and effective screening strategies for this study population.

Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa

Strengths and limitations of this study

- This is the first study to report the associations between obesity indices and cardio-metabolic risk factors in Zanzibar.
- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate, thus minimising risk of selection bias.
- The cross-sectional design prevents us from drawing conclusions regarding the impact of changes in obesity indices on risk factors.
- Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which might have underestimated adiposity in children.

Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death[1], they are also emerging as a notable public health problem in sub-Saharan African countries [2]. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles [2 3]. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus [4], with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya [5 6]. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases [7] including hypertension [8], diabetes [9] and dyslipidemia [10]. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors[11].

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardio-metabolic risk in clinical and research settings[12-14] due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population[13 15]. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status [16], which is linked to metabolic risk, e.g. in South African youth[17]. However, BMI does not distinguish well between lean mass and fat mass[18]. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The

correlation on the other hand varies significantly across ethnicities [19 20]. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies[21]. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings [22 23].

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations [2 7 18]. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas [24]. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups (≥5 to <18 years, ≥18 to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

Subjects and Methods

Study population and design

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere [25]. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of their children in writing.

Patient and Public Involvement

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting.

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study.

This observational epidemiological study examined participants in their home environment and did not enrol clinical patients.

Questionnaires and anthropometric measurements

Questionnaires were developed in English, translated into Swahili, and then back translated to control for translation errors. Trained field staff collected the survey information. Parents reported their age and sex, as well as that of their children. Age was grouped into three categories ≥5 to <18 years, ≥18 to <45 years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) [26] was used as a proxy indicator for socio-economic status (SES) of the family. Education was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented in the questionnaire. Regarding medication

for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoproteinemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards [27] [28]. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures [29] [30]. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere [25].

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m^2 and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between $>75^{th}$ and $<95^{th}$ percentile) and obesity (BMI >95th percentile) were built according to the WHO centile curves [31] [32]. For adults, overweight/obesity was defined as BMI $\geq 25kg/m^2$ as recommended by WHO [33]. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight ($\leq 75^{th}$ percentile for children and adolescents and $< 25kg/m^2$ for adults) and 2) overweight/obesity ($>75^{th}$ percentile and $\geq 25kg/m^2$). Regarding waist circumference (WC), high abdominal obesity was defined as WC $\geq 90^{th}$ percentile for children below 10 years [34];WC $\geq 90^{th}$ percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF [35]. As recommended by

McCarthy et al. [36], for boys and girls below 18 years, high body fat percentage (BF%) was set at ≥85th percentile. For adults above 18 years, high BF% was defined as ≥20 % for men and ≥32 % for women [37]. The cut-offs and references are listed in Table 1.

Cardio-metabolic risk factors

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture [38]. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. Collection, processing and storage of blood samples are described elsewhere [25].

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study [34 39]. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. [40] for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as

recommended [41]; for adolescents and adults above 16 years hypertension was defined as recommended [42]. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP) [11] and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) [35]. HbA1c for participants above 17 years was defined according to Stern et al. [43] and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. [44]. In the present study, the 75th percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al [45]. HOMA-IR was calculated from glucose (mmol/l)) and insulin (µU/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)[46].

Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children: ≤10y	BMI ≥75th percentile [1]	TC ≥90th percentile [2]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [2]	TG ≥90th percentile [2]	HOMA-IR ≥ 95th percentile [2]
	BF %≥85th percentile [3]	HDL-C ≤ 10th percentile [2]	FPG ≥ 95th percentile [2]
	SBP≥90th centile or DBP ≥90th centile [2]	LDL ≥90th percentile [2]	
Adolescents: >10 to <16 y	BMI ≥ 75th percentile [1]	TC ≥5.2 mmol/L [6]	HbA1c ≥ 97.5th percentile[10]
	WC ≥90th percentile [4]	TG ≥1.7mmol/L [4]	HOMA-IR ≥75th percentile [9]
	BF %≥85th percentile [3]	HDL-C < 1.03 [4]	FPG ≥ 5.6mmol/L [4]
	SBP≥140mmHg or DBP≥90mmHg [11]	LDL ≥3.4mmol/L [6]	
Adults: ≥16y	BMI ≥ 25 kg/m[1]	TC ≥5.2 mmol/l [6]	HbA1c ≥ 6.1% [5]
	WC ≥ 94 cm male, ≥80cm female [4]	TG ≥1.7mmol/L,[4]	HOMA-IR >4.65 or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [7]
	BF % ≥ 20 % male and	HDL-C < 1.03 male,< 1.29	FPG ≥ 5.6mmol/L[4]

	≥32 % female [8]	female [4]	
	SBP≥140mmHg or DBP≥90mmHg [12]	LDL ≥3.4mmol/L [6]	

1 WHO
2 IDEFICS Study
3 McCarthy, H.D., et al. (2006)
4 IDF
5 Stern, S.E., et al (2003) for adults above 17 years
6 NCEP
7 von Eyben, F.E., et al (2005)
8 Gallagher, D., et al (200)
9 Shashaj et al. (2015) for children and adolescents under 17 years
10 Rodoo P et al. (2013)
11, 12 National Institute of Health 3rd and 7th report respectively

Inclusion criteria for study sample

Of 1,443 individuals who participated in this study, 1,314 fulfilled the inclusion criteria (age, sex, weight, height) for the overall study analysis. Of the 1,314 participants, 1,234 provided complete waist circumference and body fat percent measurements. Among these, 557 provided complete blood samples for the cardio-metabolic risk analysis and only 505 were on fasting status. To reduce bias while estimating mean and SD in the regression analysis, we excluded the top 1% of individuals with extremely high values for cardio-metabolic risk and obesity indices, leaving us with a complete sample of 470 participants for the analysis.

Statistical analysis

Descriptive analysis was conducted to calculate the mean standard deviation (SD) and range (minimum, maximum) for continuous variables, as well as the distribution of the categorical data in N and percentages (%). As part of the regression analysis, we tested the necessary assumptions in terms of symmetry and normality using residual-plots and Q-Q-Plots. Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure

in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, the strongest relationship with cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at $\alpha = 0.05$.

Results

Distribution of obesity and cardio-metabolic risk and characteristics of the study population by age groups (n=470)

The mean age was 29 (±18) years, with the highest proportion being in the age group (≥18 to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m^2, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7) kg/m^2 for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure, 150 (± 280) mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend.

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with higher education level were aged ≥18-<45 years (150/244 = 61%) (Table 3).

Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by age group (means and standard deviation (SD))

	≥5 to <18 years (n=165)		≥18 to <45 years (n=195)		45+years (n=110)		Total (n=470)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53

DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only about 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among ≥18 to <45 year olds.

Table 3: Characteristics of the study population (n=470) by age group (n/%)

	≥5 to <18 years		**≥18 to <45 years**		**45+ years**		**Total**	
	n	(%)	n	(%)	n	(%)	n	(%)
All	165	(100)	195	(100)	110	(100)	470	(100)
Gender								
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1)
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9)
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6)
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4)
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)
High [a]	0	(0)	54	(27.7)	63	(57.3)	117	(24.9)
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0)
High [b]	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1)
Hypertension								
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5)
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1)
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5)
Hypertension medication[c]								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02)
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0)
Dyslipidaemia [d]								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9)
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11)
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3)
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68)
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5)
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4)
LDL-cholesterol								
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7)
High	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3)

	≥5 to <18 years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Diabetes Markers [e]								
HbA1c								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)

[a] High WC was defined as WC ≥90th percentile for children under 10y [34]. Adolescents between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off [35]

[b] High BF% for adults (overweight/obese)≥ 20 for men and ≥32 for women according to (NIH/WHO) BMI guidelines [37] and ≥85th percentile for children [36]

[c] Missing information from 12 participants (n=458)

[d] High dyslipidemia for adults; was defined as total serum cholesterol (≥6.2mmol/l) and LDL-cholesterol (≥3.4mmol/l) [11] low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in women high and hypertriglyceridemia (≥1.7 mmol/l) [35] and for children according to IDEFICS study [34]

[e] High diabetes risk markers; high HbA1c (>6.1%) [45], high fasting plasma glucose (≥5.6 mmol/l) [35] and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR >3.60 and BMI >27.5 kg/m^2 [43] and for children high HbA1c (≥97.5th percentile), high fasting plasma glucose ≥95th percentile and HOMA-IR ≥95th percentile.

Association between obesity indices and cardio-metabolic risk factors

Obesity indices (BMI, WC and BF %) were observed to be associated with one or more risk factors. Participants with high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52)) or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive (Table 4). Having high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) was associated with higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C, elevated glucose and HOMA-IR. As the proportion of individuals with high HOMA-IR was

very small in our sample (1,28%/n=6), the results was not considered in the final regression analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion (AIC), which estimates the quality of each model relative to that of each of the other models, showed that models including WC as an obesity index tended to have a slightly stronger relationship compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices	**High BMI**				**High WC**				**High BF%**			
Risk factors	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**	**OR**	**(95% CI)**		**AIC**
Hypertension	**2.41**	**1.33**	**4.47**	**504.86**	**3.68**	**1.81**	**7.52**	**499.79**	**2.51**	**1.40**	**4.51**	**503.46**
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	**2.52**	**1.24**	**5.13**	**452.23**	**1.91**	**1.02**	**3.58**	**454.77**
High HbA1c	**2.08**	**1.15**	**3.79**	**442.70**	**3.01**	**1.51**	**6.03**	**438.53**	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR levels was very small in our sample (1,28%/n=6), HOMA-IR was not considered in the final regression analysis.

Table 5: Associations between obesity indices (independent) and cardio-metabolic risk factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

	Combined Obesity Indices									**AIC total**
Obesity indices	**BMI**			**WC**			**BF%**			
Risk Factors	**OR**	**(95% CI)**		**OR**	**(95% CI)**		**OR**	**(95% CI)**		
Hypertension	1.19	0.48	2.95	**2.62**	**1.1**	**6.06**	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	**2.62**	**1.1**	**6.15**	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6

Discussion

This study is the first population–based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries [47]. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana [7], but higher than in Nigeria [2] and Benin [48]. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon) [49].

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C [50 51]. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years.. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C [52]. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria [2] and 80% in Botswana [53], mostly affecting individuals between 35-54 years.

In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has

not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria [54], i.e. HbA1c cut-off ≥6.5% and FPG ≥7.0mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of ≥5.6mmol/l. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty[55] and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion[56]. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Considering this, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to 0.61% when we used the WHO [54] diabetes diagnostic criteria (FPG ≥7mmol/l) for the same age group (data not shown). This, in our opinion, indicates that the majority of the children are at risk for diabetes, and that the cut-off

for HbA1c ≥6.1% as well as elevated FPG≥5.6 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC [57] as well as BF% [7]. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better indicator for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana [7].

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI [58] and BMI is one of the main risk factors for diabetes and pre-diabetes [59]. However, when all three obesity indices were combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus[60]. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari population.

This study has some limitations that should be considered. First, this study investigated the association between obesity indices and cardio-metabolic risk factors using cross-sectional

data; thus we were not able to examine the impact of changes in obesity indices on risk factors. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children [61]. Third, even though we excluded participants who reported food or beverage intake prior to blood drawing during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". The overall aim of the study was to estimate the prevalence of malnutrition in the Zanzibari population including possible correlates. Therefore, the initial sample size calculation was based on the following considerations: Assuming a prevalence of approximately 30% malnutrition in children <5 years of age, a sample size of 323 children <5 years of age was needed to estimate such a prevalence and a corresponding 95% confidence interval with a precision of ±5% [62]. To recruit this number of children, we decided to include entire households. Therefore, 1,314 individuals are sufficient to estimate prevalences up to 30% within 5 absolute percentage points with 95% confidence (in children <5 years of age, but also their fathers and mothers). The present study consists of a sub sample of the study population providing all biomarkers of interest. Even though the decreased sample size may limit the scope of the results obtained - and we acknowledge this as a limitation -, we are convinced that the results, presented in the current paper, provide important information for public health stakeholders, policy makers and researchers.

The results of this research can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult

population. There is little information on the association of multiple obesity indices with multiple cardio-metabolic risk factors in this population; hence, our study provides an important contribution towards filling this gap.

Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at ≥6.1% and/or elevated fasting glucose at ≥5.6mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group ≥18 to <45 years. These can also be used to help monitor prevention activities.

Declarations

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Competing interests

The authors declare that they have no competing interests.

Author's Contribution

The authors' responsibilities were as follows: AH and MAN were responsible for study design. AH , MAN and SK conducted data collection and developed study hypothesis. MAN and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN wrote the manuscript and had primary responsibility for final content. MAN, CB, SK, MS ,KB and AH critically revised the manuscript and gave final consent.

Data sharing statement

The datasets generated and/or analysed during the current study are not publicly available since a follow-up study is planned.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Cross-sectional study
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Completed in the abstract, please refer to *line 27-53*
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported This has been explained in the Introducion section .
Objectives	3	State specific objectives, including any prespecified hypotheses -To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. -To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper This has been presented in the abstract , please refer to *line 31-34*. **Key elements of study design** : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selecetd and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This has been described in the method section, please refer to *line 115-125*
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants This has been described in the method section, refere to *line 116-124*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This has been defined in the method section, refer to *line 150-225* including **Table 1** *line 225-237* *Since clinical patients were not included, diagnostic criteris is not applicable*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). -Please refer to method section *line 161-225* Describe comparability of assessment methods if there is more than one group

		-*Not applicable*
Bias	9	Describe any efforts to address potential sources of bias This was described in the inclusion criteria were outliers were deleted from the sample in order to reduce bias. Refer to *line 246*
Study size	10	Explain how the study size was arrived at This has been described in *line 119-122*
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why -Quantitative variables were grouped into categories according to the given cut-offs, please refer to method sections *anthropometric measurements and cardiometabolic risk factors*
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses -all the above points have been discussed in the statistical analysis , refer to *line 251-272*
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed This has been described in *line 242-246*
		(b) Give reasons for non-participation at each stage This has been described in *line 242-246*
		(c) Consider use of a flow diagram -Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Please refer to *line 277-304* and *Tables 2 and 3*
		(b) Indicate number of participants with missing data for each variable of interest -This was not described in the manuscript, the missing data for each variable of interest were deleted during data cleaning and before running the statistical analysis. Please refer to the inclusion criteria section for general overview, *line 242-248*
Outcome data	15*	Report numbers of outcome events or summary measures -Please refer to result sections table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period . *Not relevant* -Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses -This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives -This has been decribed in the discussion section, please refer to *line 348 onwards*
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias -Limitations of the study have been described in *line 427-441*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence -Please refer to the conclusion section from *line 353 onwards*
Generalisability	21	Discuss the generalisability (external validity) of the study results -Based on the findings of the study,similar epidemiological surveys could be conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based -This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012-ZMT-4. *See line 483* -The present article is based on the "Access to Food and Nutritional Status of the Zanzibari population" study, *please refer to reference no.25*

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.