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Assessment of Cardiovascular Risk in Malnourished Moroccan Haemodialysis Patients: The Interest of Atherogenic Index of Plasma and Lipid Ratios

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Abstract

Background: Protein-energy wasting (PEW) and dyslipidaemia are strongly associated with cardiovascular disease (CVD) and accelerated atherosclerosis in end-stage renal diseases patients. Our study aimed to assess the impact of malnutrition on lipid profiles and cardiovascular risk of Moroccan haemodialysis patients using lipid ratios and the atherogenic index of plasma (AIP).

Methods and patients: This cross-sectional study included 126 Moroccan haemodialysis patients aged >18 years who had undergone dialysis for >6 months. Patients were divided into three groups: well-nourished patients (group 1), moderately malnourished patients (group 2) and severely malnourished patients (group 3). For each participant, clinical markers of malnutrition such as serum albumin and prealbumin were measured. Anthropometric measurements and a fasting lipid profile were taken and specific lipid ratios were assessed, as well as the AIP.

Results: The mean age of our participants was 44.81 ± 14.01 years old. The most common lipid alteration recorded was increased non-HDL-C (88%) followed by decreased HDL-C (70%), and hypertriglyceridaemia (30%). Malnourished patients had a higher cardiovascular risk with AIP >0.21. We observed a significant decrease in lipid parameters parallel to the increasing severity of malnutrition increased. Group 3, had highly significantly lower values for serum albumin, serum prealbumin, Body mass index (p=0.0001) and non-HDL-C (p=0.01) than group 1. Group 2 presented significantly higher values compared to group 3 (p<0.0001) for albumin, prealbumin and non-HDL-C, and very significantly values (p<0.01) for BMI, LDL-C, HDL-C, TG, TC/HDL-C, non- HDL/HDL-C and AIP. Pearson's correlation coefficients of lipid ratios showed greater values than those of lipids alone. AIP was positively correlated with lipid ratios and nutritional markers such as serum albumin and prealbumin.

Conclusion: Our study is the first one in Morocco which confirms that Protein-energy wasting affects the serum lipoprotein profile of haemodialysis patients. Lipid ratios, especially atherogenic index of plasma, may be useful tools for diagnosing and assessing the risk of cardiovascular disease in malnourished haemodialysis patients.

Keywords: Atherogenic index of plasma; Cardiovascular disease; Chronic kidney disease; Dyslipidaemia; Lipid ratios; Malnutrition; Protein-energy wasting

Abbreviations

ATP: Adult Treatment Panel; BMI: Body Mass Index; CDK: Chronic Kidney Disease; CRP: C-Reactive Protein; CVD: Cardiovascular Disease; ESRD: End-Stage Renal Disease; HD: Haemodialysis; HDL-C: HDL-Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; ISRNM: International Society of Renal Nutrition and Metabolism; LDL-C: Low-Density Lipoprotein Cholesterol; LDL-C: LDL Cholesterol; MIA: Malnutrition, Inflammation and Atherosclerosis; NCEP: National Cholesterol Program; PEW: Protein-Energy Wasting; SGA: Subjective Global Nutritional Assessment; TC: Total Cholesterol; TG: Triglycerides ; VLDL-C: Very Low Density Lipoprotein Cholesterol

Introduction

The incidence and prevalence of chronic kidney disease (CKD) leading to end-stage renal disease (ESRD) is increasing at an alarming rate [1]. CKD is characterized by nutritional disorders and systemic inflammation. Nutritional disorders have been reported in the literature with numerous and confusing terms such as malnutrition, sarcopenia and cachexia [2]. In 2008, the International Society of Renal Nutrition and Metabolism (ISRNM) proposed that the term protein-energy wasting (PEW) be adopted as a unifying nomenclature and the starting point for a better knowledge and treatment of these problems in uraemic patients [3]. Many reports indicate that there is a high prevalence of protein-energy wasting (PEW) in ESRD patients, and a high risk factor for a poor quality of life with increased morbidity and mortality [4,5].

However, cardiovascular disease (CVD) still takes first place among all causes of death in these patients who have a 10 to 20 times higher risk than the general population [6]. This high risk of cardiac events does not start at the onset of ESRD or dialysis. In fact, data are rapidly emerging that suggest that there are substantial cardiovascular disease risks within the large population of patients with chronic kidney disease [7]. Therefore, the link between malnutrition and increased CVD risk in patients with CKD has been difficult to define, mainly due to the coexistence of several cardiovascular risk factors in patients with CKD [8].

It is well known that ESRD patients exhibit significant alterations in their lipoprotein metabolism, which may result in the development of severe dyslipidaemia [9]. Lipid abnormalities most often include increased serum levels of triglycerides (TG), very-low density lipoprotein cholesterol (VLDL-C), a slight increase in low-density lipoprotein cholesterol (LDL-C) in addition to low levels of high-density lipoprotein cholesterol (HDL-C) and qualitative changes in lipoprotein particles [10]. The atherogenic potential of dyslipidaemia in CKD may depend more on apolipoproteins than on lipid abnormalities, and may not always be recognised by measurement of plasma lipids alone [6,11]. Although the common risk factors of atherosclerosis are widespread in ESRD patients, this alone cannot justify the high prevalence of CVD among these patients. Previous studies have proven that chronic inflammation, which is frequently noted in ESRD patients, is the main cause of malnutrition, cardiovascular and atherosclerotic diseases [12,13]. Malnutrition, inflammation and atherosclerosis (MIA) syndrome is associated with a high mortality rate and increased cardiovascular events in patients with ESRD [14,15]. The 3 factors of MIA syndrome interact with each other and create a vicious cycle [16]. Malnutrition or PEW may aggravate existing inflammation, accelerating atherosclerosis and increasing susceptibility to infection [17].

Morocco is a country located on Northwest Africa, which undergoing demographic and dietary transition, which are responsible for the emergence of many chronic diseases including CKD and CVD. However, disparate data are available on the association of serum lipids in the malnutrition in Moroccan haemodialysis populations. Therefore, the impact of malnutrition on lipid profile and lipid metabolism needs to be further explored.

The aim of the current study was to determine the impact of malnutrition on lipid profiles and cardiovascular risk of Moroccan haemodialysis (HD) patients, using lipid ratios and the atherogenic index of plasma as significant predictors of future cardiovascular events in malnourished HD patients.

Patients and Methods

Patients

Our investigation was conducted on one hundred twenty-six ESRD patients (60 men and 66 women; ranging from 18 to 65 years) receiving HD in the Department of Nephrology-Transplantation and Haemodialysis of the University Hospital Centre of Casablanca, Morocco.

Only adult patients undergoing long-term HD (defined as >6 months on HD therapy) were included in the study. The patients received 10-12 hours of regular HD per week. Individuals who had any type of serious infection or malignancy were excluded. Patients who had either a metal stent or a pacemaker were also omitted. For the HD procedure, a high-flux polysulfone membrane was used with a bicarbonate dialysate. No patient was treated with drugs known to influence lipoprotein metabolism. Demographic data (age, gender and dialysis vintage), and comorbid conditions (diabetes mellitus, heart failure, etc.) were taken from the hospital's records. We obtained written informed consent from each subject and the research protocol was approved by the local ethics committees of the involved hospitals.

Methods

Nutritional status and body composition: There is no single measurement that can be used to determine the presence of malnutrition. Therefore, a range of measurements is recommended, including anthropometric measurements, body composition, dietary protein and energy intake, and at least one measurement of serum protein status (assessment of malnutrition). In order to understand the influence of malnutrition on lipid profile, the patients were divided into three groups according to the ISRNM diagnostic criteria recommendation and the subjective global nutritional assessment (SGA) [3,18,19]: well-nourished patients (group 1, n=32), moderately malnourished patients (group 2, n=76) and severely malnourished patients (group 3, n=18).

Blood sampling and biochemical measurements: Venous blood samples (about 5 ml) were obtained from patients after overnight fasting for a minimum of 12 hours and before the beginning of haemodialysis. The samples were centrifuged at 4000 rpm for 10 minutes to separate serum from blood cells. Serum lipids: total cholesterol (TC), HDL-cholesterol (HDL-C), triglycerides (TG) and albumin were determined using enzymatic methods. LDL cholesterol (LDL-C) was calculated using Friedwald's formula [20]. Non-HDL-C was calculated by subtracting HDL-C from TC. The atherogenic index of plasma was calculated as the logarithmically transformed ratio of serum triglycerides to HDL-C. The diagnosis of dyslipidaemia was based on the National Cholesterol Programme (NCEP) Adult Treatment Panel (ATP) III, defined as the presence of one of the following factors: LDL-C levels ≥ 1.3 g/l, HDL-C <0.40 g/l, triglycerides ≥ 1.50 g/l or lipid-lowering drug treatment. Serum albumin was determined by the bromocresol green method. Both serum prealbumin and C-reactive protein (CRP) were measured by nephelometry using the MININEPH of the Binding Site Group, Birmingham, UK.

Statistical Analysis

The results were 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. The relationships between variables were assessed by Pearson's correlation analysis and linear regression models. Odds Ratio (OR) and 95% confidence interval (95% CI) were assessed after binomial logistic regression analysis. Differences with a $p<0.05$ were considered statistically significant. All analyses were conducted using R (free software available at http://www.r-project.org/), version 3.1.1 for statistical analysis.

Results

In the present study, the mean age of participants was 44.81 ± 14.01 years old. Of 126 subjects, 52.38% were female and 47.62% were male. The demographic and biochemical comparison of the patients grouped

by their nutritional status is shown in Table 1. The causes of ESRD were hypertensive glomerulonephritis in 32 patients (26%), glomerulosclerosis in 18 patients (15%), diabetic nephropathy in 5 patients (4%) and other or unknown in 71 patients (55%). Of these patients, 76.23% had inflammation (CRP > 6 mg/l) and the elevated CRP levels were reported to be more common in malnourished dialysis patients who presented 74.61%.

	Group 1 (n =32)	Group 2 (n =76)	Group 3 (n =18)	P1	P2	P3
Gender (male/female)	20/12	46/30	10/8			
BMI (kg/m^2)	24.53 ± 6.08	21.40 ± 3.25	19.20 ± 2.62	0.001	< 0.0001	0.01
S. Albumin (g/l)	41.80 ± 3.80	39.60 ± 4.54	33.65 ± 3.60	0.01	< 0.0001	< 0.0001
S. Prealbumin (mg/l)	365.40 ± 64.06	281.70 ±72.63	207.22 ± 60.54	< 0.0001	< 0.0001	< 0.0001
T. protein(g/l)	72.32 ± 6.68	74.57 ± 6.54	70.83 ± 8.01	NS	NS	0.01
CRP (mg/l)	15.31 ± 13.83	20.78 ± 23.48	32.77 ± 39.79	NS	NS	NS
TC (g/l)	1.58 ± 0.28	1.59 ± 0.41	1.44 ± 0.365	NS	NS	NS
LDL-C (g/l)	0.82 ± 0.41	0.80 ± 0.35	0.67 ± 0.36	NS	0.01	0.01
HDL-C (g/l)	0.49 ± 0.26	0.45 ± 0.20	0.58 ± 0.61	NS	NS	0.01
TG (g/l)	1.25 ± 0.54	1.57 ± 0.66	1.20 ± 0.60	0.01	NS	0.01
TC/HDL-C	4.16 ± 2.68	4.31± 2.72	3.28 ± 2.22	NS	NS	0.01
LDL/HDL-C (g/l)	2.49 ± 2.69	2.37 ± 2.09	1.71 ± 2.09	NS	NS	0.01
TG/HDL-C	3.06 ± 1.92	3.71 ± 3.54	2.88 ± 2.41	NS	NS	NS
Non HDL-C	2.82 ± 1.00	2.95 ± 1.18	2.25 ± 0.94	NS	0.01	0.001
Non HDL/HDL-C	3.16 ± 2.68	2.95 ± 2.72	2.28 ± 2.22	NS	NS	0.01
AIP	0.41 ± 0.25	0.47 ± 0.28	0.32 ± 0.36	NS	NS	0.01

S. Albumin: Serum Albumin; S. Prealbumin: Serum Prealbumin; T.protein: Total Protein; BMI: Body mass index; CRP: *C-reactive protein;* TC: Total cholesterol ; TG: Triglyceride; HDL-C: High-Density Lipoprotein-Cholesterol; Non-HDL-C: Non-high density lipoprotein-cholesterol; LDL-C: Low-Density Lipoprotein-Cholesterol; AIP= Atherogenic Index of Plasma.

Table 1: L Comparison of Nutritional and Biochemical Parameters of Hemodialysis Patients. Group 1: Well-nourished patients; group 2: Moderately malnourished patients; group 3: Severely malnourished patients; P1 = Comparison groups 1/2; P2= Comparison groups 1/3; P3= Comparison groups 2/3.

Clinical characteristics of study population

The analysis of the lipid parameters showed that, the most common lipid alteration recorded was increased non-HDL-C (88%) followed by decreased HDL-C (70%), hypertriglyceridaemia and hyper-LDL-emia (10%). All groups of patients were at high CVD risk, represented by a high value of AIP (>0.21). 70.3% of malnourished patients had a dialysis vintage of more than 10 years (versus 64% in the well-nourished group).

Table 1 gives the description of nutritional characteristics of the study groups, classified into different SGA grades. A significant decrease in most parameters was observed as the degree of malnutrition increased. In other words, the lowest values of the measured parameters were in group 3 (severely malnourished patients), whereas the highest values were in group 1 (well-nourished patients). Patients in group 2 experienced a gradual deterioration in nutritional status compared to group 1. Group 3 had very significantly lower values for serum albumin, serum prealbumin, body mass index (BMI) and non-HDL-C (p=0.0001 and p=0.01). Comparisons between groups 1 and 2 did not reveal any significant variation in lipid ratios except for TG, with a significantly increased level (p=0.01). Group 2 presented significantly higher values compared to group 3 (p<0.0001) for albumin, prealbumin and non-HDL-C; (p<0.01) for total protein, CRP, BMI, LDL-C, HDL-C, TG, TC/HDL-C, non- HDL/HDL-C and AIP. No significant difference was observed between CRP and total cholesterol levels in all patients groups (p>0.05). However, malnourished patients had higher serum levels of CRP when compared to well-nourished subjects.

Correlation between malnutrition serum lipids and lipid ratios

To gain further insight into the relationship between lipid profile, lipid ratios and nutritional parameters, linear regression analysis provided the correlations of these variables with each other and with nutritional parameters (Table 2).

	HDL	LDLC	TG	TC/HD-C	LDL/ HDL-C	TG/ HDLc	Non HDL-C	NonHDL/ HDL-C	AIP	BMI	S.Albu-min	S. Pre albumin	CRP
TC (g/l)	0.13	0.42+	0.32+	0.33+	0.23*	0.24**	0.72+	0.34+	0.16	0.01	0.54**	0.02	0.1
HDL-C (g/l)		-0.33+	-0.04	-0.60+	-0.52+	-0.51+	-0.54+	-0.61+	-0.67+	0.02	-0.19*	-0.17	-0.1
LDL-C (g/l)			0.09	0.53+	0.69+	0.38+	0.59 +	0.53+	0.33+	-0.06	0.26**	0.06	0.04
TG				0.17	0.07	0.49+	0.27 **	0.17	0.56+	0.1	0.13	-0.12	-0.06
TC/HDL-C					0.92+	0.77+	0.70 +	1.00+	0.64+	-0.09	0.20*	0.08	0.04
LDL/ HDL-C						0.66+	0.55 +	0.92+	0.54+	-0.09	0.19*	0.09	0
TG/HDL-C							0.55 +	0.77+	0.87+	0.06	0.32***	0.17	0.03
Non HDL-C								0.70+	0.58+	-0.05	0.32***	0.12	0.16
NHDL/									0.64+	-0.09	0.20*	0.09	0.04
HDL-C													
AIP										0.07	0.36 +	0.24*	0.06
BMI (kg/m2)											-0.13	0.16	-0.11
S. Albumin (g/l)												0.32***	0.02
S.Prealbumin (mg/l)													0.01

Note: S. Albumin: Serum Albumin ; S. Prealbumin: Serum Prealbumin ; T.protein: Total Protein ; BMI: Body mass index ; CRP: *C-reactive protein;* TC: Total cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein-Cholesterol; Non-HDL-C: Non-high density lipoprotein-cholesterol; LDL-C: Low-Density Lipoprotein-Cholesterol; AIP= Atherogenic Index of Plasma. *p <0.05; ** p <0.010; ***p <0.001; +p <0.0001.

Table 2: Pearson's correlation coefficients for the study population.

In the whole sample, serum albumin was correlated with AIP (p=0.0001), TG/HDL-C, non-HDL-C and serum prealbumin (p=0.001) and inversely correlated with HDL-C (p=0.05). Other positive associations were shown between serum albumin, TC and LDL-C (p=0.001 in both). In contrast, no significant correlation was found between serum prealbumin and other parameters, except for AIP (p=0.05). There was a significant positive correlation between BMI and dialysis vintage only (p=0.05). Pearson's correlation coefficients of lipid ratios showed greater values than those of lipids alone. LDL-C/HDL-C and TC/HDL-C, were linked to each other (p=0.0001) and positively associated with non-HDL-C, non-HDL-C/HDL-C, TG/HDL-C and AIP but negatively correlated with HDL-C (p=0.0001 for all). TC/HDL-C and LDL-C/HDL-C also presented a positive correlation with serum albumin (p=0.05). Non-HDL-C and TG/HDL-C were associated with each other (p= 0.0001) and correlated with AIP and non-HDL-C/HDL-C (p=0.0001). Both non-HDL-C and TG/HDL-C were negatively linked to HDL-C (p=0.0001). TG/HDL-C was also positively correlated with TC (p= 0.01). Non-HDL-C was positively associated with LDL-C, TC (p=0.0001 for both) and TG (p=0.01). A positive significant correlation was also observed between non-HDL-C/HDL-C ratio and TC, (p=0.0001) in addition to serum albumin (p=0.05). AIP was positively correlated with LDL-C and TG and negatively with HDL-C (p=0.0001).

Association of serum lipids and lipid ratios with malnutrition in our HD patients

As seen in Table 3, binomial logistic regression showed that the severely malnourished HD patients had an increased value of Odds Ratio, i.e., were at high risk of developing CVD as compared with groups 1 and 2 in all parameters, except for TG, HDL-C and TC. In the unadjusted model, LDL-C, TC/HDL-C, LDL-C/HDL-C, non-HDL-C, non-HDL-C/ HDL-C and AIP were associated with the incidence of CVD in malnourished subjects.

However, after further adjusting our patients for age and gender, most serum lipids and lipid ratios were associated with a high risk of developing CVD in malnourished patients.

	OR1		OR 2		OR 3	
	Unadjusted OR (95%CI)	Adjusted OR (95%CI)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
TC	0.86 (0.31 - 2.33)	0.82 (0.30 - 2.22)	0.55 (0.20 - 1.52)	0.5 (1.18 - 1.36)	0.64 (0.27 - 1.53)	1.66 (0.68 - 4.09)

HDL-C	1.81 (0.65 -5.04)	1.81 (0.65 - 5.11)	0.28 (0.08 -0.98)*	1.07 (0.40 - 2.98)	0.6 (0.24 - 1.46)	1.67 (0.68 - 4.18)
LDL-C	3.42 (0.66 - 17.70)	3.12 (0.70 - 22.33)	0.34 (0.02 - 4.01)	0.25 (0.01 - 2.87)	0.09 (0.01 - 0.83) *	12.35 (2.09-236.27)*
TG	3.02 (1.01 - 9.03) *	3.14 (1.07 - 10.28)*	1.37 (0.44 - 4.22)	1.34 (0.43 - 4.50)	0.45 (0.18 - 1.09)	2.26 (0.93 - 5.67)
TC/ HDL-C	2.5 (0.83 - 7.51)	2.55 (0.87 - 8.26)	0.72 (0.21 - 2.40)	1.71 (0.21 - 2.48)	0.28 (0.10 - 0.76) **	3.63 (1.38 - 10.35)*
LDL /HDL-C	1.2 (0.32 - 4.47)	1.18 (0.32 - 4.98)	0.12 (0.01 - 1.18)	0.09 (0.04 - 0.75)*	0.1 (0.01 - 0.87) *	10.2 (1.71 - 195.92)*
TG/HDL-C	1.37 (0.44 - 4.22)	1.38 (0.44 - 4.67)	0.96 (0.30 - 3.05)	0.93 (0.28 - 3.18)	0.7 (0.26 - 1.82)	1.48 (0.55 - 4.10)
Non- HDL-C	1.13 (0.40 - 3.24)	1.13 (0.40 - 3.38)	0.28 (0.07 - 0.98)*	0.26 (0.06 - 0.91)*	0.24 (0.08 - 0.75) **	4.35 (1.45 - 15.18)*
Non- HDL/ HDL-C	2.08 (0.76 - 5.68)	2.09 (0.77 - 5.85)	0.58 (0.20 - 1.64)	0.26 (0.06 - 0.91)*	0.28 (0.11 - 0.68) ***	3.77 (1.53 - 9.80)**
AIP	3.65 (0.31 - 42.48)	3.76 (0.33 - 84.26)	0.25 (0.05 - 1.25)	0.23 (0.03 - 0.10)*	0.07 (0.08 - 0.56) **	15.78 (2.78 - 299.41)*

Note : 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; 95% CI: 95% Confidence Interval; TC: Total cholesterol; TG: Triglyceride; HDL-c: High-Density Lipoprotein-Cholesterol; non-HDL-C: non-high density lipoprotein-cholesterol; LDL-c: Low-Density Lipoprotein-Cholesterol; AIP: Atherogenic Index of Plasma. Statistically significant results:*p<0.05. **p<0.01 and ***p<0.001.

Table 3: Association of serum lipids and lipid ratios with protein-energy wasting. Patients were adjusted for age and gender.

The LDL-C, LDL-C/HDL-C and AIP were the best predictors of several cardiovascular outcomes, and their ORs were significantly higher in severely malnourished HD patients. In contrast, in well-nourished patients, TG indicated the higher significant CVD risk: OR 3.14 (95% CI of 1.07–10.28, p=0.05), in the adjusted or unadjusted model, compared to malnourished patients.

Discussion

The present study was performed to evaluate the impact of protein-energy wasting on lipoprotein profiles and cardiovascular risk in haemodialysis patients. Patients' undergoing long-term haemodialysis treatment showed lipid metabolism alterations and our results demonstrated a relationship between nutritional status and lipoprotein metabolism disturbances, leading to raised cardiovascular risk in malnourished Moroccan patients.

The increased risk of CVD has many causes, but dyslipidaemia plays a prominent role. It is commonly associated with an abnormal lipoprotein phenotype, which is characterised by increased serum triglycerides due to the enhanced production of triglyceride-rich lipoproteins such as very-low-density lipoproteins in the liver [9,21]. Regardless of the etiology, patients with CKD develop complex qualitative and quantitative abnormalities. Total and LDL-C values are usually within normal limits or slightly reduced in this population [22-24]. Similarly, to the results of Mekki et al. our study shows that hypertriglyceridaemia seems to be moderate compared with patients in developed countries. This could be due to the Mediterranean diet consumed by our population, which is characterised by a high intake of vegetable proteins, complex carbohydrates, fibre and mono-unsaturated fatty acids [25]. Despite the neutral effect of dialysis on serum lipid profile, some dialysis-related parameters may significantly affect lipoprotein metabolism and modify the features of dyslipidaemia in HD patients. It has also been demonstrated that the use of high-flux membranes is closely associated with a significant reduction in serum triglyceride levels as well as with an increase in HDL-C levels [21,26].

A low level of serum cholesterol may indicate the presence of malnutrition and is often associated with a low level of serum albumin. In our patients, the mean level of serum cholesterol was higher than that found in our previous study [6] and another Moroccan study [27]. The well-known association of high cholesterol levels with increased mortality in the general population was not observed in HD patients without malnutrition or inflammation [11,28]. If patients suffered from these conditions, a high cholesterol concentration was associated with a better outcome which might be explained by the cholesterol-lowering effect of systemic inflammation and malnutrition [29]. Hypoalbuminaemia is the strongest predictor of CVD and mortality in dialysis patients when compared with classic risk factors (hypertension, hypercholesterolaemia, obesity) [30,31] and non-traditional risk factors (anemia, oxidative stress, and dialysis modality) [32,33]. Low levels of albumin can also be influenced by inflammation and infection. Moreover, studies have reported an increased risk of CVD with high CRP levels without a decrease in albumin levels. Therefore, in the presence of normal albumin levels, CRP levels may increase [34]. Iseki et al. reported a significant relationship between albumin levels and CRP in 163 haemodialysis patients. On the contrary, no significant correlation was reported between CRP and serum albumin levels in our HD patients. Our findings are supported by several studies [35,36].

During recent decades, due to the progress made in terms of CVD management, epidemiologists and clinicians are of one mind: the evaluation of coronary artery disease risk based exclusively on LDL-C is not optimal, especially in people at intermediate risk [37].

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 can provide information that is difficult to quantify by routine analyses, by indicating metabolic interactions between different lipid variables [38,39].

In the biomedical research, it has been reported that lipid ratios might have a more integrated explanation than single lipid measurements, even TG or HDL-C [40]. According to Grover et al. either the ratio of LDL-C/HDL-C or TC/HDL-C is the best related predictor of future cardiovascular events [41]. However, our results, are in agreement with several prior studies, suggest that the use of TC/HDL-C or LDL-C/HDL-C is better than the use of TC or LDL-C alone [38]. Previous investigations reported a relationship between a high TG/HDL-C and elevated levels of small, dense LDL-C particles [42,43]. These LDL-C particles are highly atherogenic [44] and their level is considered a useful marker of insulin resistance [45]. In our study, lipid ratios, such as TC/HDL-C and TG/HDL-C, were elevated in moderately malnourished HD patients compared to well-nourished patients. This might be due to the reduction in HDL-C level or hypertriglyceridaemia. Other prospective studies agreed that a high LDL-C/HDL-C ratio combined with hypertriglyceridaemia was associated with the highest CVD risk while some studies reported that TG/HDL-C was a strong predictor of myocardial infarction [10,38].

The atherogenic index of plasma has been successfully used as an additional index when assessing cardiovascular (CV) risk factors [46-48]. It was closely correlated with the LDL-C particle size and could serve as an indicator of the atherogenic lipoprotein phenotype [46]. It has been associated with HDL-C, LDL-C and VLDL particle sizes and proposed as a predictor of insulin resistance and all-cause mortality [49]. Indeed, it has been 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 is associated with high CV risk [46]. The mean value of AIP in our patients was >0.21 in all groups, especially in moderately malnourished patients. We also, found that AIP was strongly associated with TC, HDL-C, LDL-C, TG, TC/HDL-C, LDL-C/HDL-C, TG/HDL-C, non-HDL-C, and non-HDL-C/HDL-C. These results are in agreement with those of other studies [50,51].

Non-HDL-C can easily be calculated by the difference between TC and HDL-C. This value includes all of the cholesterol present in the atherogenic lipoprotein particles (e.g. LDL-C, VLDL-C, IDL, and lipoprotein A) and excludes HDL-C, which is anti-atherogenic [52]. The substitution of LDL-C by non–HDL-C as a marker for cardiovascular risk in the HD population would dispense with the 12-hour fasting before sample collection, which is very difficult for diabetic patients undergoing dialysis, especially for those with dialysis scheduled in the afternoon and evening [53]. Gardner et al. suggested that non-HDL-C be substituted for LDL-C as a risk factor for coronary diseases [54]. Our results showed a significant increase in non-HDL-C in the presence of malnutrition. At the baseline, the mean value of the non-HDL-C level was 2.95 g/L in moderately malnourished group versus 2.82 g/L in well-nourished HD patients. Cui et al. demonstrated that the mortality of adults with cardiovascular diseases was better estimated by levels of non-HDL-C than of LDL-C [55]. A study with a sample of 186 patients undergoing HD showed that having a non–HDL-C level of >130 mg/dL, independent of the values of TG and HDL-C, was a possible predictor of the non-traditional risk factors for dialysis patients [55].

It is conceivable that malnutrition is not a risk factor for cardiovascular disease, but cardiovascular disease is more fatal in malnourished than in well-nourished patients. To the best of our knowledge, our study is the first to demonstrate that high values of AIP can serve as a significant predictor of future cardiovascular events in malnourished HD patients. However, the limitation of our study was the size of our study groups. It would have been interesting to increase the number of participants and to include private centers, in order to reduce statistical biases and to test the lipid ratios in a larger Moroccan population.

Conclusion

In conclusion, the present study suggests a significant association between specific markers of protein-energy wasting and cardiovascular diseases among patients with end-stage renal diseases. Low albumin levels appeared to precede clinically evident cardiovascular diseases, suggesting that protein-energy wasting may have an important pathogenic role in the development of cardiovascular diseases. Future studies need to clarify the pathogenic mechanisms underlying these findings. Moreover, lipid ratios, non-HDL-C and especially 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.

Our study reveals the important role of nutrition in the prognosis in hemodialysis patients, which implies the importance of nutrition education in dialysis centers to improve the quality of life of patients, this nutritional management must be individualized for each patient these personal circumstances, and according to his stage of dialysis.

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