Inflammation and Cardiovascular Risk Assessment in Moroccan Obese Patients with and without Metabolic Syndrome: Importance of Lipoproteins Ratios

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Background: Obesity predisposes an individual to numerous risk factors for cardiovascular diseases. Inflammation, reported as a link between obesity and cardiovascular disease, contributes to the development of atherosclerosis.

Objectives: The aim of our study was to assess the relationship between lipid parameters, low grade inflammation and metabolic syndrome in a sample of obese Moroccan adults with or without metabolic syndrome (MetS).

Patients & methods: Our study included 235 obese patients, mean aged 53.30 ± 9.73 years, with or without MetS. Our data included anthropometric measurements, lipoprotein and apolipoproteins profiles and several lipid ratios.

Results: In patients with MetS, lipoprotein profile alterations and low-grade inflammation were observed. Lipid ratios were better predictors of cardiovascular risk than lipids alone because of their relative associations with lipoproteins and apolipoproteins.

Conclusion: Our study shows that Moroccan obese adults with MetS have altered lipoproteins profiles and suffer from low-grade inflammation. Indeed, we have detected a high level of small dense LDL particles and HDL particles defectiveness. Hence, we propose that risk management of cardiovascular events should be based on lipoprotein ratios rather than lipids alone. Treatments should also take into account inflammatory markers and LDL heterogeneity. (*Ethn Dis.* 2014;24[4]:462–468)

Key Words: Obesity, Metabolic Syndrome, Inflammation, Lipids, Cardiovascular Risk Factors

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Introduction

Obesity is associated with multiple atherosclerosis risk factors such as abdominal obesity, insulin resistance (IR), atherogenic dyslipidemia and hypertension. The cluster of these risk factors has been termed metabolic syndrome (MetS).[1,2] Obesity represents a major public health problem in an increasing number of countries[3,4] and the raising prevalence of MetS[2] is reported as a consequence of the ongoing obesity epidemic.[5,6]

Recently, some forms of obesity were reported to be associated with chronic low-grade inflammation,[4,7] which is a fundamental mechanism of the pathogenesis of atherosclerotic vascular disease and MetS,[6,8] allowing recognition of atherosclerosis as an inflammatory process.[9] Considered as emergent risk factors, inflammatory markers can be potentially used in the clinical stratification of cardiovascular diseases (CVD).[10–12] Moreover, some people exhibit chronically elevated levels of C-reactive protein (CRP), the most common inflammatory marker of cardiovascular and metabolic disorders, within upper normal range, which indicates a systemic low-grade inflammation.[13,14]

To date, few studies on MetS were conducted in the North-African population.[6,15] Therefore, the aim of our study was to assess the relationship between lipid parameters, low-grade inflammation, MetS and its components in a population of obese Moroccan adults with or without MetS. Furthermore, we also evaluated the association of lipid and apolipoproteins ratios, atherogenic index of plasma (AIP) and non-HDL-cholesterol (non-HDL-C) with particular lipid parameters.

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Patients and Methods

Our study included 235 obese patients (160 women, 75 men), mean age 53.30 ± 9.73 years, with or without MetS. At the time of enrolment, they completed a health and lifestyle questionnaire indicating sociodemographic characteristics, medical history, and lifestyle factors. Participants were considered to be smokers if they smoked at the time of data collection or had stopped smoking less than one year before. Patients having some diseases affecting the lipoprotein metabolism were excluded from this study. All participants were Moroccan adult volunteers living in Casablanca and its neighboring areas and all provided their written informed consents.

Anthropometric measurements, lipids parameters analyses, cardiovascular risk assessment and definitions of obesity and MetS adopted have been detailed in

a previous publication.[15,16] Moreover, low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) levels were calculated according to the Friedwald's formula. We have assessed apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B) and CRP concentrations using nephelometry techniques. Apolipoproteins ratios, such as apolipoprotein B to apolipoprotein A1 (Apo B/ Apo A1), LDL to Apo B (LDL/Apo B) and HDL to Apo A1 (HDL/Apo A1), were calculated; AIP was defined as the logarithm of the TG/HDL ratio.

Serum equivalent CRP concentrations >10.0 mg/L were considered clinically elevated and indicative of current infection.

Statistical Analysis

Mean levels and standard deviations of lipid parameters were calculated in each group of participants. The differences between each mean value of the lipid levels were assessed by ANOVA tests. Linear regression analysis was performed to test associations between lipids ratios and predicted risks of developing CVD, myocardial infarction (MI), stroke and coronary heart disease (CHD). Odds Ratio and 95% Confidence Interval were assessed after binomial logistic regression analysis. Differences with $P<.05$ were considered statistically significant. All analyses were conducted using R free software, version 2.12.0 for statistical analysis.

Table 1. Baseline characteristics of the study population

Parameters	Obese without MetS (*n*=115)	Obese with MetS (*n*=120)
Sex-ratio (male/female)	.29	.35
Age, years	52.10 ± 9.99	54.45 ± 9.33
BMI, kg/m^2	33.49 ± 3.26	34.68 ± 4.41[a]
WC, cm	108.18 ± 7.90	111.10 ± 9.45[a]
sBP, mm Hg	122.07 ± 18.91	133.13 ± 17.55[c]
dBP, mm Hg	73.48 ± 9.81	79.43 ± 11.78[c]
MetS components number, %		
1	17.02	
2	31.92	
3	33.19	
4	13.62	
5	4.26	
Type of MetS components, %		
High WC	96.52	100[a]
High TG,	8.70	56.67[c]
Low HDL-C,	7.83	39.17[c]
Hypertension	33.91	75.00[c]
Diabetes	21.74	68.33[c]
CRP category stratification, %		
CRP <3 mg/dL	36.11	34.69
CRP 3–10mg/dL	41.67	38.78
CRP >10 mg/dL	22.22	26.53
Lipid parameters		
TC, mmol/L	4.98 ± .83	5.24 ± 1.10[a]
HDL-C, mmol/L	1.43 ± .27	1.23 ± .31[c]
LDL-C, mmol/L	3.01 ± .78	3.12 ± .95
TG, mmol/L	1.21 ± .53	2.01 ± .94[c]
VLDL-C, mmol/L	.55 ± .24	.92 ± .43[c]
Apo AI, mg/dL	158.61 ± 36.70	168.42 ± 44.10
Apo B, mg/dL	106.45 ± 24.47	127.01 ± 27.28[c]
TC/HDL	3.60 ± .87	4.47 ± 1.23[c]
TG/HDL	.91 ± .53	1.80 ± 1.16[c]
LDL/Apo B	1.14 ± .19	.99 ± .21[b]
HDL/Apo A1	.33 ± .06	.28 ± .06[c]
Apo B/A1	.70 ± .21	.85 ± .44
Non HDL-C, mg/dL	137.34 ± 32.21	154.98 ± 41.76[c]
AIP	−.10 ± .21	.19 ± .25[c]

Data are mean ± SD unless indicated otherwise.

AIP, atherogenic index of plasma; Apo, apolipoprotein; BMI, body mass index; CRP, C-reactive protein; dBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MetS, metabolic syndrome; sBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; VLDL-C, very low density lipoprotein cholesterol; WC, waist circumference.

[a] $P<.05$.

[b] $P<.001$.

[c] $P<.0001$.

RESULTS

Baseline characteristics of our study population are summarized in Table 1. Obese patients with MetS presented higher body mass index (BMI), waist circumference (WC), systolic and diastolic blood pressures (sBP and dBP) values than those without MetS. Of the studied population, 17.02%, 31.92%, 33.19%, 13.62% and 4.26% had one, two, three, four or five MetS components, respectively. The most prevalent MetS components were high WC, hypertension and diabetes while low HDL-C was the least in both groups. Most participants had CRP levels between 3 and 10 mg/dL with no difference between both groups.

Obese participants with MetS showed higher levels of total cholesterol (TC), triglycerides (TG), VLDL-C and Apo B levels as compared to those without MetS, while LDL-C and Apo A1 were similar between both groups. The reduction of high-density lipoprotein cholesterol (HDL-C), observed in patients with MetS, leads to higher lipid and apolipoproteins ratios such as TC/HDL and TG/HDL. LDL/ Apo B and HDL/Apo A1 decreased in presence of MetS while Apo B/A1 remained similar

Table 2. Spearman's correlation coefficients in the whole population

										Predicted Risks of				
	TC/HDL	TG/HDL	Non HDL-C	AIP	Apo A1	Apo B	LDL/Apo B	Apo B/A1	HDL/Apo A1	CHD	MI	Stroke	CVD	CVD Death
TC	.64[d]	.28[b]	.96[d]	.36[c]	NS	.80[d]	NS	.56[d]	NS	.36[c]	.35[c]	NS	.26a	NS
HDL-C	−.66[d]	−.56[d]	NS	−0.68[d]	.53[d]	NS	NS	−.26[a]	−.44[d]	−.38[d]	−.33[b]	NS	−.26a	−.29[b]
LDL-C	.59[d]	NS	.85[d]	NS	NS	.74[d]	.47[d]	.58[d]	NS	.26[a]	.25[a]	NS	NS	NS
TG	.65[d]	.95[d]	.52[d]	.90[d]	NS	.35[c]	−.30[b]	.24[a]	.40[d]	.49[d]	.47[d]	NS	.40d	.36c
VLDL-C	.65[d]	.95[d]	.52[d]	.90[d]	NS	.35[c]	−.30[b]	.24[a]	.40[d]	.49[d]	.47[d]	NS	.40d	.36c
TC/HDL		.71[d]	.82[d]	.78[d]	−.35[c]	.62[d]	NS	.55[d]	.32[b]	.59[d]	.55[d]	NS	.42d	.36c
TG/HDL			.44[d]	.88[d]	NS	.25[a]	−.27[a]	.22[a]	.45[d]	.49[d]	.47[d]	NS	.38d	.38d
Non HDL-C				.55[d]	NS	.81[d]	NS	.62[d]	NS	.46[d]	.44[d]	NS	.33b	.22a
AIP					−.74[a]	.39[d]	−.22[a]	.34[b]	.48[d]	.56[d]	.52[d]	.21[a]	.45d	.40d
Apo A1						NS	−.50[d]	−.30[b]	−.47[d]	NS	NS	NS	NS	NS
Apo B							NS	.47[d]	−.29[b]	.40[d]	.36[c]	NS	.32[b]	NS
LDL/Apo B								NS	.57[d]	NS	NS	−.25[a]	NS	NS
Apo B/A1									NS	NS	NS	NS	NS	NS
HDL/Apo A1										−.38[d]	−.33[b]	−.29[b]	−.36[c]	−.35[c]

AIP, atherogenic index of plasma; Apo, apolipoprotein; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; VLDL-C, very low density lipoprotein cholesterol; CVD, cardiovascular disease; CHD, coronary heart disease; MI, myocardial infarction, NS, not significant.

[a] $P<.05$.
[b] $P<.01$.
[c] $P<.001$.
[d] $P<.0001$.

in both groups. We also noticed greater values of non-HDL-C and atherogenic index of plasma (AIP) in obese with MetS as compared to those without MetS.

Table 2 presents Spearman's correlation coefficients between lipid parameters and predicted risks of different cardiovascular outcomes. Associations between different cardiovascular outcomes and lipid ratios were stronger as compared to those of lipoproteins alone and apolipoproteins ratios. The highest Spearman's coefficients with predicted risks of CHD, MI, CVD and CVD death were found with TC/HDL and AIP. Moreover, LDL/Apo B's correlation with predicted risk of stroke was stronger than AIP's.

Lipid parameters variations according to the presence or the absence of low grade inflammation, number and types of MetS features and sex are shown in Table 3. There was no significant variation in all parameters due to inflammation, high WC, hypertension and/or diabetes. Men, as compared to women, had greater values of TG, VLDL-C, TC/HDL, TG/HDL and AIP due to the decrease of HDL-C levels. According to the number of MetS components, variations in HDL-C, TG, VLDL-C, TC/HDL, TG/HDL, non HDL-C, AIP and Apo B began when people had at least 2 MetS features. Total cholesterol and Apo B/A1 levels increased in people with 5 MetS components. LDL-C and Apo A1 did not present any significant modification according to increasing number of MetS components. Obese patients with 2 MetS features had higher LDL/Apo B level but it decreased in those with 4 MetS components. The ratio of HDL/Apo A1 increased in obese participants with at least 3 MetS features.

Regarding the type of MetS component, we noticed that hypertriglyceridemia and hypo-HDL-emia were accompanied by variations in all lipid parameters panel, except Apo A1 and LDL/Apo B. Hypo-HDL-emia did not affect LDL-C, non-HDL-C, Apo B and Apo B/A1 levels while hypertriglyceridemia did not affect HDL/Apo A1 level.

Table 3. Lipid parameter variations according to low-grade inflammation, sex and number of MetS features, mean (SD)

	CRP		Sex		Number of MetS Components				
	< 3 mg/dL	3–10 mg/dL	Women	Men	1	2	3	4	5
TC, mmol/L	5.45 (.94)	5.19 (1.15)	5.11 (.98)	5.11 (1.01)	4.87 (.81)	5.04 (.84)	5.13 (1.07)	5.35 (1.13)	5.73 (1.06)[a]
HDL-C, mmol/L	1.25 (.32)	1.25 (.29)	1.36 (.30)	1.20 (.29)[c]	1.47 (.25)	1.40 (.28)[d]	1.27 (.34)[b]	1.18 (.21)[d]	1.01 (.08)[d]
LDL-C, mmol/L	3.31 (.82)	3.27 (.96)	3.07 (.86)	3.05 (.91)	2.91 (.85)	3.07 (.74)	3.06 (.93)	3.10 (.95)	3.62 (.93)
TG, mmol/L	1.93 (1.07)	1.66 (1.08)	1.50 (.66)	2.01 (1.25)[d]	1.14 (.69)	1.25 (.41)[d]	1.83 (1.00)[d]	2.33 (.74)[d]	2.39 (.45)[d]
VLDL-C, mmol/L	.88 (.49)	.75 (.49)	.68 (.30)	.91 (.57)[d]	.52 (.31)	.57 (.18)[d]	.83 (.46)[d]	1.06 (.33)[d]	1.09 (.20)[d]
TC/HDL	4.66 (1.49)	4.33 (1.27)	3.91 (1.06)	4.47 (1.37)[b]	3.42 (.87)	3.70 (.86)[d]	4.26 (1.25)[d]	4.56 (.76)[d]	5.76 (1.41)[d]
TG/HDL	1.77 (1.37)	1.48 (1.36)	1.21 (.70)	1.88 (1.54)[d]	.84 (.69)	.94 (.40)[d]	1.63 (1.28)[d]	2.05 (.81)[d]	2.40 (.60)[d]
Non-HDL-C, mg/dL	162.17 (39.46)	152.56 (43.54)	144.89 (37.98)	151.11 (39.44)	131.55 (33.31)	140.43 (31.17)[d]	149.00 (41.40)[a]	161.00 (38.10)[b]	182.40 (41.98)[c]
AIP	.14 (.30)	.07 (.29)	.01 (.25)	.17 (.30)[d]	−.15 (.30)	−.07 (.19)[d]	.12 (.27)[d]	.28 (.17)[d]	.37 (.10)[d]
Apo A1, mg/dL	159.14 (33.14)	158.01 (42.04)	165.41 (41.98)	162.97 (40.74)	166.4 (30.17)	152.38 (40.12)	171.77 (42.06)	160.49 (40.77)	170.18 (63.15)
Apo B, mg/dL	120.68 (24.03)	117.87 (32.76)	115.13 (30.90)	121.88 (23.90)	104.28 (21.76)	108.19 (26.31)[d]	124.46 (24.50)[b]	118.75 (19.24)	175.75 (22.42)[d]
LDL/Apo B	1.06 (.14)	1.10 (.26)	1.09 (.20)	1.01 (.22)	1.08 (.14)	1.19 (.20)[b]	1.02 (.23)	.91 (.145)[b]	1.00 (.20)
HDL/Apo A1	.30 (.05)	.32 (.07)	.32 (.07)	.29 (.05)	.33 (.04)	.33 (.08)	.28 (.05)[c]	.29 (.07)[a]	.24 (.06)[b]
Apo B/A1	.79 (.22)	.85 (.51)	.78 (.46)	.78 (.21)	.65 (.18)	.74 (.21)	.85 (.52)	.77 (.14)	1.13 (.29)[c]

AIP, atherogenic index of plasma; Apo, apolipoprotein; CRP, protein-C-reactive; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MetS, metabolic syndrome; TC, total cholesterol; TG, triglycerides; VLDL-C, very low density lipoprotein cholesterol.

[a] $P<.05$.
[b] $P<.01$.
[c] $P<.001$.
[d] $P<.0001$.

Binomial logistic regression of some lipoproteins and apolipoproteins ratios and predicted risks of several cardiovascular outcomes are shown in Table 5. The ratio of TC/HDL and AIP were the best predictors of MetS and their ORs were significantly higher in men than in women. All cardiovascular outcomes predicted risks were elevated with increased number of MetS components, in men and in participants with MetS.

DISCUSSION

Our study reports a relationship between the MetS, low-grade inflammation and lipoprotein metabolism disturbances in Moroccan obese patients, leading to raised cardiovascular risk.

We have shown that most of obese patients with MetS present CRP levels >3 mg/dl, which is in agreement with several reports.[2,6,17–19] Recently, some scientists suggested that CRP predicted future MetS independent of age and its 5 components, and that it should be added as a MetS component.[2,19–22] Indeed, low-grade inflammation and its association with obesity may promote IR in various tissues.[3,20] Besides, IR leads to an increased flux of free fatty acids (FFA) into various tissues because of enhanced lipolysis and reduced FFA uptake and esterification. Since FFA competes with glucose for cellular uptake and metabolism, it can further reduce insulin sensitivity, instituting a vicious cycle.[23]

We have shown that most of obese patients with MetS present CRP levels >3 mg/dl, which is in agreement with several reports.[2,6,17–19]

Table 4. Lipid parameters variations according to types of MetS components, mean (SD)

	High WC		Hypertriglyceridemia		Hypo-HDL-emia		High BP		Hyperglycemia	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
TC, mmol/L	4.69 (.22)	5.12 (.99)	4.86 (.89)	5.62 (.97)[d]	5.18 (.95)	4.88 (1.07)[a]	5.00 (.90)	5.20 (1.04)	5.07 (.94)	5.16 (1.04)
HDL-C, mmol/L	1.29 (.18)	1.32 (.31)	1.39 (.31)	1.19 (.25)[d]	1.42 (.27)	1.00 (.16)[d]	1.32 (.30)	1.33 (.31)	1.33 (.32)	1.32 (.29)
LDL-C, mmol/L	2.50 (.72)	3.08 (.87)	2.92 (.79)	3.35 (.96)[d]	3.09 (.87)	2.98 (.89)	3.00 (.83)	3.12 (.90)	3.04 (.86)	3.09 (.89)
TG, mmol/L	1.93 (1.17)	1.62 (.84)	1.20 (.51)	2.47 (.81)[d]	1.52 (.82)	1.94 (.92)[b]	1.55 (.90)	1.68 (.83)	1.57 (.89)	1.69 (.82)
VLDL-C, mmol/L	.88 (.79)	.73 (.38)	.55 (.23)	1.12 (.37)[d]	.69 (.37)	.88 (.42)[b]	.71 (.41)	.76 (.38)	.71 (.40)	.77 (.37)
TC/HDL	3.72 (.65)	4.05 (1.16)	3.64 (.95)	4.87 (1.09)[d]	3.76 (1.00)	4.94 (1.15)[d]	3.97 (1.07)	4.11 (1.21)	4.03 (1.15)	4.06 (1.16)
TG/HDL	1.70 (1.78)	1.36 (.99)	.94 (.64)	2.22 (1.07)[d]	1.16 (.87)	2.01 (1.14)[d]	1.32 (1.06)	1.40 (.96)	1.33 (1.05)	1.40 (.96)
Non-HDL-C, mg/dL	131.25 (14.53)	146.61 (38.65)	134.02 (33.17)	171.17 (36.18)[d]	145.21 (37.90)	150.00 (39.78)	142.18 (34.97)	149.78 (40.71)	144.74 (36.73)	148.27 (40.25)
AIP	.04 (.38)	.05 (.27)	−.08 (.21)	.31 (.18)[d]	−.02 (.26)	.25 (.20)[d]	.03 (.28)	.07 (.26)	.03 (.28)	.07 (.25)
Apo A1, mg/dL	154.1 (38.63)	164.39 (41.65)	165.85 (43.03)	161.99 (38.88)	165.87 (38.65)	158.99 (48.98)	160.77 (35.61)	168.02 (46.56)	161.79 (38.77)	166.68 (43.71)
Apo B, mg/dL	111.4 (29.27)	118.39 (28.19)	107.16 (25.13)	134.23 (23.98)[d]	116.77 (22.23)	123.28 (41.23)	113.75 (25.47)	123.19 (29.77)	113.21 (24.64)	123.27 (26.50)
LDL/Apo B	1.08 (.15)	1.05 (.21)	1.07 (.20)	1.02 (.23)	1.07 (.18)	.98 (.28)	1.09 (.24)	1.01 (.17)	1.07 (.21)	1.04 (.21)
HDL/Apo A1	.33 (.08)	.30 (.06)	.31 (.07)	.29 (.06)	.32 (.06)	.25 (.06)[d]	.31 (.06)	.30 (.07)	.31 (.06)	.30 (.06)
Apo B/A1	.72 (.33)	.78 (.37)	.67 (.20)	.94 (.48)[c]	.78 (.39)	.81 (.29)	.79 (.45)	.77 (.25)	.73 (.24)	.83 (.45)

AIP, atherogenic index of plasma; Apo, apolipoprotein; BP, blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MetS, metabolic syndrome; TC, total cholesterol; TG, triglycerides; VLDL-C, very low density lipoprotein cholesterol; WC, waist circumference.

[a] $P<.05$.
[b] $P<.01$.
[c] $P<.001$.
[d] $P<.0001$.

In our work, lipoproteins and apolipoproteins disturbances found in obese patients with MetS agreed with previous studies.[24–26] One explanation would be that excess fat disturbs lipoprotein levels: in obese persons, an increased flux of FFA from fat to the liver might stimulate production of TG-rich lipoproteins leading to a pro-inflammatory state owing to altered production of inflammatory and anti-inflammatory mediators and the recruitment of macrophages to adipose tissue.[17] Otherwise, TC, TG, HDL-C, LDL-C, Apo B, Apo AI were all significant predictors of risk:[24,26] Apo A1 and Apo B were better predictors of MI and CHD than HDL-C and LDL-C levels because of their respective associations with these lipoproteins.[26–29]

Low-grade inflammation, high WC, hypertension and diabetes did not affect lipid profiles nor apolipoprotein concentrations. Variations of lipoproteins and apolipoproteins concentrations according to number and type of MetS features, sex and/or low-grade inflammation, demonstrated in our study, were also reported by Davidson et al.[11] The pathophysiological mechanism leading to hypertriglyceridemia in MetS is not fully understood but seems to involve lipoprotein metabolism enzymes abnormalities: In obese patients, cholesteryl ester transfer protein (CETP) activity and mass are increased, contributing to the increased flux of FFA but also to the rise of circulating TG levels.[23] The overproduction of VLDL and Apo B particles is due to the stimulation of hepatic TG synthesis, which in turn results from the increased flux of FFA from the periphery to the liver. The increase of Apo B levels in plasma may also result from reduced apo B degradation.[23]

The low HDL-C concentrations in IR appear to be linked to the overproduction of TG-rich lipoproteins. Although the mechanisms remain unclear, the enrichment of HDL particles with TG appears to be implicated, leading to HDL particle instability and degradation. On the other hand, in presence of hypertriglyceridemia, action of CETP

Table 5. Binomial logistic regression of lipid ratios and risks of cardiovascular outcomes, odds ratios (95% CI)

	Presence vs Absence of MetS	Men vs Women	Number of MetS Components (vs 1 MetS)			
			2	3	4	5
TC/HDL	2.21 (1.65–2.95)[d]	1.49 (1.15–1.94)[b]	1.47 (.91–2.38)[d]	2.04 (1.35–3.09)[c]	5.14 (2.33–11.31)[d]	6.91 (2.10–22.78)[b]
Non HDL-C	3.57 (1.72– 7.41)[d]	1.51 (.70– 3.29)	1.02 (1.00–1.04)	3.36 (1.15–9.83)[a]	1.03 (1.00–1.06)	1.08 (1.00–1.18)
AIP	2.09 (1.69–2.57)[d]	1.27 (.93– 1.74)[d]	1.37 (1.09–1.72)[a]	1.96 (1.56–2.47)[d]	2.83 (1.30–6.16)[d]	2.89 (.97–8.57)[b]
Apo B/A1	1.42 (1.31–1.56)	.97 (.63– 1.49)	1.39 (1.09–1.72)	1.51 (1.20–1.90)	2.24 (.91–5.57)[a]	2.40 (.80–7.23)[a]
Predicted risks of						
CHD	1.23 (1.15–1.31)[d]	1.13 (1.08–1.19)[d]	1.27 (1.10–1.46)[b]	1.41 (1.21–1.63)[d]	1.59 (1.30–1.96)[d]	1.49 (1.15–1.92)[b]
MI	1.41 (1.25–1.59)[d]	1.24 (1.14–1.35)[d]	1.53 (1.12–2.08)[b]	1.97 (1.42–2.74)[d]	2.51 (1.66–3.78)[d]	2.24 (1.31–3.84) [b]
Stroke	1.41 (1.21–1.64)[d]	1.13 (1.02–1.26)[a]	3.49 (1.74–7.01)[c]	3.79 (1.91–7.52)[c]	4.02 (2.64–6.19)[d]	4.48 (1.53–13.11) [b]
CVD	1.12 (1.08–1.17)[d]	1.07 (1.04–1.10)[d]	1.22 (1.10–1.35)[c]	1.28 (1.15–1.43)[d]	1.39 (1.20–1.62)[d]	1.33 (1.10–1.61) [b]
CVD Death	1.27 (1.13–1.42)[d]	1.19 (1.09–1.29)[d]	1.71 (1.06–2.77)	2.22 (1.31–3.76)[b]	2.54 (1.37–4.74)[a]	1.90 (1.23–2.93) [b]

AIP, atherogenic index of plasma; Apo, apolipoprotein; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MetS, metabolic syndrome; TC, total cholesterol; CVD, cardiovascular disease; CHD, coronary heart disease; MI, myocardial infarction.

[a] $P<.05$.
[b] $P<.01$.
[c] $P<.001$
[d] $P<.0001$.

results in TG-rich and CE-depleted HDL particles, which are prone to degradation. Enhanced catabolism of HDL is due to hydrolysis of these HDL particles by hepatic lipase.[23]

In our study, participants with MetS, hypo-HDL-emia and/or at least 3 MetS components showed lower values of HDL/Apo A ratio, which indicates HDL impairment. Indeed, Apo A is dissociated from HDL particles, leading to a non-effective reverse cholesterol transport and to attenuated anti-atherogenic activity of HDL in MetS.[20] Another possibility is that the altered lipid flux in the liver may reduce the hepatic production of Apo A.[23]

On one hand, lipoprotein size modulates the ability of the lipoproteins to cross the endothelial barrier to enter the arterial intima.[30] Using LDL/Apo B, TC/HDL and TG/HDL ratios as surrogates of LDL size, our data have shown that patients with MetS presented greater number of small dense LDL (sdLDL) particles than those without MetS. Moreover, according to AIP cut-off points proposed by Dobiášová et al,[31] our obese patients without MetS are classified at low cardiovascular risk, while those with MetS are in the medium cardiovascular risk category. We also noted AIP associations with all lipoproteins and apolipoproteins, lipid and apolipoproteins ratios, and all cardiovascular outcomes studied, which is in accordance with many international reports.[24,28,29,32–37] But, AIP has been associated with HDL, LDL and VLDL particles sizes and is proposed as a predictor of insulin resistance and all-cause mortality.[31] Therefore, IR had effects on lipoprotein size and subclass particle levels for VLDL, LDL and HDL.[34]

According to Apo B and Non-HDL-C values, our results showed greater number of sdLDL particles in patients with at least two MetS components, and hypertriglyceridemia, leading to a higher cardiovascular risk. The sdLDL is considered more atherogenic than the large buoyant LDL particles.[24,28,30,33] While a total LDL-C value cannot distinguish between both types of LDL particles, a high Apo B and non-HDL-C levels may indicate an increased number of sdLDL particles, which is more important than the LDL size itself.[27–29]

On the other hand, using TC/HDL and Apo B/A1 ratios, we have noticed a cholesterol imbalance between atherogenic and anti-atherogenic lipoprotein particles in obese with MetS, adults with 5 MetS features and/or hypertriglyceridemia. Consequently, those people have more cholesterol circulating in the plasma compartment, and this cholesterol is likely to be deposited in the arterial wall, provoking atherogenesis and risk of cardiovascular events.[24,26] Our findings were consistent with others publications where these ratios were found to be related to MetS and its components.[6,24–26,38]

CONCLUSION

Our study suggests that Moroccan obese adults with MetS have lipoprotein metabolism alterations and suffer from low-grade inflammation. These data provide additional support for previously reported associations between inflammation, MetS and CVD. Thus, we propose that risk management could be based on lipoprotein and apolipoprotein ratios rather than lipids alone, since it presents clear advantages due to its high predictive value, its associations with lipid parameters and does not require any additional expense beyond the standard lipid panel. Management of clinical treatments should also take into account inflammatory markers and LDL heterogeneity.

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