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ORIGINAL ARTICLE

# EPIDEMIOLOGICAL ASPECTS OF THE ASSOCIATION OF THE HYPERTRIGLYCERIDEMIC WAIST PHENOTYPE WITH METABOLIC SYNDROME AND CARDIOVASCULAR RISK FACTORS IN MOROCCO. CASE THE AMAZIGH POPULATION FROM A GEOGRAPHIC REGION CALLED SOUSS

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# ABSTRACT

**Background.** The global prevalence of metabolic syndrome (MetS) increases susceptibility to non-communicable diseases such as obesity, type 2 diabetes, and cardiovascular disease, posing significant health risks. Effective prevention and management require objective tools. The hypertriglyceridemic waist (TG+WC+) phenotype is proposed as a less expensive approach to identify individuals with metabolic syndrome and other cardiovascular risk factors.

**Objective.** The current aim of this investigation is to study the epidemiological characteristics of the hypertriglyceridemic waist phenotype and their correlations with cardiovascular risk factors and MetS in the Moroccan Amazigh ethnic group from the Souss region of Morocco.

**Material and Methods.** A total of 827 Amazigh adults from the Sousse region of Morocco were divided into four distinct phenotype groups: TG-WC-, TG+WC-, TG-WC+, and TG+WC+ (normal TG- or high TG+ triglycerides/normal WC- or high WC+ waist circumference). The association of the different phenotypes with MetS and other cardiovascular risk factors was established by logistic regression analysis.

**Results.** The prevalence of the TG+WC+ phenotype was 27.7% and varied according to age group and sex. Among subjects with the TG+WC+ phenotype, most were 41-60 years old (53.3%) and in women (74.2%). Participants with the TG+WC+ phenotype had the highest prevalence of dyslipidemia (87.3%), hypoHDLaemia (69.9%), and general obesity (37.12%). The three phenotypes TG-WC-, TG+WC- and TG-WC+ were less associated with MetS and other cardiovascular risk factors. Moreover, people with the TG+WC+ phenotype had a very high odds ratio for MetS.

**Conclusion.** These findings suggest that the TG+WC+ phenotype exhibits a robust correlation with MetS and additional variables connected to cardiovascular risk. The TG+WC+ phenotype serves as a valuable clinical instrument for detecting individuals vulnerable to MetS and cardiovascular diseases.

**Keywords:** hypertriglyceridemic waist phenotype, cardiovascular risk factors, metabolic syndrome, epidemiology, Morocco

# **INTRODUCTION**

Metabolic syndrome (MetS), is characterized by a range of interconnected clinical and biochemical irregularities and dysfunctions. The combined impact of these elements represents a notable factor at risk for the onset of cardiovascular disease (CVD), type 2 diabetes (T2D), and additional health complications [1]. Metabolic syndrome prevalence is on the rise across the globe, varying from 12.5% to 31.4%, contingent upon the adopted definition and the geographical region studied. The Eastern Mediterranean and the Americas show the highest prevalence rates, which correlate with the standard of living and income levels [2].

The growing prevalence of MetS globally is attributed to the shift in epidemiological and nutritional patterns known as the epidemiological and nutritional transition that accompanies rapid economic growth. This phenomenon arises from unhealthy lifestyle choices, including sedentary behavior and inadequate

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dietary habits, which have become pervasive across all nations due to continuous cultural globalization [3].

Morocco, like all other nations, has undergone an epidemiological transition, leading to adverse outcomes for both public health and the economy [3]. It was reported that Moroccan population presents a high risk of cardiovascular disease (37%), significantly elevated in older adults [4]. It is evident that cardiovascular disease continues to be the major reason behind mortality [5, 6]. Also, the prevalence of MetS varies by age, gender, ethnicity, and area [7]. However, there is no national average, for example, among adult women in southern Morocco, it was 16.3% in 2002 [8], but among post-menopausal women in northern Morocco, it was 74.18% in 2020 [9].

Metabolic syndrome (MetS) is generally indicated by the coexistance of at least three of the following characteristics, although other health organizations may have different diagnostic standards: obesity, either general or central located, high triglyceride (TG), low HDL-cholesterol, hypertension, and hyperglycemia [10]. The main causes of MetS are considered to be central obesity and insulin resistance [11]. According to Engin [12], central obesity is the most observed aspect of MetS. Waist circumference (WC) measurement is considered the classic marker screening for MetS and a more effective parameter for predicting CVD risk indicators [13, 14]. But which index best predicts MetS remains controversial. While WC is one of the components of MetS [15], its limitations lie in its inability to distinguish between subcutaneous and visceral abdominal fat [16]. Indeed, it has been demonstrated that visceral fat is strongly linked with various cardiovascular risk triggers and CVD [17, 18, 19]. The presence of elevated TG and WC is known as the hypertriglyceridemic waist phenotype (TG+WC+). Lemieux et al. in 2000 [20] suggested that males displaying atherogenic metabolic traits and facing a heightened risk of coronary heart disease might be detectable through an inexpensive screening approach involving the assessment and analysis of waist circumference and triglyceride levels.

Recent studies have employed the TG+WC+ phenotype, an inexpensive index to identify hypertension [21], type 2 diabetes [22, 23] and MetS as part of initial population screening efforts. For identifying metabolic problems, hypertriglyceridemic waist phenotypes may be more predictive value than individual anthropometric markers [24, 25]. One of the most potent indicators of breast cancer risk is the TG+WC+ phenotype [26]. For screening the risk of cardiovascular disease, this marker may be a useful tool [27].

The objective of this study is to elucidate the epidemiological characteristics of the TG+WC+ phenotype and investigate its possible associations with MetS and cardiovascular factors at risk in a cross-

sectional sample drawn from the Moroccan Amazigh ethnic group in the Souss region of Morocco.

# **MATERIAL AND METHODS**

### The target population

This is a prospective epidemiological study carried out between January 2023 and December 2023 at the Hassan 1st Provincial Hospital in Tiznit city. The study involved a population of Amazigh origin, 827 healthy individuals (254 men and 573 women aged between 20 and 80). The study was carried out in conjunction with a lipid panel. Participants are volunteers and each of them had written consent prior to their inclusion in this study. We excluded pregnant women, disabled people, senile individuals over 80, hemodialysis patients, cancer patients, and cardiac patients.

#### Anthropometric measurements

Weight measurements were taken utilizing an electronic scale with a sensitivity of 0.1 kg, with participants being weighed wearing only light underwear. The height of each subject was assessed with precision, to the nearest millimeter using a wall measuring device. The subjects were placed with their backs to the wall, with their feet, buttocks, back, shoulders and head in contact with the surface. WC was determined using a tape measure halfway between the last rib of the thorax and the tip of the hip bone at the end of a natural exhalation. The test subject is required to stand with their feet 25 cm [28].

### Blood pressure measurement

The automated sphygmomanometer (MICOLIF, Germany) was utilized to test the blood pressure. While the subjects were at rest, measurements were taken. Three measurements of the blood pressure were made, and the analysis was done using the mean value.

# Blood tests

After a 12-hour overnight fast, blood samples were obtained by venipuncture from trained medical personnel. The lipid profile analysis was conducted at the medical biology unit of the Provincial Hospital in Tiznit city using an automated analyzer (BioSystems BA400).

### Definitions

MetS is defined according to the harmonized criteria outlined in the Joint Interim Statement (JIS) definition [29], considering specific WC cut-off points for Mediterranean region. When three or more of the following risk-factors indicators were met, the patient was considered with MetS: WC in women  $\geq$ 80 cm and in men  $\geq$ 94 cm; fasting plasma glucose (FPG)  $\geq$ 1 g/L or taking anti-diabetic drugs; systolic blood pressure

(SBP) ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg or confirmed treatment history of hypertension, elevated fasting triglycerides (FGT) ≥1.5 g/L or under treatment for hypertriglyceridemia and low HDL-cholesterol <0.40 g/L in male and <0.5 g/L in female or under therapy for hypoHDLemia. Elsewhere, hypertension is manifested by systolic pressure value ≥140 mmHg, diastolic pressure value ≥ 90 mmHg, or taking anti-hypertensive drugs [30], type 2 diabetes is defined as a fasting blood glucose ≥1.26 g/L, HbA1c ≥6.5%, or taking anti-diabetic drugs [31].

### Anthropometric indices

The body mass index (BMI), also referred to as the Quetelet index, is calculated by dividing an individual's weight in kilograms by the square of their height in meters (kg/m<sup>2</sup>) [32]. Thus, general obesity has been defined by a BMI≥30.0 kg/m<sup>2</sup>.

# Definition of the triglyceridemic-waist circumference phenotype

To identify triglyceridemic-waist phenotypes TGWC, subjects were divided into four phenotypic categories according to strict JIS criteria based on fasting serum TG levels and WC [29].

- Phenotype TG-WC- was considered normal phenotype: WC<94 cm in male and <80 cm in female; TG<1.50 g/L.
- Phenotype TG+WC-: WC<94 cm in male and <80 cm in female; TG≥1.5 g/L.
- Phenotype TG-WC+: WC $\geq$ 94 cm for male and  $\geq$ 80 cm for female; TG<1.5 g/L.
- Phenotype TG+WC+known as hypertriglyceridemic waist phenotype: WC≥94 cm for male and ≥80 cm for female; TG≥1.50 g/L.

# Statistical analysis

The data is presented in the form of mean values accompanied by standard deviation or as a numerical percentage. Analysis of variance (ANOVA) was performed to compare quantitative characteristics and the *chi*-square test for qualitative characteristics. The link between MetS and cardiovascular factors at risk with the TG+WC+ phenotype were tested using logistic regression models. Model 1 can fit. In Model 2, adjustments were made for both age and sex. Model 3 further expanded upon Model 2 by incorporating additional adjustments for all examined variables: MetS, diabetes mellitus, dyslipidemia, general obesity, hypertension, hypercholesterolemia, hyperLDLemia, and hypoHDLemia.

The results are expressed as odds ratios (OR) along with their corresponding 95% confidence intervals (CI) in both univariate and multivariate analyses. IBM SPSS Statistics 25.0 software was utilized for all statistical computations and data analysis.

# RESULTS

Our study has enrolled 827 adults (mean age 52.9±14.7); 30.7% were men (mean age 56.5±14.9 years) and 69.3% were women (mean age  $51.2\pm14.4$  years). Subjects were grouped into four groups based on their phenotype (TGWC). The prevalence of the TG- WC-, TG+ WC-, TG- WC+ and TG+ WC+ phenotypes were 14.4%, 1.9%, 56%, and 27.7%, respectively (Tables 1 and 2). Among subjects with the TG+WC+ phenotype, 8.7% were people aged 20 to 40 years, 53.3% were adults aged 41 to 60 years and 38% were senior adults aged 61 to 80 years (Figure 1.a). According to the sex, the distribution was unequal. Indeed, in men the prevalence was 23.2%, while in women it was 29.7% (Figure 1.b). However, women had the highest TG-WC+, 81.2%, closely followed by TG+WC+, 74.2%. Conversely, men had the highest TG+WC- (87.5%) and TG-WC- (79%) (Table 2).

Based on the four TGWC phenotypes, Table 1 presents the anthropometric and biochemical measurements of the subjects. It was observed a significant increase in all measured quantitative indicators within the four groups. The TG+WC+ phenotypic participants showed the highest values, while, the TG-WC- phenotype participants had the lowest values. Table 2 shows that the TG+WC+ phenotypic participants had the highest prevalence of cardiovascular risk-factors including 69.9% hypoHDLemia, 37.12% obesity, and 87.3%





		value	000		000	000	000	000	001	000		000	000	000	000	000				
	, ,	-d ID	to 0.		) 42 0.	0	$\begin{bmatrix} 1\\ 62 \end{bmatrix} 0.$	2 0. 36 0.	2 52 0.	$\begin{array}{c c}1\\65&0.\end{array}$		0.	5 0.	1 37 0.	1 90 0.	0 0				
	type ()	95% (	54.74 57.81		74.10 to 77.4	1.612 to 1.6	101.1 to 103.	28.21 to 29.3	84.62 to 87.6	141.5 to 146.		2.12 to 2.2	1.49 to 1.6	0.411 to 0.43	1.291 to 1.39	2.02( to 2.1				
	+ phenoi 9 (27.7%	Mean ±SD	56.28 ±11.76		75.76 ±12.74	$1.62 \pm 0.08$	102.37 ±9.63	28.79 ±4.41	86.12 ±11.53	144.08 ±19.74		2.17 ±0.41	$\begin{array}{c} 1.57 \\ \pm 0.6 \end{array}$	$\begin{array}{c} 0.42 \\ \pm 0.1 \end{array}$	$1.34 \pm 0.38$	2.11 ±0.65	lesterol; totypes			
	IG+WC- N=22	Max	80		116	1.84	135	45.312	131	206		3.39	3.91	0.86	2.52	5.72	otal chol ur phen			
		Min	21		47	1.45	80	18.671	62	100		0.9	0.87	0.17	0.57	1.51	TC - tc tross fc			
	'pe	95% CI	50.44 to 53.13		71.49 to 73.94	1.61 to 1.63	98.20 to 100.027	27.315 to 28.14	82.13 to 84.02	136.88 to 140.48		1.861 to 1.9	1.27 to 1.36	0.471 to 0.492	1.198 to 1.261	0.96 to 1.01	glucose; nificant ac			
	- phenoty 3 (56%)	Mean ±SD	51.78 ±14.73		72.72 ±13.39	$\begin{array}{c} 1.62 \\ \pm 0.08 \end{array}$	99.12 ±9.97	27.73 ±4.52	83.07 ±10.33	138.68 ±19.71		$\begin{array}{c} 1.9 \\ \pm 0.41 \end{array}$	$\begin{array}{c} 1.32 \\ \pm 0.52 \end{array}$	$\begin{array}{c} 0.48 \\ \pm 0.11 \end{array}$	$\begin{array}{c} 1.23 \\ \pm 0.34 \end{array}$	$\begin{array}{c} 0.98 \\ \pm 0.28 \end{array}$	; plasma 0.05 sigr			
	CG-WC+ N=46	Max	80		125	1.9	133	43.58	135	207		4.59	3.98	0.88	3.97	1.5	- fasting value <(			
	Г	Min	20		44	1.46	80	16.162	59	87		0.8	0.75	0.2	0.44	0.34	FPG – erol; p-			
	- phenotype 6 (1.9%)	95% CI	53.21 to 66.29		60.44 to 71.81	1.59 to 1.70	81.85 to 88.52	22.67 to 25.89	83.51 to 94.86	143.66 to 160.96		1.89 to 2.50	1.19 to 2.50	0.394 to 0.505	1.085 to 1.608	1.81 to 2.19	ic blood; n choleste			
		Mean ±SD	59.75 ±12.28	cal data	66.13 ±10.66	$\begin{array}{c} 1.65 \\ \pm 0.1 \end{array}$	85.19 ±6.26	24.28 ±3.03	89.19 ±10.65	152.31 ±16.24	tory data	2.19 ±0.57	$1.84 \pm 1.23$	$\begin{array}{c} 0.45 \\ \pm 0.1 \end{array}$	$1.35 \pm 0.49$	2 ±0.35	<ul> <li>diastol</li> <li>ipoprotei</li> </ul>			
	G+WC N=10	Max	80	Clinic	06	1.84	92	32.051	110	170	Labora	3.43	5.33	0.66	2.35	2.78	e; DBP ensity li			
	Γ	Min	39		48.5	1.47	74	20.761	74	110		1.46	0.7	0.25	0.6	1.52	bressur low-de			
	be	95% CI	46.21 to 52.83		60.11 to 63.62	1.65 to 1.67	80.62 to 83.01	21.88 to 22.91	80.54 to 84.97	131.13 to 138.77		1.57 to 1.74	1.18 to 1.39	0.471 to 0.530	1.009 to 1.126	0.78 to 0.90	lic blood <sub>1</sub> LDL-C –			
	- phenoty 9 (14.4%)	Mean ±SD	49.52 ±18.25			-		$61.87$ $\pm 9.69$	$\begin{array}{c} 1.66 \\ \pm 0.08 \end{array}$	81.81 ±6.59	22.4 ±2.85	82.76 ±12.2	$134.95 \pm 21.04$		$\begin{array}{c} 1.65 \\ \pm 0.47 \end{array}$	1.28 ±0.57	0.5 $\pm 0.16$	1.07 ±0.32	$\begin{array}{c} 0.85 \\ \pm 0.3 \end{array}$	0 – systol lesterol;
	FG-WC- N=119	Max	79		92	1.83	93	32.466	121	196		2.63	3.41	1.41	1.9	1.5	ce; SBI tein chc			
at not he		Min	20		42	1.46	64	16.298	65	102		0.33	0.7	0.12	0.43	0.08	mferen			
ascille utal acteristics of study p		95% CI	51.85 to 53.86		70.96 to 72.79	1.62 to 1.63	96.47 to 98.05	26.86 to 27.51	83.25 to 84.74	138.53 to 141.27		1.91 to 1.98	1.35 to 1.43	0.460 to 0.48	1.214 to 1.264	1.25 to 1.34	aist circu -density l			
	27 (100 %	Mean ±SD	52.86 ±14.71		71.87 ±13.42	$\begin{array}{c} 1.63 \\ \pm 0.08 \end{array}$	97.26 ±11.59	27.19 ±4.74	83.99 ±11.06	139.9 ±20.125		$\begin{array}{c} 1.94 \\ \pm 0.45 \end{array}$	$\begin{array}{c} 1.39\\ \pm 0.59\end{array}$	$\begin{array}{c} 0.47 \\ \pm 0.12 \end{array}$	$1.239 \pm 0.36$	$\begin{array}{c} 1.29 \\ \pm 0.67 \end{array}$	; WC – w C – high			
	ALL=8	Max	80		125	1.9	135	45.312	135	207		4.59	5.33	1.41	3.97	5.72	s index.			
		Min	20		42	1.45	64	16.162	59	87		0.33	0.7	0.12	0.43	0.08	dy mass yceride			
			Age (years)		Weight (kg)	Height (m)	WC (cm)	BMI (kg/m <sup>2</sup> )	SBP (mm Hg)	DBP (mm Hg)		TC (g/L)	FPG (g/L)	HDL-C (g/L)	LDL-C (g/L)	TG (g/L)	BMI – boc TG – trigl			

e nhenotynes 1mfar Table 1 Baseline characteristics of study narticinants in the triolyceridemia-waist circo

	Total N=827 (100%)	Phenotype TG-WC- N=119 (14.4%)	Phenotype TG+WC- N=16 (1.9%)	Phenotype TG-WC+ N=463 (56%)	Phenotype TG+WC+ N=229 (27.7%)	p-value
Men	254 (30.71%)	94 (79%)	14 (87.5%)	87 (18.8%)	59 (25.8%)	0.000
Women	573 (69.29%)	25 (21%)	2 (12.5%)	376 (81.2%)	170 (74.2%)	0.000
		Clin	ical data			
Metabolic syndrome	548 (66.26%)	11 (9.2%)	13 (81.3%)	300 (64.8%)	224 (97.8%)	0.000
Diabetes mellitus	356 (43.05%)	40 (33.6%)	10 (62.5%)	169 (36.5%)	137 (59.8%)	0.000
Dyslipidemia	517 (62.5%)	45 (37.8%)	11 (68.8%)	261 (56.4%)	200 (87.3%)	0.000
General obesity	225 (27.21%)	1 (0.84%)	1 (6.25%)	138 (29.81%)	85 (37.12 %)	0.000
Central obesity	692 (83.68%)	0 (0%)	0 (0%)	463 (100%)	229 (100 %)	0.000
Hypertension	447 (54.05%)	47 (39.5%)	12 (75%)	244 (52.7%)	144 (62.9%)	0.000
Hypercholesterolemia	105 (12.7%)	7 (5.9%)	3 (18.8%)	37 (8%)	58 (25.3%)	0.000
HyperLDLemia	128 (15.5%)	9 (7.6%)	3 (18.8%)	54 (11.7%)	62 (27.1%)	0.000
HypoHDLemia	427 (51.6%)	33 (27.7%)	5 (31.3%)	229 (49.5%)	160 (69.9%)	0.000

Table 2. Prevalence of cardiovascular risk factors in the triglyceridemia-waist circumference phenotypes

dyslipidemia. Except for hypertension and diabetes mellitus which showed the highest values in TG+WC-phenotypic group (75.0% and 62.5%, respectively), their prevalence in TG+WC+ group were 62.9% and 59.8%, respectively. Concerning the TG-WC- phenotype group had the lowest values. In Figure 2, it was observed that the TG+WC+ phenotype group was associated with the highest prevalence of MetS (97.8%), whereas the TG-WC- phenotype was associated with the lowest prevalence (9.2%).

The use of univariate and multivariate binary logistic regression to identify any relationship between cardiovascular risk factors or MetS and the four TGWC phenotypes has showed that the three phenotypes TG-WC-, TG+WC- and TG-WC+ were less associated to MetS and the cardiovascular disease risk factor with an odds ratio (OR) ranging from 0.01 to 0.86 (Table 3). After caring out adjustment in Models 2 and 3, there was a significant increased risk of 13.89 times (OR) of dyslipidemia in the TG+WC- phenotype. Furthermore, the TG+WC+ phenotype showed a stronger and statistically significant positive association with MetS  $(p < 10^{-3})$  and the other cardiovascular risk factors  $(p < 10^{-3})$  in both Model 1 and adjusted Model 2. Indeed, individuals with the TG+WC+ phenotype had very high odds ratio for MetS and dyslipidemia, as well as high odds ratio for the other risk factors of cardiovascular diseases. The probability of participants with the TG+WC+ phenotype to develop the MetS was higher in Model 1; OR=37.89 for a 95% CI: [15.39 to 93.25]; (p<10<sup>-3</sup>) and Model 2; OR=35.47; for a 95% CI: [14.28 to 88.12]; (p<10<sup>-3</sup>). Moreover, for diabetes mellitus, the OR was 2.59; 95% for a CI: [1.67 to 3.52];  $(p < 10^{-3})$ ; adjusted by age and gender OR=2.31; for a 95% CI: [1.67 to 3.22];  $(p < 10^{-3})$ . For dyslipidemia, the OR was 6.11; for a 95% CI: [4.01 to 9.32]; (p<10<sup>-3</sup>), adjusted by age and gender OR=5.88; for a 95% CI: [3.84 to 8.99];



Figure 2. Prevalence of metabolic syndrome in the triglyceridemia-waist circumference phenotypes

 $(p < 10^{-3})$ . The probability that participants exhibiting the TG+WC+ phenotype developing was for hypertension OR=1.65; for a 95% CI: [1.21 to 2.25]; (p<10<sup>-3</sup>), adjusted by age and gender OR=1.43; for a 95% CI: [1.03 to 1.99]; (p < 0.05); for hypercholesterolemia OR=3.98; for a 95% CI: [2.61 to 6.06]; (p<10<sup>-3</sup>), adjusted by age and gender OR=3.69; 95% CI: [2.41 to 5.66]; (p<10<sup>-3</sup>); for hyperLDLemia OR=2.99; for a 95% CI: [2.03 to 4.41]; (p<10<sup>-3</sup>), adjusted by age and gender OR =2.71; for a 95% CI: [1.83 to 4.02];  $(p<10^{-3})$ ; and for hypoHDLemia OR=2.87; for a 95% CI: [2.08 to 3.98]; (p $<10^{-3}$ ), adjusted by age and gender OR=2.86; for a 95% CI: [2.05 to 3.98]; (p<10<sup>-3</sup>). It should be considered that, according to the data of this study, the TG+WC+ phenotype is highly correlated with MetS, and the underlying risk factors with cardiovascular disease. After adjustment by all predictors in analysis Model 3, the association of MetS (p<10-3), dyslipidemia (p<10<sup>-3</sup>), for hyperLDLemia (p<10<sup>-3</sup>), hypoHDLemia (p<10<sup>-3</sup>), and TG+WC+ persisted. The risk of MetS was doubled, dyslipidemia and hypertension halved, while hypercholesterolemia remained stable.

able 3. Binary logistic <sub>1</sub> yndrome	regression ana	ılysis evaluating associati	ions betwee	en triglyceridemia-wais	t circumfere	ence phenotypes and cau	diovascul	ar risk factors and metab	olic
		Phenotype TG-W N=119	VC-	Phenotype TG+V N=16	VC-	Phenotype TG-W N=463	C+	Phenotype TG+W N=229	/C+
Characterist	ics	Odds ratio (95%CI)	p-value	Odds ratio (95%CI)	p-value	Odds ratio (95%CI)	p-value	Odds ratio (95%CI)	p-value
	Model 1	0.03 (0.02 to 0.06)	0.000	0.03 (0.02 to 0.06)	0.000	0.86 (0.64 to 1.15)	0.314	37.89 (15.39 to 93.25)	0.000
Metabolic syndrome	Model 2	0.02 (0.01 to 0.04)	0.000	0.02 (0.01 to 0.05)	0.000	0.72 (0.52 to 1.01)	0.055	35.47 (14.28 to 88.12)	0.000
	Model 3	0.01 (0 to 0.02)	0.000	5.10 (0.91 to 28.55)	0.063	1.09 (0.69 to 1.74)	0.703	68.21 (15.66 to 297.05)	0.000
	Model 1	0.63 (0.42 to 0.94)	0.026	0.63 (0.42 to 0.94)	0.026	0.54 (0.41 to 0.72)	0.000	2.58 (1.89 to 3.52)	0.000
Diabetes mellitus	Model 2	0.57 (0.35 to 0.93)	0.025	0.57 (0.35 to 0.93)	0.025	0.57 (0.42 to 0.77)	0.000	2.31 (1.67 to 3.22)	0.000

> The abbreviations are as presented in Table 1. Model 1 is applicable. Model 2 was adjusted for age and sex. Model 3 was adjusted for Model 2 in addition to all variables studied, namely metabolic syndrome, diabetes mellitus, dyslipidemia, general obesity, hypertension, hypercholesterolemia, hyperLDLemia, and hyoHDLemia

0.05 (0.01 to 0.45)

0.547

1.75 (0.28 to 10.74)

Model 3

Model 2

HypoHDLemia

Model

0.38 (0.24 to 0.62)

No 2

0.000

2.86 (2.05 to 3.98)

0.75 (0.38 to 1.49)

2.87 (2.08 to 3.98)

0.159 0.006 0.574

> 0.66 (0.49 to 0.89) 1.20 (0.63 to 2.31)

2.6040.008

0.82 (0.62 to 1.08)

0.20 (0.47 to 0.00) 1.62 (4.18 to 0.00)

0.0000.000

0.31 (0.20 to 0.47)

0.83 (0.14 to 4.99)

0.48 (0.22 to 1.04) 0.22 (0.01 to 3.42)

0.48 (0.22 to 1.04)

Model 2

HyperLDLemia

Model

Model 3

0.4 (0.2 to 0.82)

0.012 0.063 0.843

1.02 (0.57 to 1.82)

0.409

0.785 0.000

0.92 (0.5 to 1.69)

2.99 (2.03 to 4.41)

2.58 (1.3 to 5.11)

0.021 0.001

0.47 (0.24 to 0.89)

0.52 (0.35 to 0.76) 0.46 (0.31 to 0.69)

0.000

0.44 (0.19 to 1.04) 0.84 (0.08 to 8.42)

0.0600.697

0.44 (0.19 to 1.07) 1.46 (0.22 to 9.78) 0.41 (0.20 to 0.82)

Model 2 Model 3

Hypercholesterolemia

0.019

0.39 (0.176 to 0.86)

1.14 (0.47 to 2.76)

Model 3

Model

Model 2

Hypertension

Model

0.000

0.38 (0.25 to 0.58) 0.33 (0.21 to 0.52)

0.161 0.591

2.71 (1.83 to 4.02)

0.0000.952

90	Epidemiological aspects of the as	ociation of the hypertriglyceridem	ic waist phenotype with me	etabolic syndrome
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0.000 0.0000.065 0.000 0.030

1.93 (1.39 to 2.68)

1.79 (1.28 to 2.52) 1.48 (0.98 to 2.25) 1.65 (1.21 to 2.25) (1.43 (1.03 to 1.99) 0.58 (0.38 to 0.88) 3.98 (2.61 to 6.06) 3.69 (2.41 to 5.66)

> 0.813 0.379

1.05 (0.72 to 1.53)

0.36 (0.04 to 3.51)

0.004

0.03 (0.00 to 0.33)

0.000

Model 2 Model 3

Obesity general

0.88 (0.67 to 1.16)

0.001

1.09 (0.8 to 1.48) 1.30 (0.9 to 1.88)

0.000 0.850 0.020 0.060 0.8840.012 0.063 0.283 0.306

0.34 (0.21 to 0.55)

0.000

0.34 (0.21 to 0.55)

0.5 (0.34 to 0.75)

0.001

0.50 (0.34 to 0.75)

1.15 (0.26 to 5.14) 0.39 (0.18 to 0.86)

0.771

0.001

0.000 0.0000.006 0.0000.000

0.012

0.000

5.88 (3.84 to 8.99) 3.97 (1.76 to 8.95)

0.000 0.006 0.059 0.686

0.43 (0.31 to 0.59) 0.37 (0.18 to 0.76) 1.35 (0.99 to 1.85) 1.07 (0.77 to 1.49)

(13.89 (1.28 to 150.37)

0.02 (0 to 0.13) 0.03 (0 to 0.18)

0.000

0.02 (0.00 to 0.13) 0.03 (0.00 to 0.18)

1.41 (0.21 to 9.3)

0.37 (0.23 to 0.58)

0.30 (0.2 to 0.45)

0.000 0.0000.720

0.30 (0.20 to 0.45) 0.37 (0.23 to 0.58)

Model 2

Dyslipidemia

Model

Model 3

Model 1

0.55 (0.41 to 0.73)

6.11 (4.01 to 9.32)

0.000

0.113 0.000

1.39 (0.92 to 2.1)

0.003

0.58 (0.4 to 0.83)

0.273 0.000 0.000 0.030 0.000 0.000 0.382

0.46 (0.12 to 1.84)

0.061

2.64 (0.96 to 7.26)

Model 3

### DISCUSSION

To our knowledge, there is no comparative data linking triglyceridemic-waist circumference (TGWC) phenotypes with MetS or cardiovascular risk factors among different ethnic groups in Morocco. This epidemiological investigation is the first study conducted among the Amazigh population in the geographic region called Souss, aiming to examine the relationship between TGWC phenotypes and MetS or some other cardiovascular diseases risk factors.

According to the finding of this survey, 27.7% of Amazigh participants presented a WC+TG+ phenotype, with a higher prevalence among women (29.7%) compared to men (23.2%).

According to the previous published papers, the prevalence of WC+TG+ phenotype in our studied sample was close to that observed in Norfolk, UK, which is 27.81% in women and 31.20% in men [33], higher to the ones found in a studies carried out in Nigeria 23.4% [34], in the municipality of Shanghai 21.2% [35] and almost double that the ones recorded in China 15.22% and 15.93% [36, 37]. However, it is lower than that observed in other countries or regions like in Spain (38.2%) [38], South Asian Indians (35.4%) [39], and in Quebec City metropolitan area (80%) [20].

Regarding the MetS prevalence, the lowest (9.2%) was observed in individuals with the TG-WCphenotype, and the highest value (97.8%) was recorded within individuals with the TG+WC+ phenotype group which indicates that individuals with the TG+WC+ phenotype are predominantly affected by multiple abnormal metabolic parameters. This same finding was also reported in South African by Prakaschandra and Naidoo in 2022 [39] in which the prevalence of MetS was equal to 88.7% in the TG+WC+ phenotype group. Therefore, it may be suggested that the TG+WC+ phenotype constitutes a more accurate predictor of MetS than previously thought and can be used as a way for early screening and identification of individuals with an elevated risk of developing MetS. It is well known that MetS is a condition that includes a cluster of risk factors specific for cardiovascular disease, thus this study reports higher, even alarming, prevalence of cardiovascular risk factors in individuals exhibiting the TG+WC+ phenotype compared to those who are considered normal (TG-WC-). Indeed, the prevalence of seven risk factors investigated in this study were 87.3%, 62.9%, 69.9%, 59.8%, 37.12%, 25.3% and 27.1% for dyslipidemia, hypertension, low HDL levels, type 2 diabetes, obesity, hypercholesterolemia and hyperLDLemia, respectively.

Also, subjects with the TG+WC+ phenotype seems to be at a higher risk than those with other phenotypes to develop MetS (37 to 68 times more), dyslipidemia (4 to 6 times more), type 2 diabetes (3 to 2 times more), hypertension (1 to 2 times more), hypercholesterolemia (4 times more), general obesity (2 to times more), hyperLDLemia and low HDL (3 times more).

This finding confirms what was previously published from several studies. Gazi and all reported that people with the TG+WC+ phenotype presented also a dyslipidemia, high LDL-cholesterol, and low HDL cholesterol [40, 41]. In a meta-analysis study carried out by Ma and all on a sample of 242 879 subjects from the general population of 19 countries, the pooled odds ratio for type 2 diabetes related to the TG+WC+ phenotype was equal to 2.89 in non-diabetic subjects [42]. In a prospective cohort study of 95 015 participants in China reported that the TG+WC+ phenotype is associated with a nearly 1.24 to 2 times increased risk of developing CVD [43]. Moreover, in a cohort study conducted in Norfolk, UK, it was observed that men and women who had the TG+WC+ phenotype faced 2.4 and 3.84 times higher risk of developing coronary heart disease in comparison to healthy population (TG-WC-) [33] confirming the ability of TG+WC+ phenotype to identify individuals at elevated risk factors for CVD [17, 33, 37].

# CONCLUSIONS

This study presents novel findings regarding the prevalence of the TG+WC+ phenotype and confirms its relation to metabolic syndrome and cardiovascular diseases risk factors among the Amazigh population living in Morocco. The findings suggest that the TG+WC+ phenotype is associated with a heightened risk of MetS and cardiovascular diseases risk factors, persisting even after adjusting for confounding factors such as sex, age, and other relevant risk factors.

The simplicity, reproducibility, and low cost of the TG+WC+ phenotype make it a valuable and practical tool to identify individuals at an elevated risk of cardiovascular disease. However, further studies involving other ethnic groups from Morocco are recommended to confirm the present findings and evaluate the efficacy of using TG+WC+ phenotype as a clinical or epidemiological tool.

This study presents the first data on the prevalence of the TG+WC+ phenotype and its association with MetS and cardiovascular diseases risk factors in a representative sample of the Amazigh ethnic group from the geographical region of Souss in Morocco.

# **Ethics statement**

The protocol for this survey has been reviewed and validated by the Ethics Committee (N° IRB00012973) and authorized by the Ministry of Health and Social Protection. Participants were informed of the aims and objectives of the study, and informed consent was obtained in writing.

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# **Conflict of interest**

The authors disclose no conflicts of interest.

# REREFENCES

- Xu H, Li X, Adams H, Kubena K, Guo S. Etiology of Metabolic Syndrome and Dietary Intervention. Int J Mol Sci. 2018;20(1):128. doi: 10.3390/ijms20010128.
- Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, Nkeck JR, Nyaga UF, Ngouo AT, et al. Geographic distribution of metabolic syndrome and its components in the general adult population: A meta-analysis of global data from 28 million individuals. Diabetes Res Clin Pract. 2022;188:109924. doi: 10.1016/j.diabres.2022.109924.
- Chadli S, Taqarort N, Houate BE, Oulkheir S. Epidemiological transition in Morocco (1960-2015). Médecine Santé Trop. 2018;28(2):201-205. doi: 10.1684/ mst.2018.0800.
- De Vries TI, Cooney MT, Selmer RM, Hageman SHJ, Pennells LA, Bois A, et al. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. Eur Heart J. 2021;42(25):2455-2467. doi: 10.1093/eurheartj/ ehab312.
- Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J Am Coll Cardiol. 2020;76(25):2982-3021. doi: 10.1016/j. jacc.2020.11.010.
- Mensah GA, Fuster V, Murray CJL, Roth GA, Abate Y H, Abbasian M, et al. Global Burden of Cardiovascular Diseases and Risks, 1990-2022. J Am Coll Cardiol. 2023;82(25):2350-2473. doi: 10.1016/j.jacc.2023.11.007.
- Najeh H, Rherissi B, Ezzikouri S, Belmouden A, Chadli S. Genetic study of the metabolic syndrome in the Moroccan population: A scoping review. E3S Web Conf. 2023;460:11014. doi: 10.1051/e3sconf/202346011014.
- Rguibi M, Belahsen R. Metabolic syndrome among Moroccan Sahraoui adult women. Am J Hum Biol. 2004;16(5):598-601. doi: 10.1002/ajhb.20065.
- Harraqui K, Oudghiri DE, Hannoun Z, Naceiri Mrabti H, Aboulghras S, Assaggaf H, et al. Frequency of Metabolic Syndrome and Study of Anthropometric, Clinical and Biological Characteristics in Peri- and Postmenopausal Women in the City of Ksar El Kebir (Northern Morocco). Int J Environ Res Public Health. 2022;19(10):6109. doi: 10.1002/ajhb.20065.

- Cornier M-A, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, et al. The metabolic syndrome. Endocr Rev. 2008;29(7):777-822. doi: 10.3390/ijerph19106109.
- Samson SL, Garber AJ. Metabolic Syndrome. Endocrinol Metab Clin North Am. 2014;43(1):1-23. doi: 10.1016/j. ecl.2013.09.009.
- Engin A. The Definition and Prevalence of Obesity and Metabolic Syndrome. In: Obesity and Lipotoxicity. (Engin AB, Engin A. eds). Advances in Experimental Medicine and Biology Springer International Publishing: Cham; 2017; pp. 1-17. doi: 10.1007/978-3-319-48382-5\_1.
- 13. Zhu S, Wang ZM, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesityassociated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. Am J Clin Nutr. 2002;76(4):743-749. doi: 10.1093/ajcn/76.4.743.
- 14. Ford ES. The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality Study. Atherosclerosis 2004;173(2):307-312. doi: 10.1016/j.atherosclerosis.2003.12.022.
- Lee BJ, Kim JY. Identification of metabolic syndrome using phenotypes consisting of triglyceride levels with anthropometric indices in Korean adults. BMC Endocr Disord. 2020;20:29. doi: 10.1186/s12902-020-0510-0.
- 16. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obes Rev Off J Int Assoc Study Obes. 2002;3(3):141-146. doi: 10.1046/j.1467-789X.2002.00065.x.
- Lemieux I, Poirier P, Bergeron J, Alméras N, Lamarche B, Cantin B, et al. Hypertriglyceridemic waist: a useful screening phenotype in preventive cardiology? Can J Cardiol. 2007;23(Suppl B):23B-31B. doi: 10.1016/S0828-282X(07)71007-3.
- Sam S, Haffner S, Davidson MH, D'Agostino Sr RB, Feinstein S, Kondos G, et al. Hypertriglyceridemic Waist Phenotype Predicts Increased Visceral Fat in Subjects With Type 2 Diabetes. Diabetes Care. 2009;32(10):1916-1920. doi: 10.2337/dc09-0412.
- Laurent-Jaccard A. Is excess weight a cardiovascular risk factor? Rev Med Suisse. 2002;2383:542-544. doi: 10.53738/REVMED.2002.-2.2383.0542.
- 20. Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Alméras N, et al. Hypertriglyceridemic waist: A marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? Circulation. 2000;102(2):179-184. doi: 10.1161/01.CIR.102.2.179.
- Chen S, Guo X, Yu S, Yang H, Sun G, Li Z, et al. Hypertriglyceridemic waist phenotype and metabolic abnormalities in hypertensive adults. Medicine (Baltimore) 2016;95(49):e5613. doi: 10.1097/ MD.000000000005613.
- 22. Shi WR, Wang HY, Chen S, Guo XF, Li Z, Sun YX. Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study. Lipids Health Dis. 2018;17(1):236. doi: 10.1186/ s12944-018-0886-2.

- 23. Li K, Cao B, Ke J, Yang L, Zhao D. Association of Hyper-Triglyceridemic Waist Phenotype and Diabetic Vascular Complication in the Chinese Population. Diabetes Metab Syndr Obes [Internet]. 2023;16:2233-41. doi: 10.2147/ DMSO.S416668.
- 24. Lee BJ, Nam J, Kim JY. Predictors of metabolic abnormalities in phenotypes that combined anthropometric indices and triglycerides. BMC Complement Altern Med. 2016;16:59. doi: 10.1186/ s12906-016-1024-1.
- 25. de Cuevillas B, Alvarez-Alvarez I, Riezu-Boj JI, Navas-Carretero S, Martinez JA. The hypertriglyceridemicwaist phenotype as a valuable and integrative mirror of metabolic syndrome traits. Sci Rep [Internet]. 2021;11:21859. doi: 10.1038/s41598-021-01343-x.
- 26. Xiang Y, Zhou W, Duan X, Fan Z, Wang S, Liu S, et al. Metabolic Syndrome, and Particularly the Hypertriglyceridemic-Waist Phenotype, Increases Breast Cancer Risk, and Adiponectin Is a Potential Mechanism: A Case–Control Study in Chinese Women. Front Endocrinol. 2020;10:905. doi: 10.3389/fendo.2019.00905.
- 27. Czernichow S, Bruckert E, Bertrais S, Galan P, Hercberg S, Oppert JM. Hypertriglyceridemic waist and 7.5-year prospective risk of cardiovascular disease in asymptomatic middle-aged men. Int J Obes. 2007;31(5):791-796. doi: 10.1038/sj.ijo.0803477.
- Thomas MC, Zimmet P, Shaw JE. Identification of Obesity in Patients With Type 2 Diabetes From Australian Primary Care: The NEFRON-5 Study. Diabetes Care. 2006;29(12):2723-2725. doi: 10.2337/dc06-1288.
- 29. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International atherosclerosis society; And international association for the study of obesity. Circulation. 2009;120(16):1640-1645. doi: 10.1161/CIRCULATIONAHA.109.192644.
- 30. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. Guía de práctica clínica de la ESH/ ESC para el manejo de la hipertensión arterial (2013). Hipertens Riesgo Vasc. 2013;30:4-91. doi: 10.1016/S1889-1837(13)70027-8.
- Blonde L, Umpierrez GE, Reddy SS, McGill JB, Berga SL, Bush M, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Pland 2022 Update. Endocr Pract. 2022;28(10):923-1049. doi: 10.1079/BJN19910073.
- 32. Deurenberg P, Weststrate JA, Seidell JC. Body mass index as a measure of body fatness: age- and sex-specific prediction formulas. Br J Nutr. 1991;65(2):105-114. doi: 10.1079/BJN19910073.
- 33. Arsenault BJ, Lemieux I, Després JP, Wareham NJ, Kastelein JJ, Khaw KT et al. The hypertriglyceridemicwaist phenotype and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. CMAJ Can Med Assoc J. 2010;182(13):1427-1432. doi: 10.1503/cmaj.091276.

- 34. Amadi CE, Mbakwem AC, Duro DC, Udenze IC, Akinsola CM, Ajuluchukwu JN, et al. Prevalence, patterns and predictors of metabolic abnormalities in Nigerian hypertensives with hypertriglyceridemic waist phenotype: A cross sectional study. PLOS Glob Public Health. 2022;2(12):e0001203. doi: 10.1371/journal. pgph.0001203.
- 35. Xuan Y, Shen Y, Wang S, Gao P, Gu X, Tang D, et al. The association of hypertriglyceridemic waist phenotype with hypertension: A cross-sectional study in a Chinese middle aged-old population. J Clin Hypertens. 2022;24(2):191-199. doi: 10.1111/jch.14424.
- 36. Wang A, Li Z, Zhou Y, Wang C, Luo Y, Liu X, et al. Hypertriglyceridemic waist phenotype and risk of cardiovascular diseases in China: results from the Kailuan Study. Int J Cardiol. 2014;174(1):106-109. doi: 10.1016/j.ijcard.2014.03.177.
- Zheng X, Ren X, Jiang M, Han L. Association between hypertriglyceridemic-waist phenotype and cardiovascular disease: A cohort study and metaanalysis. Front Cardiovasc Med. 2022;9:940168. doi: 10.3389/fcvm.2022.940168.
- Fernández-García JC, Muñoz-Garach A, Martínez-GonzálezMÁ, Salas-Salvado J, Corella D, Hernáez Á, etal. Association Between Lifestyle and Hypertriglyceridemic Waist Phenotype in the PREDIMED-Plus Study. Obes Silver Spring Md. 2020;28(3):537-543. doi: 10.1002/ oby.22728.
- 39. Prakaschandra R, Naidoo DP. The association between the hypertriglyceridaemia waist phenotype, cardiovascular risk factors and the metabolic syndrome in South African Asian-Indians. Diabetes Metab Syndr Clin Res Rev. 2022;16(6):102524. doi: 10.1016/j.dsx.2022.102524.
- 40. Gazi IF, Filippatos TD, Tsimihodimos V, Saougos VG, Liberopoulos EN, Mikhailidis DP, et al. The hypertriglyceridemic waist phenotype is a predictor of elevated levels of small, dense LDL cholesterol. Lipids. 2006;41(7):647-654. doi: 10.1007/s11745-006-5015-8.
- 41. Dikaiakou E, Athanasouli F, Fotiadou A, Kafetzi M, Fakiolas S, Michalacos S, et al. Hypertriglyceridemic Waist Phenotype and Its Association with Metabolic Syndrome Components, among Greek Children with Excess Body Weight. Metabolites. 2023 Feb 3;13(2):230. doi: 10.3390/metabol3020230.
- 42. Ma CM, Liu XL, Lu N, Wang R, Lu Q, and Yin FZ. Hypertriglyceridemic waist phenotype and abnormal glucose metabolism: a system review and meta-analysis. Endocrine. 2019;64(3):469-485. doi: 10.1007/s12020-019-01945-6.
- 43. Wang A, Li Z, Zhou Y, Wang C, Luo Y, Liu X, et al. Hypertriglyceridemic waist phenotype and risk of cardiovascular diseases in China: results from the Kailuan Study. Int J Cardiol. 2014;174(1):106-109. doi: 10.1016/j.ijcard.2014.03.177.

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