USEFULNESS OF LIPID RATIOS AND ATEROGENIC INDEX OF PLASMA IN OBESE MOROCCAN WOMEN WITH OR WITHOUT METABOLIC SYNDROME

Fadwa Essiarab, MPH; Hassan Taki, PhD; Halima Lebrazi, PhD; Maati Sabri, MD; Rachid Saile, PhD

INTRODUCTION

Non-communicable diseases (NCDs) are the leading cause of death worldwide. In 2008, almost two thirds (36 million) of all recorded deaths were due to NCDs, of which 80% occur in low- and middle-income countries. Epidemiological studies have shown that 48% (17 million) of NCDs were due to cardiovascular disease (CVD). The leading cause of death and disability in a growing number of developing countries, CVD is responsible for premature morbidity and mortality and to preventable losses of employment, earnings, and quality of life.

Obesity, type 2 diabetes mellitus, dyslipidemia and hypertension remain major cardiovascular risk factors, whose prevalence and impact on overall cardiovascular risk are increasing, particularly in Western societies. Worldwide prevalence of obesity has nearly doubled during the last 30 years. In 2008, 297 million women and 205 million men (respectively, 14% and 10% of adults worldwide) were obese. In Morocco, obesity became a significant health problem; many Moroccan studies reported ranges from 13.5% to 46% in women. Other studies also reported a high prevalence of co-morbidities associated with obesity and their consequences on lipid metabolism, steadily increasing risks of CVDs. Each year, at least 2.8 million die from obesity or overweight; indeed, increased body mass index (BMI) leads to high risks of coronary heart diseases (CHD) and ischemic strokes.

Clustering of several CVD risk factors, such as insulin resistance, glucose intolerance, atherogenic dyslipidemia, high blood pressure, and visceral adiposity, has been termed metabolic syndrome (MetS) and was first described by Kylin. These metabolic and hemodynamic abnormalities independently predict the development of atherosclerosis and CVD. Clinically, it is of great significance, since identifying patients at risk of developing CVD and/or diabetes mellitus will enable preventive intervention to promote lifestyle modifications. Many meta-analyses have shown associations between MetS and increased risks of CVDs.

Morocco is a Mediterranean country that has known much development in the last decades. On the one hand, Morocco is passing through a nutritional transition characterized by a higher caloric intake, on the other hand, the status of the Moroccan woman has changed from “housewife” to “independent, active and dynamic woman” who has reduced her physical activity. Most of the biomedical literature occurring about health concerns in Morocco are focused on the Saharoui or North West’s population. To our knowledge, no work group has previously focused on Casablanca, which was chosen for our study because of its high urbanization, its fast and recent development, as well as its cultural and ethnic melting pot, fruit of a great migration of individuals from all over Morocco.

Our study aimed to investigate the impact of obesity and metabolic syndrome on lipoprotein profiles and cardiovascular risk through lipid ratios and atherogenic index of plasma (AIP) in Moroccan obese women.

METHODS

Our study included 240 Moroccan women aged 33 to 65 years (mean-age

From the Laboratory of Biology and Health - URAC 34-Hassan II University Mohammadia-Casablanca, Faculty of Sciences Ben M’Sik, Avenue Cdt Driss El Harti, B.P 7955, Sidi Othmane, Casablanca, Morocco (EF, TH, LH, SR) and the Cardiology Department, CNSY Ziraoui Polyclinic, Casablanca, Morocco (SM).

Address correspondence to Professor Saile Rachid; Laboratory of Biology and Health - URAC 34-Hassan II University Mohammadia-Casablanca, Faculty of Sciences Ben M’Sik, Avenue Cdt Driss El Harti, B.P 7955, Sidi Othmane, Casablanca, Morocco. +212 5 22 70 46 71; +212 5 22 70 46 75 (fax); sailorachid@yahoo.fr

Objective: Our study aimed to study the impact of obesity and metabolic syndrome (MetS) on lipoprotein profiles and cardiovascular risk through lipid ratios and atherogenic index of plasma (AIP) in Moroccan women.

Methods: Our study included 240 Moroccan women, aged 53.31 ± 8.51 years, divided into three groups: controls (group 1, n=80), obese without MetS (group 2, n=80) and obese with MetS (group 3, n=80). Anthropometric and lipid measurements were taken and specific lipid ratios assessed, as well as Non-HDL cholesterol (Non-HDL-C) and atherogenic index of plasma (AIP).

Results: Group 2 presented similar lipoprotein profiles compared with group 1. Group 3 had higher triglyceride (TG) levels than group 1, which, in turn, increased HDL and AIP values. Dyslipidemia in group 3 was demonstrated by higher TG levels, lipid ratios and AIP and lower HDL-C levels compared with group 2. All of these abnormalities are responsible for elevations of risks of cardiovascular diseases. Closer associations were found between cardiovascular risk and lipid ratios and AIP than lipids alone.

Conclusion: Our study confirms that MetS affects the serum lipoprotein profile of obese women. Lipid ratios, non HDL-C and AIP remain useful tools for the diagnosis and prognosis of cardiovascular disease by their associations with lipid parameters and their high predictive values.
Our study aimed to investigate the impact of obesity and metabolic syndrome on lipoprotein profiles and cardiovascular risk through lipid ratios and atherogenic index of plasma (AIP) in Moroccan obese women.

53.31 ± 8.51 years). In these women, metabolic syndrome was assessed according to a modified definition of the National Cholesterol Education Program III, which is reported as the $R$5,1 FS Chemistry System.

IN

P

W

AIP

30 kg/m² (free software available at http://www.r-project.org/), version 2.12.0 for statistical analysis.

All data are expressed as mean ± standard deviation. 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 lipid ratios and predicted risk of developing a CVD, MI, stroke and CHD. Odds ratio (OR) and 95% confidence interval (95% CI) were assessed after binomial logistic regression analysis. Differences with a $P<.05$ were considered statistically significant. All analyses were conducted using R (free software available at http://www.r-project.org/), version 2.12.0 for statistical analysis.

RESULTS

Table 1 summarizes baseline characteristics and biochemical variables of our study participants. Groups 2 and 3 presented higher anthropometric values while compared to group 1 (in both groups: $P<.0001$ for BMI and WC). Elevation of systolic blood pressure in group 2 was not statistically significant, contrary to group 3 ($P<.01$) as compared with group 1. Diastolic blood pressure values were not significantly increased in groups 2 and 3 in comparison with group 1. Comparisons between group 2 and 3 showed no significant differences in BMI and WC but, group 3 had higher systolic and diastolic blood pressures ($P<.0001$ and $P<.001$, respectively) than group 2. Comparisons between groups 1 and 2 did not present any significant variation for sBP or dBP. While comparing group 3 to group 2, we noticed greater triglycerides and lower HDL-C levels in group 3 ($P<.0001$ for both), but not significant differences for TC and LDL-C. Group 3 presented highly significant elevations of TC/HDL, TG/HDL, and AIP values than group 2 ($P<.0001$ for all) while LDL/HDL and Non-HDL-C presented a weaker significance ($P<.01$ and $P<.05$, respectively). In group 3, we noted higher triglycerides, TG/HDL and AIP as compared to group 1 ($P<.001$, $P<.01$ and $P<.0001$, respectively). All others parameters showed no significant differences.

In Table 2, we noted that predicted risks of developing MI and CVD were increased in group 2 as compared with group 1. The predicted risk of developing MI and stroke are even more increased in group 3 in comparison with group 1. Significant elevations of predicted risks of developing MI, Stroke, CVD were observed while comparing group 2 and 3. We also noticed an increase in predicted risk of mortality due to CVD in these groups.

Linear regression analyses results are presented in Table 3. TC/HDL and
LDL/HDL, linked to each other \((P<0.001)\), were positively associated with TC, LDL-C, TG, non HDL-C, TG/HDL and AIP but negatively correlated to HDL-C \((P<0.001\) for all). TC/HDL and LDL/HDL also presented strong positive correlations with predicted risks of CHD, MI, CVD \((P<0.001\) for all) and CVD death \((P<0.01\) and \(P<0.05\), respectively).

Non HDL-C and TG/HDL, associated with each other \((P<0.001)\), were correlated to TG, AIP, CHD, MI, CVD and CVD death predicted risks \((P<0.001\) for all, except for CVD death, \(P<0.05\)). Both non HDL-C and TG/HDL were also linked to TC \((P<0.001\) and \(P<0.01\) respectively for Non HDL-C and TG/HDL). Non HDL-C was positively associated with LDL-C while TG/HDL was negatively linked to HDL-C \((P<0.001\) for both).

Strong positive correlations were found between AIP and TG and predicted risks of CHD, MI and CVD while a negative association was found between AIP and HDL-C \((P<0.001\) for all). Other positive associations between AIP and TC \((P<0.01)\), LDL \((P<0.01)\) and predicted risk of CVD death \((P<0.05)\) were also observed.

Predicted risks of CHD and MI were strongly positively associated with TC, LDL-C and TG while they presented a negative correlation with HDL-C \((P<0.001\) for all). Predicted risk of stroke was correlated to neither lipid parameters, nor lipid ratios, nor AIP.

Predicted risks of CVD was linked to these parameters \((P<0.05\) for HDL-C, \(P<0.01\) for TC and LDL-C, and \(P<0.001\) for TG). Predicted risk of mortality from CVD was only associated with TG \((P<0.05)\).

CHD and MI Pearson’s correlation coefficients of lipid ratios showed greater values than those of lipids alone. For predicted CVD and CVD death risks, they remained higher and even more significant. TC/HDL had the highest Pearson’s correlation coefficients for CHD and MI predicted risks \((r=.52\) and .50, respectively) while AIP and TG/HDL presented the smallest values \((r=.42\) and .41, respectively). For predicted CVD and CVD death risks, the smallest values of Pearson’s correlation coefficients were for Non HDL-C \((r=.30\) and .15, respectively) while TC/HDL had the greatest ones \((r=.34\) and .21, respectively).

### Table 2. Odds ratio and 95% CI determination after binomial logistic regression

<table>
<thead>
<tr>
<th>Predicted Risks</th>
<th>OR 1 (95%CI)</th>
<th>OR 2 (95%CI)</th>
<th>OR 3 (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>1.10 (0.95–1.27)</td>
<td>1.07 (0.97–1.18)</td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>MI</td>
<td>4.52 (1.80–11.40)</td>
<td>5.25 (1.86–14.84)</td>
<td>1.35 (1.21–1.52)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.89 (0.80–4.39)</td>
<td>4.30 (1.59–11.62)</td>
<td>1.94 (1.50–2.51)</td>
</tr>
<tr>
<td>CVD</td>
<td>1.53 (1.16–1.89)</td>
<td>1.15 (0.97–1.32)</td>
<td>1.42 (1.16–1.75)</td>
</tr>
<tr>
<td>CVD Death</td>
<td>3.57 (0.68–3.23)</td>
<td>1.72 (0.84–3.55)</td>
<td>2.92 (1.72–4.94)</td>
</tr>
</tbody>
</table>

\(^{a} P<0.001\)  
\(^{b} P<0.01\)  
\(^{c} P=0.05\)  

OR 1 = Odds ratio between groups 1 and 2; OR 2 = Odds ratio between groups 1 and 3; OR 3 = Odds ratio between groups 2 and 3.

CHD = coronary heart disease; CVD = cardiovascular disease; MI = myocardial Infarction.

**Discussion**

Our study in Moroccan women showed that obesity and its associated comorbidities led to higher anthropometric values while the presence of metabolic syndrome in obese women led to higher sBP and TG, which,

Ethnicity & Disease, Volume 24, Spring 2014 209

lipid ratios and AIP in obese women - Essiarab et al
LIPID RATIOS AND AIP IN OBESE WOMEN - Essiarab et al

Table 3. Pearson’s correlation coefficients for study participants

<table>
<thead>
<tr>
<th>Predicted Risks of</th>
<th>CHD</th>
<th>Stroke</th>
<th>MI</th>
<th>CVD</th>
<th>CVD Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-C</td>
<td>0.36^d</td>
<td>0.20</td>
<td>0.34^d</td>
<td>0.24^b</td>
<td>0.10</td>
</tr>
<tr>
<td>LDL-C</td>
<td>0.28^d</td>
<td>0.00</td>
<td>-0.27^d</td>
<td>-0.18^a</td>
<td>-0.14</td>
</tr>
<tr>
<td>TG</td>
<td>0.37^d</td>
<td>0.10</td>
<td>0.34^d</td>
<td>0.23^b</td>
<td>0.11</td>
</tr>
<tr>
<td>TC/HDL</td>
<td>0.40^d</td>
<td>0.11</td>
<td>0.40^d</td>
<td>0.30^d</td>
<td>0.16^a</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>0.52^d</td>
<td>0.07</td>
<td>0.50^d</td>
<td>0.34^d</td>
<td>0.21^a</td>
</tr>
<tr>
<td>Non HDL-C</td>
<td>0.49^d</td>
<td>0.05</td>
<td>0.46^d</td>
<td>0.31^d</td>
<td>0.19^a</td>
</tr>
<tr>
<td>TG/HDL</td>
<td>0.43^d</td>
<td>0.06</td>
<td>0.42^d</td>
<td>0.30^d</td>
<td>0.15^a</td>
</tr>
<tr>
<td>AIP</td>
<td>0.42^d</td>
<td>0.10</td>
<td>0.41^d</td>
<td>0.30^d</td>
<td>0.18^a</td>
</tr>
</tbody>
</table>

* P<0.05.
^b P<0.01.
^c P<0.001.
^d P<0.0001.

AIP = atherogenic index of plasma; HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol; TC = total cholesterol; TG = triglycerides; CHD = coronary heart disease; CVD = cardiovascular disease; MI = myocardial Infarction.

turn, was reflected by an approximate 2-fold increased TG/HDL and AIP values. All of these abnormalities are responsible for elevations of risks of cardiovascular disease and coronary heart disease, morbidity and mortality.

Indeed, in obese women in all groups and made relatively homogenous by their obesity level, persons with MetS presented higher levels of sBP, dBP and TG, and lower HDL-C levels. This might be due to the fact that hypertension, hypertriglyceridemia and hypo-HDL-emia had been more prevalent in the third group than in the second one, since these factors fall within MetS definition. Our findings agreed with some authors who reported that obesity effects are mediated through hypertension and dyslipidemia.

Dyslipidemia is a well-known major risk factor for CHD, as well as a component of MetS. TG and HDL-C are not only independent risk factors of CVD, but also components of MetS. Hypertriglyceridemia and low HDL-C levels result from insulin resistance, a central factor of MetS leading to higher levels of VLDL, which contains a high concentration of TG. Although atherosclerosis is a multifactorial process, abnormalities in lipoprotein metabolism are one of the key factors, representing around 50% of the population-attributable risk of developing cardiovascular disease. Our results showed that Moroccan obese women are also at high risk for CVDs, since hypertriglyceridemia and hypo-HDL-emia are highly prevalent (5%–6.25% in obese women without MetS and 50% - 46.25% in obese women with MetS), which is in agreement with other research.

During the last decades, according to progress made in terms of CVD management, epidemiologists and clinicians are of one mind: artery coronary disease risk evaluation based exclusively on LDL-C is not optimal, especially in people at intermediate risk. Our review of the literature in this area revealed the importance of many lipid ratios or “atherogenic indexes” in the optimization of the predictive power of the lipid profile. These ratios have the ability to present information that are difficult to quantify by routine analyses, by indicating metabolic interactions between different lipid variables.

Several lipid ratios have been proposed as simple clinical indicators because of the integrative information of the multiple variables. These lipid ratios are strong indicators of cardiovascular risk by its expressions of imbalance between atherogenic and protective lipoproteins. Indeed, TC/HDL and LDL/HDL ratios have been shown as two components and indicators of vascular risk in large observational studies. Our study showed strong correlations between lipid ratios and CHD, MI, CVD and CVD death predicted risks. In the biomedical literature, it is reported that lipid ratios might have a more integrated explanation than single lipid measures, even TG or HDL-C. However, our results, contrary to those of several prior studies, do suggest that the use of either TC/HDL-C or LDL/HDL is better than the use of TC or LDL-C alone. Since almost two-thirds of plasma cholesterol found in LDL-C, TC and LDL-C, are closely related and the predictive values of their ratios have been shown to be greater than the isolated parameters.

In our study, lipid ratios, such as TC/HDL, LDL/HDL and TG/HDL, were significantly elevated in obese women with MetS while compared to obese women without MetS. This might be due to the reduction of HDL-C level, or hypertriglyceridemia, or both found in MetS. Our findings agreed with other publications. On the other hand, our data confirm those of the Helsinki Heart Study which has demonstrated that cardiovascular risk is even greater when hypertriglyceridemia is present in addition to high lipid ratios. Other prospective studies agreed that a high LDL/HDL-C ratio combined with
In our study, we noted that AIP mean value in obese women without MetS was >0.21 and that it had been multiplied by two in the presence of MetS.

hypertriglyceridemia was associated with highest CVD risk while some studies reported that TG/HDL was a strong predictor of myocardial infarction.\(^{23,26}\)

Measurement of Non-HDL-C has been proposed because it includes both cholesterol-rich and triglyceride-rich atherogenic apolipoprotein-B containing lipoproteins and the measurement does not require overnight fasting.\(^{27}\)

Our results showed a significant increase of Non-HDL-C in presence of MetS. At baseline, the mean value of Non-HDL-C level was 138 mg/dL. The Framingham Heart Study, Women’s Health Study, Lipid Research Clinical program Follow Up Study, showing relationship between Non HDL-C increase and CHD risk elevation, reported higher mean values at baseline (160, 155 and 172 mg/dL, respectively, for women).\(^{28}\)

We also reported that Non–HDL-C was associated with increased predicted risks of developing CHD, MI, CVD and predicted risk of CVD death. Recent observational and intervention studies proposed Non HDL-C as a risk marker for atherosclerosis, CHD, CHD death, non fatal myocardial infarction, CVD and cardiovascular mortality.\(^{1,2,21,25,27–29}\)

Atherogenic index of plasma (AIP) has been recently described as a biomarker of plasma atherogenicity.\(^{22,30}\) It has been associated with HDL, LDL and VLDL particle sizes and proposed as predictor of insulin resistance and all-cause mortality in women.\(^{22,31}\)

Dobišová and co-workers have suggested that AIP values of -0.3 to 0.11 are associated with low CV risk while values of 0.11 to 0.21 suggest medium CV risk and > 0.21 associated with high CV risk.\(^{30}\)

In our study, we noted that AIP mean value in obese women without MetS was >0.21 and that it had been multiplied by two in the presence of MetS. This can be explained by the fact that 23.75% of obese women without MetS and 5% of those with MetS were considered as low-risk while 56.25% and 85%, respectively, were in the high risk category. We found that AIP was associated with TC, HDL-C, LDL-C, TG, TC/HDL, LDL/HDL, Non HDL-C, TG/HDL, CHD, MI, CVD and CVD death predicted risks. Our results are similar to those of Rašlová and al.\(^{22}\)

The presence of the MetS is a strong predictor of future CVD and CVD death and the increase in risk begins with the presence of at least one MetS component.\(^{32}\)

This syndrome confers an increased risk for the development of diabetes mellitus and for cardiovascular morbidity and mortality.\(^{33}\)

Our study showed that MetS was associated with an approximate 2-fold increase in risk of CVD, MI, stroke and 3-fold increase in risk of CVD mortality. Others studies reported equivalent findings.\(^{34,35}\)

One limitation of the study was the size of our study groups. It would have been interesting to increase the number of participants and to include men, in order to reduce statistical biases and to test the lipid ratios in Moroccan men. Furthermore, other metabolic and inflammatory parameters should be investigated.

CONCLUSION

Our study confirms that the metabolic syndrome affects serum lipoprotein profile in obese women. We showed that, in presence of obesity, it leads to higher cardiovascular risk. This study is also one of the first that has considered Moroccan obese women with or without MetS. The Moroccan population, which has been subjected to a nutritional transition, is experiencing lifestyle changes due to a recent and widespread urbanization. These new habits lead to a greater risk of cardiovascular disease.

To address these risks, solutions, including intensive pharmacotherapy for dyslipidemia, hypertension, hypertriglyceridemia, and diabetes, are available. Yet, intensive management targeting lifestyle changes, such as low-caloric and low-fat diets and regular physical activity resolving abdominal obesity problem, may also avoid cardiovascular and other complications.

Lipid ratios, Non–HDL-C and AIP remain useful tools for the diagnosis and prognosis of cardiovascular disease. By their associations with lipid parameters and their high predictive values, these biomarkers could be helpful in the management of clinical treatments.

REFERENCES


6. Rahim S, Badaï A. Étude de l’obésité et quelques facteurs associés chez un groupe de femmes marocaines résidentes de la ville de

Ethnicity & Disease, Volume 24, Spring 2014

211
LIPID RATIOS AND AIP IN OBSESE WOMEN - Essiarab et al


AUTHOR CONTRIBUTIONS

Design and concept of study: Sabri, Saile
Acquisition of data: Essiarab, Taki, Lebrazi, Sabri, Saile
Data analysis and interpretation: Essiarab, Taki, Lebrazi, Sabri, Saile
Manuscript draft: Essiarab, Saile
Statistical expertise: Essiarab
Acquisition of funding: Taki, Lebrazi, Sabri, Saile
Administrative: Essiarab, Taki, Lebrazi, Saile
Supervision: Sabri, Saile