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Original Research Article

Non-High-Density-Lipoprotein Cholesterol in Morocco Hemodialysis Patients

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Abstract

Introduction*:** Disturbances in lipid profile are very common in hemodialysis patients. Non-high-density lipoprotein cholesterol (non-HDL-c) has been proposed as a good predictor of atherogenic potential in the general population, but there is little data on this parameter in hemodialysis patients. The objective of this study is to assess the prevalence of lipid abnormalities in a series of hemodialysis patients and to appreciate the contribution of non-HDL-c in the identification of non-traditional risk factors related to lipoprotein subclasses. ***Materials and methods: we performed a case-control study which included 100 chronic hemodialysis patients, from October 2014 to February 2015. We evaluated anthropometric markers and lipids parameters in HD patients and control patients, and the correlation between them was investigated. ***Results:*** One hundred chronic hemodialysis patients with a mean age of 48 ± 17 years participated in this study. The most common lipid abnormality was a decrease in HDL-c (47%), followed by an increase in HDL-c (27%) and hypertriglyceridemia (20%). Total cholesterol (TC), LDL-c, and CT/HDL-C ratio are significantly higher in the group of patients with high non-HDL-c compared to the low non-HDL-c group. In addition, a significant correlation was demonstrated between the levels of non-HDL-c and either LDL-C ($r = 0.917$, $p = 0.000$) or TC ($r = 0.941$, $p = 0.000$). ***Conclusion:*** Our study suggests that non-HDL cholesterol is an indicator valuable in the diagnosis, monitoring of dyslipidemia and assessment of cardiovascular risk in hemodialysis patients. It amply deserves to be included in the parameters of the lipid balance within the framework of the follow-up of hemodialysis patients.

Keywords: Hemodialysis, lipid profile, non-high-density-lipoprotein (HDL) cholesterol.

1. INTRODUCTION

Chronic Kidney Disease (CKD) is acute pathology characterized by a progressive alteration of the exocrine and endocrine renal functions leading to clinical and biological disorders designated to as uremic syndrome [1].

The high incidence of cardiovascular disease in chronic hemodialysis patients (HD) are related of "traditional" (hypertension, diabetes, dyslipidemia) and "nontraditional" risk factors (anemia, bone mineral disorders, hyperparathyroidism, inflammation) [3, 4]. However, prevention and management of cardiovascular risk factors can reduce the rate of cardiovascular mortality in hemodialysis patients.

Dyslipidemia is one of the traditional risk factors in HD patients; it is characterized by qualitative and quantitative anomalies of plasma lipoproteins. In clinical practice, screening for dyslipidemia in the general population is based on the determination of total cholesterol, triglycerides and high-density lipoprotein cholesterol (HDL-c) in fasting blood. The low-density lipoprotein cholesterol (LDL-c) is calculated by Friedewald's equation for triglycerides <4 g / l, beyond the dosage of c-LDL is recommended.

Non-HDL cholesterol is not included in the routine lipid profile but can be calculated by subtracting c-HDL from total cholesterol. It corresponds to the sum of intermediate density lipoproteins IDL, very high density VLDL and LDL. It is strongly correlated with apoprotein B known by its atherogenicity. It is one of the parameters to be monitored during the management of dyslipidemia in CKD according to the recommendations of the NKF / K-DOQI.

Numerous studies have shown that c-non-HDL has a higher predictive value than c-LDL in the

prevention and management of cardiovascular disease in the general population and in CKD.

The objective of this study is to assess the prevalence of lipid abnormalities in chronic hemodialysis patients from the Meknes region (Morocco) compared to a control population and to assess the contribution of non-HDL cholesterol in the monitoring of this category of patients.

2. MATERIALS AND METHODS

This is a case-control study which included 100 chronic renal patients treated by hemodialysis at a rate of 3 sessions per week, over a period of 04 months, from October 2014 to February 2015. We included all participants who have agreed to participate in the study and have signed an informed consent.

For the control group, we recruited 100 subjects in good health at the blood donation service of the Moulay Ismail Military Hospital (HMMI) in Meknes-Morocco. Controls were matched (pair) for sex and age with the study population.

The following information were collected: age, sex, duration of dialysis and presence of co-morbid factors (diabetes, hypertension, cardiovascular disease). Blood samples were taken on a heparinized tube in the morning after a 10h fast.

Plasma lipids were measured after overnight fast. The laboratory data collected for the study were the cholesterol, triglyceride, HDL-c, CRP, urea, creatinine and fasting blood sugar. These parameters were evaluated on Cobas® 6000 from Roche Diagnostic.

Total cholesterol (TC) and triglyceride (TG) was measured by enzymatic method using respectively cholesterol esterase and cholesterol oxidase, lipoprotein lipase and glycerol kinase. HDL-c was determined by enzymatic method direct measurement in homogeneous phase. The LDL-c was indirectly measured using the Friedewald equation (LDL=TC – HDL- TG/5), for TG values <4 g / l. Non-HDL-c was calculated by subtracting from HDL-c from total cholesterol.

Dyslipidemia is defined according to the "Adult Treatment Panel III" (ATP III) guideline of the national cholesterol education program (NCEP) [4,5] by the presence of one of the factors: LDL-c> 1,20 g / l (3.36 mmol / L), HDL-c <0.40 g / l (1 mmol / L), TG> 1.70 g / l (1.70 mmol / L or taking a lipid-lowering treatment.

For the other lipid parameters, the atherogenicity seuil are resumed in Table 1. The statistical study was performed using SPSS 11.5 software. Quantitative variables were expressed as mean ± standard deviation, and the qualitative variables were expressed as a percentage. The comparison of the means was carried out by Student's t test. The comparison of percentages was performed by Pearson's chi-square test. P values <0.05 were considered statistically significant.

3. RESULTS

The mean age of the 100 included chronic hemodialysis patients was 48 ± 17 years with an M / F sex ratio of 1.5. The duration of hemodialysis was on average 72 months at the time of the study. The mean age of the control population was 47 ± 15 years with extremes of 23 to 78 years. The prevalence of systemic arterial hypertension, diabetes and cardiovascular disease in the studied population 41%, 12% and 9 % respectively.

The mean and standard deviation values of the lipid parameters of the HD patients and controls was: 2.45 ± 0.46 vs 1.50 ± 0.24, p <0.05 for TC, 1.97 ± 0.70 vs 0.91 ± 0.30, p <0.05 for TG, 1.41 ± 0.37 vs 0.85 ± 0.31, p <0.05 for LDL-c, 0.39 ± 0.12 vs 0.42 ± 0.11, p = 0.095 for HDL-c and 1.09 ± 0.34 vs 0.84 ± 0.24, p <0.05 for non-HDL-c (Table 2). TC, TG, LDL-c and non-HDL-c were significantly higher in HD compared to controls. Whereas, the mean of HDL-c did not show a significant difference between hemodialysis patients and controls.

The prevalence of dyslipidemia was 65% in HD patients. The dyslipidemia profile was characterized by hypoHDLemia (46.9%), followed by hypertriglyceridemia (20%), total hypercholesterolemia (19%) and LDL hypercholesterolemia (12%). The atherogenic index were higher in 27% of patients

Non-HDL-c was elevated in 24% of HD patients. A very positive correlation between non-HDL-c and respectively TC (r = 0.94) and LDL-c (r = 0.91) was found (Figures 1 and 2).

Table 3 shows lipid parameters distribution of hemodialysis patients and controls compared to the atherogenic risk Seuil. For TG, 20% of the patients were in the risk zone vs 2.8% of the controls. The non-HDL-c and atherogenicity index levels were respectively abnormal in 24% and 27% of patients compared to 7.6% and 11.5% in controls.

The demographic and biological characteristics of the two groups of HD patients with low and high non-HDL-c levels are shown in Table 4. TC, TG, LDL-c, and blood glucose are significantly elevated in patients with high non-HDL-c levels. Urea and creatinine did not show a significant difference between the two groups. CRP is significantly low in patients with high non-HDL-c levels.

Table-1: The different seuil of parameters and lipid indices for the assessment of atherogenic risk

Parameter	Seuil
HDL-c	0,4 (g/l)
LDL-c	1,2 (g/l)
Triglycerides	1,7 (g/l)
Rapport CT/C-HDL	4,85
C-non HDL	1,3 (g/l)

Table-2: Lipid parameters, non-HDL cholesterol and atherogenic Index in chronic hemodialysis patients and controls

Lipid Parameters	Hemodialysis (n=100)	Controls (n=100)	p
TC (g/l)	2.45 +/- 0.46	1.50 +/- 0.24	< 0.05
TG (g/l)	1.97 +/- 0.70	0.91 +/- 0.30	< 0.05
LDL-c (g/l)	1.41 +/- 0.37	0.85 +/- 0.31	< 0.05
HDL-c (g/l)	0.39 +/- 0.12	0.42 +/- 0.11	0.095 (NS)
Non-HDL-c (g/l)	1.09 +/- 0.34	0,84 +/- 0.24	< 0.05

Results expressed as mean ± standard deviation p: probability

Table-3: The distribution of hemodialysis patients and controls according to atherogenicity thresholds

	Hemodialysis Number (%)	Controls Number (%)	p
TC > 2 (g/l)	19	6.7	< 0.05
TG > 1.7 (g/l)	20	2.8	< 0.05
LDL-c > 1.2 (g/l)	12	5.7	< 0.05
HDL- c≤ 0.4 (g/l)	46.9	23.1	0.0865
Non-HDL- c> 1.3 (g/l)	24	7.6	< 0.05
AI= CT/c-HDL>4.85	27	11.5	< 0.05

Table-4: Comparison of demographic and biological parameters between the two groups of patients with a low level (group I) and a high level of non-HDL-c (group II).

Biological Parameters	Groupe I	Groupe II	p	r
CRP	10.17 +/- 20.44	5.83 +/- 5.76	0.003	-0.3
Creatinine	93.58 +/- 23.81	97.64 +/- 27.96	0.872	0.012
Urea	1.15 +/- 0.33	1.22 +/- 0.24	0.2	0.01
Blood glucose	1.03 +/- 0.71	1.12 +/- 0.98	0.006	0.2
TC	1.34 +/- 0.22	1.95 +/- 0.33	0.000	0.941
LDL-c	0.70 +/- 0.19	1.32 +/- 0.28	0.000	0.917
TG	1.23 +/- 0.61	1.68 +/- 0.97	0.000	0.5
HDL-c	0.38 +/- 0.12	0.40 +/- 0.12	0.831	0.016

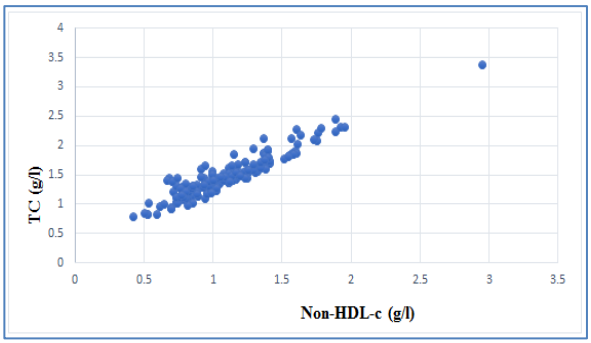

Fig-1: The relationship between non-HDL-c and TC (r = 0.94).

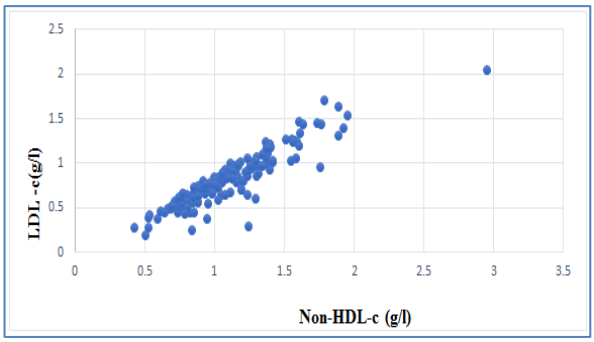

Fig-2: The relationship betwen non-HDL-c and LDL-c (r=0,91).

4. DISCUSSION

CKD is associated with several types of metabolic disorders. These alterations are the source of serious complications that can affect the prognosis and life quality of patients. These complications include dyslipidemia, secondary hyperparathyroidism with renal osteodystrophy, insulin resistance, anemia, inflammation and undernutrition which contribute to an increased prevalence of cardiovascular morbidity and mortality.

Both qualitative and quantitative disturbances in lipid parameters are common in chronic uremic patients at the hemodialysis stage and have been widely reported in the literature [6, 7]. The prevalence of dyslipidemia in chronic hemodialysis patients varies between studies. It is 40% in the study reported by Fox et al. [8], by 63% in the series by Cofan et al. [9] and 67% in that of Kronenberg et al. [10].

Our study confirms literature reports, as we have indeed found a prevalence of dyslipidemia of around 65%. This relatively high rate is most likely related to the age of our patients (48 ± 17 years) as well as the duration of hemodialysis (72 months). Indeed, dyslipidemia increases with age and duration of hemodialysis [8-10].

In our series, hemodialysis subjects exhibited a significant increase in serum triglyceride concentration compared to the control group. This hypertriglyceridemia affected 20% of patients; it is related to the accumulation of lipoproteins rich in TG, mainly very low-density lipoproteins (VLDL) and intermediate density lipoproteins (IDL). This accumulation appears to be due to a decrease in the lipolytic activities of LPL and hepatic lipase (LH) [11].

As for cholesterol metabolism, according to literature data, the most significant abnormality was a decrease in HDL cholesterol in the hemodialysis group. This anomaly affected nearly 47% of patients. The elevation of the uraemic level of VLDL and the alteration of the activity of certain enzymes (lipoprotein lipase (LPL), hepatic lipase (LH) and lecithin cholesterol acyltransferase (LCAT)) would contribute to the disruption of the metabolism of the blood. -HDL [12].

Total cholesterol and LDL cholesterol levels also showed a significant difference compared to the control group. These quantitative anomalies would be related to the qualitative disturbances of LDL particles which would increase atherogenicity. The increased oxidative susceptibility of LDL and the accumulation of the small, dense, highly atherogenic LDL sub-fraction (subclass LDL-6) have been described [13, 14].

The relationship between dyslipidemia and atherosclerosis, on the one hand, and cardiovascular risk, on the other hand, is currently being demonstrated. The concentrations of certain lipid parameters have variable predictive powers depending on the studies, with respect to cardiovascular events [15, 16]. The use of certain ratios has been advocated to account for the risk of atherogenicity. In our study, we used the atherogenic index (AI = TC / HDL-c). In addition, the evaluation of non-HDL-c would allow better identification of non-traditional risk factors linked to subclasses of lipoproteins.

The chronic hemodialysis patients showed a significant increase in AI compared to the control group: this is explained both by the increase in TC and by the significant decrease in HDL-c compared to controls. An AI greater than 4.85 supports a high risk for atherogenicity. In the hemodialysis group, AI was greater than 4.85 in 27% of cases while non-HDL-c was significantly higher, around 24%. When comparing the hemodialysis group with a low non- HDL-c level (group I) and the group with a high non-HDL-c level (group II), we found that the levels of TC, TG, LDL-c are significantly higher and HDL-c levels are significantly lower in group II compared to group I.

This was previously revealed by a study carried out in May 2012 on an Algerian cohort of hemodialysis patients [17], as well as by a cross-sectional study carried out in 2016 in Tunisia [18].

In addition, a significant correlation was demonstrated between the levels of non-HDL-c and either LDL-c ($r = 0.917$, $p = 0.000$) or TC ($r = 0.941$, $p = 0.000$). This agrees with the data described in the literature. We also found a negative association between CRP and non- HDL-c ($r = -0.3$, $p = 0.003$).

5. CONCLUSION

The prevalence of dyslipidemia is very high in hemodialysis patients in our study. The most common abnormalities are decreased HDL, non-HDL hypercholesterolemia and hypertriglyceridemia. Thus, the lipid profile of our hemodialysis patients is very atherogenic, characterized by a significant accumulation of VLDL, LDL and IDL, the concentration of which is estimated by calculating non-HDL cholesterol. Also, non-HDL cholesterol makes it possible to identify non-traditional risk factors linked to these very atherogenic lipoproteins. Consequently, the intake of non-HDL cholesterol appears to be greater than that of LDL cholesterol and deserves to be included in the parameters of the lipid profile in the context of the follow-up of hemodialysis patients.

Declaration of interest

The authors declare that they have no conflicts of interest concerning this article.

REFERENCES

1. Fox, C. S., Matsushita, K., Woodward, M., Bilo, H. J., Chalmers, J., Heerspink, H. J. L., ... & Chronic Kidney Disease Prognosis Consortium. (2012). Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. The Lancet, 380(9854), 1662-1673.
2. Cozzolino, M., Mangano, M., Stucchi, A., Ciceri, P., Conte, F., & Galassi, A. (2018). Cardiovascular disease in dialysis patients. Nephrology Dialysis Transplantation, 33(suppl_3), iii28-iii34.
3. Longenecker, J. C., Coresh, J., Marcovina, S. M., Powe, N. R., Levey, A. S., Giaculli, F., ... & Klag, M. J. (2003). Lipoprotein (a) and prevalent cardiovascular disease in a dialysis population: The Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study. American journal of kidney diseases, 42(1), 108-116.
4. Song, Y., Liu, X., Zhu, X., Zhao, B., Hu, B., Sheng, X., ... & Zhao, J. (2016). Increasing trend of diabetes combined with hypertension or hypercholesterolemia: NHANES data analysis 1999–2012. Scientific reports, 6(1), 1-9.
5. National Cholesterol Education Program (US). Expert Panel on Detection, & Treatment of High Blood Cholesterol in Adults. (2002). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) (No. 2). The Program.
6. Moulin, B. (2000). Anomalies lipidiques au cours de l'insuffisance rénale: conséquences sur la progression de l'insuffisance rénale et le risque cardiovasculaire. Néphrologie, 21(7), 339-342.
7. Shoji, T., Nishizawa, Y., Kawagishi, T., Emoto, M., & Morii, H. (1998). Secondary hyperparathyroidism, decreased hepatic triglyceride lipase, elevated intermediate density lipoprotein and atherosclerosis in hemodialysis patients. Nephron, 78(1), 121-122.
8. Fox, C. S., Longenecker, J. C., Powe, N. R., Klag, M. J., Fink, N. E., Parekh, R., & Coresh, J. (2004). Undertreatment of hyperlipidemia in a cohort of United States kidney dialysis patients. Clinical nephrology, 61(5), 299-307.
9. Cofan, F., Vela, E., & Cteries, M. (2006). Collaborative Study Group for Dyslipidemia. Atherosclerosis, 184, 94-102.
10. Kronenberg, F., Lingenhel, A., Neyer, U., Lhotta, K., König, P., Auinger, M., ... & Dieplinger, H. (2003). Prevalence of dyslipidemic risk factors in hemodialysis and CAPD patients. Kidney International, 63, S113-S116.
11. Verzola, A., Perini, L., Gatto, S., Gilli, P., & Bedani, P. L. (1998). Causes and risks of hyperlipidemia during dialysis and after renal transplantation. Recenti progressi in medicina, 89(11), 590-597.
12. Lacour, B., Massy, Z. A., Jungers, P., & Drueke, T. (1993). Anomalies du métabolisme des lipoprotéines dans l'insuffisance rénale chronique. Néphrologie (Genève), 14(2), 75-90.
13. Wanner, C., & Quaschning, T. (2001). Dyslipidemia and renal disease: pathogenesis and clinical consequences. Current opinion in nephrology and hypertension, 10(2), 195-201.
14. Rajman, I., Harper, L., Mcpake, D., Kendall, M. J., & Wheeler, D. C. (1998). Low-density lipoprotein subfraction profiles in chronic renal failure. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association-European Renal Association, 13(9), 2281-2287.
15. Frey, J., & Couderc, R. (1998, October). Valeur séméiologique du cholestérol-LDL et de l'apolipoprotéine B dans le risque athéromateux. In Annales de Biologie Clinique (Vol. 56, No. 5, pp. 517-20).
16. Yamamoto, S., & Kon, V. (2009). Mechanisms for increased cardiovascular disease in chronic kidney dysfunction. Current opinion in nephrology and hypertension, 18(3), 181.
17. Gouri, A., Dekaken, A., Yakhlef, A., Bentorki, A. A., & Kouicem, N. (2012). Non-high-density-lipoprotein (HDL) cholesterol in Algerian hemodialysis patients. Immuno-analyse & Biologie Spécialisée, 27(6), 357-361.
18. El Ati, Z., Sioud, O., Sbaa, M., & Bouzidi, H. (2014). Apport de non-HDL-cholestérol en hémodialyse. Néphrologie & Thérapeutique, 10(5), 330.