Response to the comment on "IgM nephropathy in children: clinicopathologic analysis"

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Dear Editor,

We thank to Dr Mubarak for his interest in and comment on our article "IgM nephropathy in children: clinicopathologic analysis". We agree with Dr, Mubarak that IgM nephropathy (IgMN) is a very controversial entity, with variable definitions in the different case series published. As in all series of glomerulopathy cases, the percentage frequency variability depends largely on the subjectivity of diagnosis in many cases, the characteristics of each study population and the denominator used to determine the percentage. We decided use all renal biopsies because it gives us an idea of the total frequency of cases and permit to compare with other glomerulopathies frequencies. In our series, 138 children were biopsied due to nephrotic syndrome, so IgMN percentage frequency in children with nephrotic syndrome was 9.4%. With respect minimum threshold of IgM positivity used for us in order to define IgM Nephropaty was "++".

The evolution time in ours patients was 1 year until 21 years, (diagnostic moment until last observation); but, we used the time between the first evaluation in this hospital and one year more like follow up.

Dr Mubarak his appreciations about Table 1 is correct, we mistake this information because at moment of diagnosis, seven patients present hematuria and three hypertension. About laboratory information, ours creatine values are mg/dL and for proteinuria mg/m^2/hours, and for last, those patients were classified like cortico-resistant or cortico-dependent in the last evaluations that we found.

Thank you for his correction.

Conflicts of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Prevalence of chronic kidney disease in patients infected by the human immunodeficiency virus

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To the Editor

Antiretroviral therapy has dramatically improved the prognosis and survival of patients infected with the human immunodeficiency virus (HIV).[1] This new situation has allowed pathologies to develop that in previous decades were considered to be less significant. Within this context, there is a growing interest in chronic kidney disease (CKD), and there are discrepancies both in terms of its prevalence and the factors involved in its development, including antiretroviral drugs (Table 1).[2-11]

With these objectives in mind (prevalence and risk factors), we reviewed patients treated at the Infectious Diseases Clinic of Zamora over a 6 month-period (October 2012-April 2013). Inclusion criteria: HIV infection, with at least two consecutive visits. Patients with concomitant acute disease at the time of the visit and/or those with a follow-up period of less than three months were excluded. We reviewed their medical histories and recorded their age, sex, weight, body mass index, follow-up time, concomitant chronic diseases (diabetes mellitus [DM], high blood pressure [HBP], chronic hepatitis B and/or C virus), smoking status, creatinine, phosphorus, proteinuria (measured by

the albumin/creatinine ratio [A/CR]), urinary sediment, current CD4 count, CD4 nadir, the presence of AIDS, HIV RNA, antiretroviral therapy and tenofovir therapy (current and/or previous).

Estimated glomerular filtration rate (eGFR) was calculated using the MDRD (Modification of Diet in Renal Disease) and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations, with six categories being assigned in accordance with the recommendations of the National Kidney Foundation. CKD was defined as a decrease in kidney function, expressed by a glomerular filtration rate of <60ml/min/1.73m^2 and/or persistent proteinuria (A/CR >30mg/g) for at least 3 months.

For statistical analysis, we used the SPSS 11.5.1 software. The association study was carried out using X^2, exact tests, the Student's *t*-test or ANOVA and multivariate logistic regression.

Table 1. Prevalence of chronic kidney disease in different cohorts and related risk factors.

Study	Origin	Nº patients	CKD criteria	CKD prevalence in % and related risk factors
Fernando SK[2]	Connecticut	473 (HIV)	eGFR[a] <60ml/min/1.73m^2 and/or proteinuria (dipstick)	23.7% African American, HBP, DM
Wyatt CM[3]	New York	1239 (HIV)	eGFR[a] <60ml/min/1.73m^2 and/or proteinuria >100 mg/dl	15.5% Age >50 years old, African American, HCV and low CD4
Sorlí ML[4]	Barcelona	854 (HIV)	eGFR[a] <60ml/min/1.73m^2	7.6% Age, female, lipoatrophy and HIV symptoms
Mocroft[5]	EUROSIDA	4474 (HIV)	eGFR <60ml/min/1.73m^2 measured by Cockcroft-Gault and MDRD	3.5% Cockcroft-Gault 4.7% MDRD Advanced age, low CD4 nadir, diagnosed with AIDS, indinavir/tenofovir therapy
Overton [6]	St. Louis	845 (HIV)	eGFR[a] <60ml/min/1.73m^2	8% Low CD4 nadir, HBP and proteinuria
Lucas GM[7]	Baltimore	4227 (HIV)	eGFR[a] <60ml/min/1.73m^2	6.7% African American
Cheung CHY[8]	Hong Kong	322 (HIV)	eGFRa <60ml/min/1.73m2 and/or proteinuria (PR/CR >0.3g/g)	16.8% Age, HBP, DM, indinavir (no tenofovir), low CD4 nadir and viral load peak
Colson AW[9]	Belgium	5905 (HIV)	eGFR[a] <60ml/min/1.73m^2	3% Age >50 years old, low CD4 nadir, Caucasian
Calza L[10]	Bolonia	894 (HIV)	eGFR[a] <60ml/min/1.73m^2 and/or kidney damage (abnormalities in renal biopsy, urine analysis or renal ultrasound)	21.3% Age >50 years old, male, African American, HBP, DM, proteinuria, TG >200, low CD4 nadir, tenofovir
Otero A[11]	Spain (EPIRCE)	2746 (General population)	eGFR[a] <60ml/min/1.73m^2 and/or proteinuria (A/CR >30mg/g)	9.16% Aged[b], obesity, HBP

A/CR: albumin/creatinine ratio, DM: diabetes mellitus, eGFR: estimated glomerular filtration rate, CKD: chronic kidney disease, HBP: high blood pressure, MDRD: Modification of Diet in Renal Disease, PR/CR: proteinuria/creatinine ratio, TG: triglycerides, HCV: hepatitis C virus, HIV: human immunodeficiency virus.

[a] Measured by MDRD.

[b] Distribution by ages: 20-39 years old (1.93%), 40-64 years old (6.13%) and >64 years old (23.62%).

In accordance with the above mentioned criteria, we excluded 5 patients and included 195, whose epidemiological and clinical characteristics are displayed in Table 2. eGFR, calculated by MDRD, was 99.8±26.6ml/min/1.73m^2, and by CKD-EPI, it was 98.4±18.4ml/min/1.73m^2. The distribution by category was as follows: G1 124 patients (63.6%), G2 67 (34.4%), G3a 3 (1.5%), G3b 0, G4 0, G5 1 (0.5%) with MDRD, and G1 140 (71.8%), G2 52 (26.6%), G3a 2 (1.0%), G3b 0, G4 0, G5 1 (0.5%), with CKD-EPI. A total of 15 patients (7.7%) had proteinuria and 4 of them had an eGFR <60ml/min/1.73m^2. On applying the MDRD formula, we found CKD in 18 (9.2%), and using CKD-EPI, in 17 (8.7%) (Table 2). Furthermore, 14

Table 2. Demographic and clinical characteristics and comorbidities (the estimated glomerular filtration rate was calculated by MDRD).

Characteristics	Total (n=195)	Without CKD (n=177)	With CKD (n=18)	*P*
Male, n (%)	153 (78.5%)	138 (78%)	15 (83.3%)	0.598
Age (years)	47.62±9.86	46.92±9.16	54.5±13.61	0.017
Age ranges, years, n (%) < 40 40-64 ≥ 65	 23 (11,8 %) 162 (83,1 %) 10 (5,1 %)	 23 (13 %) 147 (83,1 %) 7 (4 %)	 0 (0 %) 15 (83,3 %) 3 (16,7 %)	0,024
Months of follow-up	127,21 ± 76,26	125,3 ± 75,6	143,67 ± 82,8	0,999
Obesity, n (%)	64 (32,8 %)	58 (32,8 %)	6 (33,3 %)	0,961
HBP, n (%)	63 (32,6 %)	53 (30,3 %)	10 (55,6 %)	0,029
DM, n (%)	20 (10,3 %)	16 (9,0 %)	4 (22,2 %)	0,079
Smoking, n (%)	114 (58,8 %)	100 (56,8 %)	14 (77,8 %)	0,085
HBV, n (%)	13 (6,7 %)	11 (6,2 %)	2 (11,1 %)	0,428
HCV, n (%)	98 (50,3 %)	87 (49,2 %)	11 (61,1 %)	0,334
Total cholesterol (mg/dl)	195,78 ± 35,94	194,58 ± 35,15	207,44 ± 42,21	0,149
Hypercholesterolaemia, n (%)	81 (41,8 %)	72 (40,9 %)	9 (50 %)	0,456
HDL cholesterol (mg/dl)	49,9 ± 17,56	49,86 ± 17,47	50,17 ± 18,87	0,946
HDL <40, n (%)	44 (27,2 %)	38 (26,2)	6 (35,3 %)	0,425
LDL cholesterol (mg/dl)	116,27 ± 32,11	115,64 ± 31,56	121,7 ± 37,33	0,463
LDL >100, n (%)	50 (30,9 %)	45 (31 %)	5 (29,4 %)	0,891
Triglycerides (mg/dl)	168,19 ± 121,23	166,55 ± 124,86	184,27 ± 77,9	0,556
TG >200, n (%)	42 (21,5 %)	38 (21,5 %)	4 (22,2 %)	0,941
Dyslipidaemia, n (%)	115 (59,6 %)	101 (57,7 %)	14 (77,8 %)	0,099
CVRF, n (%)	170 (87,2 %)	152 (85,9 %)	18 (100)	0,088
Hypophosphataemia, n (%)	16 (9,9 %)	16 (11 %)	0 (0 %)	0,149
Glycosuria, n (%)	5 (2,7 %)	3 (1,8 %)	2 (11,8 %)	0,017
Haematuria, n (%)	14 (7,7 %)	11 (6,7 %)	3 (17,6 %)	0,106
Diagnosed with AIDS, n (%)	69 (35,4 %)	61 (34,5 %)	8 (44,4 %)	0,399
CD4 nadir <200 cells/mm^3, n (%)	95 (48,7 %)	82 (46,3 %)	13 (72,2 %)	0,036
CD4 (cells/mm^3)	646,74 ± 325,68	645,56 ± 324,54	658,33 ± 346,18	0,740
CD4 <200 cells/mm^3, n (%)	12 (6,2 %)	11 (6,2 %)	1 (5,6 %)	0,912
Viral load <50 copies/ml, n (%)	169 (87,6 %)	152 (86,9 %)	17 (94,4 %)	0,353
Antiretroviral therapy, n (%)	180 (92,3 %)	163 (92,1 %)	17 (94,4 %)	0,721
Tenofovir therapy, n (%)[a]	153 (78,9 %)	140 (79,5 %)	13 (72,2 %)	0,469

DM: diabetes mellitus, CKD: chronic kidney disease, CVRF: cardiovascular risk factors, HBP: high blood pressure, HDL: high-density lipoproteins, LDL: low-density lipoproteins, TG: triglycerides, HBV: hepatitis B virus, HCV: hepatitis C virus.

Data are displayed as a mean ± (SD) standard deviation, number and percentage.

[a] Current or previous therapy with tenofovir.

patients had microhaematuria, 5 had glycosuria (2 without DM) and 16 had hypophosphataemia. If we took into account any of these abnormalities, that is, eGFR <60 and/or proteinuria and/or microhaematuria and/or glycosuria and/or hypophosphataemia, 45 patients (23.1%) would be diagnosed with renal dysfunction. One or several cardiovascular risk factors (CVRF) were found in 87.2% and in 100% of those with CKD. Hyperlipidaemia and smoking were the most prevalent CVRF, followed by HBP and DM (Table 2). Differences in CKD prevalence were not found in patients with or without antiretroviral therapy, or between those treated and not treated with tenofovir (current and/or previous).

Variables associated with CKD were age, HBP and a low CD4 nadir (CD4 <200 cells/mm^3) (Table 2). In the multivariate analysis, CKD was significantly associated with HBP (*odds ratio* [OR]: 3.1, p=.028) and a low CD4 nadir (OR=3.3, p=.03).

CKD prevalence was 9.2%, which is similar to that observed in the general Spanish population (9.16%).[11] In patients infected with HIV, the data were conflicting, probably due to the lack of homogeneity in the criteria used for defining CKD. In Barcelona and in the EUROSIDA cohort, the results were similar to those expressed herein[4,5] (Table 1).

In line with other publications, the data presented suggest that the development of CKD is associated with HBP and with a low CD4 nadir[2,3,5,6,8-10] (Table 1). It was not observed that antiretroviral therapy or specifically tenofovir had a significant influence in this regard. We believe that this finding is particularly relevant, given its high use in this series.

We consider that these observations once again reveal similarities between those infected by HIV and the rest of the population: similar CKD, with HBP as the main risk factor. Its control, as with the rest of patients, seems to be essential in preventing CKD development. Furthermore, as has been demonstrated in many studies, poor immunity (low CD4 nadir) implies a worse prognosis and facilitates the development of many complications, among which we should probably include CKD.

The results presented suggest that CKD development in patients infected with HIV depends on two modifiable factors: low CD4 nadir and HBP. The control of both should be a main target in the daily work, and our task decisive.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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