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Onchocerciasis is an independent risk factor for renal damage in high endemicity : a case-control study from the Democratic Republic of Congo

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Summary

In order to determine the frequency and determinant of the CKD in an onchocercal hyper-endemic area, this work was conducted in the health zone of Kalunguta. This is a case-control study of 443 subjects, or 111 cases of onchocerciasis and 332 controls, in January 2015 and February 2016. The mean age of the patients is 45 years (range 18 years and 85 years old) 39±8.9 years, with a sex ratio women/man of 2.1. Proteinuria was more common in onchocerciasis carriers than controls (29.7% Versus 10.5%) and higher creatinine levels in cases than controls (p =0.032). the strength of association observed in univariate analysis persisted for the status of onchocerciasis and parasite density as major major determinants of proteinuria (p<0.005) and compared with non-carriers of onchocerciasis, onchocerciasis carriers increased the risk of CKD by 3 (OR = 2.8, 95% CI: 1.46-6.19, p = 0.007). The age ≥65 years multiplied this risk by 5 (OR = 5.2, 95% CI: 2.1-12.99, p = 0.000). The personal antecedent of HBP increased this risk by 4 (OR = 4.1, 95% CI: 1.57-10.65, p = 0.004). Personal diabetes mellitus antecedent multiplied this risk by 7 (OR = 6.9, 95% CI: 1.69-70.19, p = 0.009).

In view of these results, the search for renal involvement in a hyperendemic zone of onchocerciasis must be systematic and the prescription of the molecules must take into account the presence or absence of the CKD.

Key words : Onchocerciasis, Risk factor, Chronic Kidney Disease, High endemicity.

Introduction

Chronic Kidney Disease (CKD) is a major public health problem in terms of increased incidence and prevalence, morbidity and high cost of care [1-3]. Glomerulopathy remains predominant in sub-Saharan Africa as a cause of Chronic Kidney Disease (CKD), but the burden of kidney damage associated with filariasis remains paradoxically little known. The preponderance of glomerulopathy is not yet very well understood but may be due to the persistence or re-emergence of tropical diseases [4-9]. In Africa, the CKD is attributed in decreasing order of importance to glomerular disease, hypertension and diabetes [10-14]. In this regard, the work of Sumaili *et al.* have described the epidemiological peculiarities of the CKD in Democratic Republic of Congo (DRC) and have

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shown a high prevalence of proteinuria in subjects without traditional risk factors that may be secondary to glomerulonephritis related to tropical diseases such as malaria, filariasis, schistosomiasis and onchocerciasis [2,15-17]. These parasites are considered to be the source of the majority of antigens involved in the formation of immune complexes, which under appropriate conditions lead to the destruction of renal tissue [18-26]. Loa loa is responsible for minimal glomerular lesions. Membrano-proliferative Glomerulonephritis (GMP) and Extrame-mbranous Glomerulonephritis (GEM) are more likely to occur with Onchocerca Volvulus [5,7,21,27]. However, the incidence and prevalence of renal damage during filariasis is not very well known specifically for Onchocerca Volvulus disease [5,8].

The objective of this study is to investigate the impact of onchocerciasis in chronic kidney disease (CKD) in endemic areas.

Methods

It is a case-control study, 443 subjects (111 onchocer-ciasis cases versus 332 controls) living in the health zone of KALUNGUTA / North Kivu in the East of the Democratic Republic of Congo, were examined between January 2015 and February 2016. Each case was matched to three controls, based on age, sex, size, level of education and location. We did a multi-stage draw before reaching the volunteers. In order to ensure the representativeness of the target population (adult of the selected health areas) and to have external validity of our analyzes, we verified that the volunteers who responded to this study and the non-respondents had the same socio-demographic characteristics and that they were exposed to the same risk factors studied. To be eligible, participants should meet the following inclusion criteria: Cases: be 18 years old, have a diagnosis of onchocerciasis after Skin-test, Have lived at least 6 months in the community. Study. And the witnesses: be 18 years old, be free from onchocerciasis after the skin test, no oncocerciasis antecedent and / or treatment of onchocerciasis, freely give consent to participate in the study.

To determine the onchocercal status, we performed a sampling in 4 cutaneous zones (with 2 iliac crests, scapula, and calf). The participant was declared non-carrier of onchocerciasis, in the absence of microfilariae. It was positive in the presence of at least one microfilariae, in a fragment of skin removed. Semi-quantitative proteinuria was investigated in fresh morning urine in the test strip and plasma creatinine was assayed by enzymatic method using a COBAS automaton. GFR was estimated using the MDRD and CKD-EPI formulas. The CKD has been defined and classified according to KDIGO 2012.

Operational Definitions

Onchocerciasis was defined by the presence of at least ≥1 microfilariae in a skin fragment removed. In this study, any subject with a negative skin test was considered negative. Pathological proteinuria was defined as testicular proteinuria ≥ 1+ corresponding to at least 30 mg / dl after the second control 3 months later. CKD was defined as GFR <60 ml / min / 1.73m ² and / or proteinuria> 30mg / dl [28,29]. HTA: SBP ≥140mmHg and / or DBP ≥90 mmHg (HTA unknown) or antihypertensive drug use (known hypertension) [30-33]. Diabetes (DS) was defined as fasting plasma glucose ≥126 mg / dL or case-by-case 200 mg / dL or concept of antidiabetic therapy [32,34-36]. Overweight and obesity were defined, respectively, by a BMI of 25-29.9 Kg / m² and ≥ 30 Kg / m²; abdominal obesity, by waist size> 80 cm and> 90 cm, respectively, in women and men [32,34,35]. Was considered a smoker, anyone who had smoked at least 1 cigarette / day for more than 5 years or more, or who had quit for less than 5 years [36,37]. Was considered to be a risky drinker, anyone who consumed > 2 glasses of beer/day or equivalent for at least one year [36]. Use of herbal medicinal products at risk was defined by any insecure plant intake reported by the patient for the purpose of curing or preventing a disease.

The data were encoded using Excel 2010 software, after cleaning and checking its consistency and quality, they were exported to SPSS 21.0 for analysis. The independent determinants of the CKD were sought by the logistic regression method. For all the tests used the value of p <0.05 was the threshold of statistical significance. The protocol of the study was approved by the ethics committee of the school of public health of the University of Kinshasa.

Results

Table 1 summarizes the main characteristics of the study population. There is a predominance of female patients: 302 women against 67 men, a sex ratio F / H of 2.1. Their average age was 45 (median age 45 years, range 18 to 85 years). Except for age and religion; the proportions of occupation (p = 0.025), marital status (p = 0.004) and education level (p = 0.005) differed significantly in both case and control groups.

The clinical characteristics of the patients studied are shown in Table 2. Compared with the controls, participants with onchocerciasis drank more alcohol (p =

0.019) and had a lower mean pulse pressure value (p = 0.034). a lower average waist circumference (p = 0.034) and a lower average hip circumference (p = 0.002). Of the 443 participants in the study, 167 had an High Blood Pressure with a frequency of 37.7%; 29 had diabetes mellitus with a frequency of 6.5%. The majority of participants had fasting blood glucose levels in the normal range, such as a mean blood glucose level of 140 mg / dl; but this blood glucose was significantly higher on average in controls compared to cases (p <0.05).

Table 1. Sociodemographic characteristics of the study population

Variables	Total n=443	Cases n=111	Control n=332	p
Age (years)	45,4±15,7	43,6±14,4	46,0±16,1	0,164
Gender(%)				0,519
Male	141(31,8)	35(31,5)	106(31,9)	
Female	302(68,2)	76(68,5)	126(68,1)	
Occupation(%)				0,025
Cultivator	367(82,8)	99(89,2)	268(80,7)	
Others	76(17,2)	12(10,8)	64(19,3)	
Civil Status(%)				0,004
Maried	279(63,0)	82(73,9)	197(59,3)	
Others	164(37,0)	29(26,1)	135(40,7)	
Religion(%)				0,657
Catholic	335(75,6)	89(80,2)	246(74,1)	
Protestanting	59(13,3)	11(9,9)	48(14,5)	
Revival Church	15(3,4)	0(0,0)	15(4,5)	
Others	34(7,7)	11(9,9)	23(6,9)	
Level of study(%)				0,005
No study	177(40,0)	33(29,7)	144(43,4)	
Primary	199(44,9)	66(59,5)	133(40,1)	
Secondary	59(13,3)	11(9,9)	48(14,5)	
Universty	8(1,8)	1(0,9)	7(2,1)	

*Data are expressed in absolute numbers or relative frequencies or mean plus standard deviation (SD) as appropriate. * p <0.05.*

The frequency of proteinuria in the study population is shown in Figure 1. Semi-quantitative proteinuria in the urine dipstick was positive in 15.3% for all participants, but this frequency was more significantly cases as witnesses (p <0.0001).

The table 3 describes the glomerular filtration parameters, which shows that the controls had a high mean creatinine level compared to the cases significantly (p = 0.032). Compared with eGFR, the two groups did not show any significant difference.

In univariate analysis, the status of onchocerciasis, marital status, pulse, height and parasite density had emerged as the main determinants of proteinuria. Compared with non-carriers of onchocerciasis, onchocerciasis carriers increased the risk of proteinuria by 4 (OR = 3.59, 95% CI: 2.098-6.142, p <0.0001). Married status multiplied this risk by 2; compared with subjects with parasite density between 1 and 25 microfilariae/mg skin, those with a parasite density between 26-50 and> 50 microfilariae/mg skin increased the risk of proteinuria by 3 and 4, respectively. Height increased the risk of proteinuria by 1.035. On the other hand, the pulse, the low case-specific glucose, decreased this risk by 1.03 and 1.02 respectively. After adjusting for multivariate analysis, the strength of association observed in univariate analysis persisted for the status of onchocerciasis and parasite density as major major determinants of proteinuria and increased the risk of proteinuria by 5 for carrier subjects. onchocerciasis, by 3 for subjects with a parasite density between 26-50 microfilariae / mg of skin and by 6 for those with a parasite density> 50microfilariae / mg of skin (table 4).

Table 2. Clinical and Biological Characteristics of the Study Population by Onchocerciasis Status

Variables	Total n=443(%)	Case n=111(%)	Control n=332(%)	p
HBP HF, n(%)	92(20,8)	28(25,2)	68(19,3)	0,223
DM HF, n(%)	50(11,3)	17(15,3)	33(9,9)	0,087
CKD HF, n(%)	2(0,5)	0(0,0)	2(0,6)	0,561
Known HBP, n(%)	53(12,0)	10(9,0)	43(13,0)	0,174
Known DM, n(%)	4(0,9)	0(0,0)	4(1,2)	0,314
Known CKD, n(%)	3(0,7)	2(1,8)	1(0,3)	0,154
Taken tabaco, n(%)	45(10,2)	16(14,5)	29(8,7)	0,062
Alcohol intake, n(%)	80(18,1)	28(25,2)	52(15,7)	0,019
Medicinals Plants, n(%)	81(18,3)	19(17,1)	62(18,7)	0,416
HBP, n(%)	167(37,7)	46(41,4)	121(36,4)	0,204
DM, n(%)	29(6,5)	4(3,6)	25(7,5)	0,106
Obésity, n(%)	15(3,4)	3(2,7)	12(3,6)	0,457
Overweight, n(%)	74(16,7)	16(14,4)	58(17,5)	0,278
SBP (mmHg)	131,8±23,7	130,1±20,5	132,4±24,7	0,376
DBP (mmHg)	84,3±12,6	86,3±11,2	83,5±12,9	0,102
MPP (mmHg)	100,1±15,4	100,9±13,2	99,9±16,1	0,053
PP, (mmHg)	47,5±15,9	43,8±15,0	48,8±16,1	0,034
Pulse (Bpm)	83,0±14,7	82,6±14,5	83,2±14,8	0,641
BMI (kg/m^2)	22,4±3,7	22,1±3,6	22,5±3,7	0,563
Waist circumference (cm)	75,7±8,8	73,5±8,3	76,5±8,8	0,002
Hip circumference (cm)	86,8±8,8	84,8±8,0	87,5±8,9	0,004
WHP ratio	0,87±0,05	0,87±0,05	0,87±0,05	0,276
Fasting Blood glucose (mg/dl)	78,5±32,3	59,9±13,9	83,7±34,1	0,002
Casual Blood Glucose (mg/dl)	140,3±65,1	119,9±77,6	147,5±58,6	<0,0001

HBP = high blood pressure, HF = family history, DM = diabetes mellitus, BMI = body mass index; SBP = systolic blood pressure; DBP= diastolic blood pressure; PP = pulsed pressure; CKD = chronic Kidney disease;

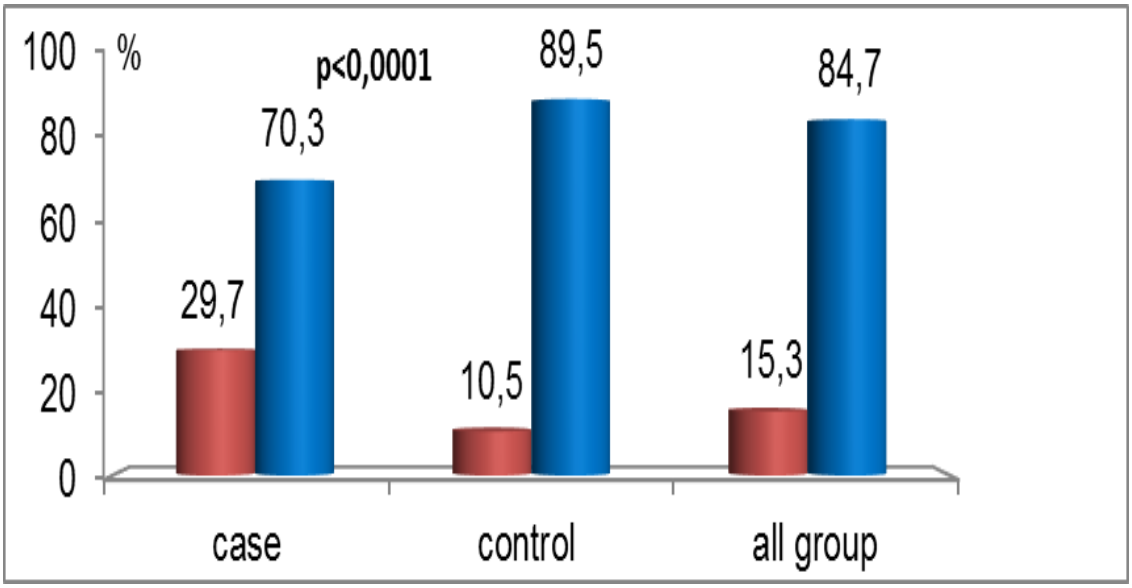

Figure 1. Frequency of proteinuria in the study population

Table 3. Kidney function of respondents according to the status of onchocerciasis

	All Group n=443	Case n=111	Control n=332	p
Créatinine (mg/dl)	0,86±0,41	0,85±0,16	0,86±0,46	**0,032**
eGFR (ml/min/1,73m²)				
MDRD	91,9±29,1	91,6±30,2	92,0±28,7	0,895
CKD-EPI	91,6±20,9	91,5±20,9	91,6±21,0	0,966
CG (ml/min)	58,6±37,4	58,8±39,6	58,6±36,7	0,223

Table 4. Determinants of proteinuria in univariate and multivariate analysis (logistic regression)

	Univariate				Multivariate			
Variables	**β**	**p**	**OR**	**IC 95%**	**β**	**p**	**OR**	**IC 95%**
Onchoceriasis								
No			**1**				1	
Yes	1,278	**0,000**	3,590	2,098-6,142	1,506	**0,000**	4,509	2,289-8,883
Civil status								
Others			1				1	
Maried	0,572	**0,002**	1,771	1,994-3,155	0,980	0,109	2,664	0,803-8,847
Pulse*	-0,023	**0,021**	0,977	0,959-0,997	-0,022	0,220	0,978	0,944-1,013
Height*	0,035	**0,033**	1,035	1,003-1,069	-0,017	0,573	0,983	0,926-1,044
Casual Blood glucose*	-0,015	**0,003**	0,985	0,976-0,995	-0,005	0,350	0,995	0,984-1,006
Parasit Density								
1-25			1				1	
26-50	1,052	**0,010**	2,865	1,801-10,242	0,987	**0,015**	2,684	1,684-10,5
>50	1,356	**0,028**	3,879	1,159-12,987	1,752	**0,009**	5,768	1,538-21,6
					2,466	0,641	11,774	

In univariate analysis, the status of onchocerciasis, age, personal antecedent of HBP and diabetes mellitus, the presence of HBP marital status, parasite density had emerged as key determinants of CKD. Compared with non-carriers of onchocerciasis, onchocerciasis carriers increased the risk of CKD by 3 (OR = 2.8, 95% CI: 1.46-6.19, p = 0.007). The age ≥65 years multiplied this risk by 5 (OR = 5.2, 95% CI: 95% CI 2.1-12.99, p = 0.000). The personal history of HBP increased this risk by 4 (OR = 4.1, 95% CI, 1.57-10.65, p = 0.004). Personal diabetes mellitus antecedent multiplied this risk by 7 (OR = 6.9, 95% CI, 1.69-70.19, p = 0.009) Compared to subjects with parasite density between 1 and 25 microfilariae/mg skin those with a parasite density between 26-50 and> 50 microfilariae/mg of skin increased the risk of proteinuria by 3 and 4 respectively. However, a normal SBP and DBP decreased the risk by 1.03 and 1.04, respectively. After adjusting for multivariate analysis, the strength of association observed in univariate analysis persisted only for onchocerciasis status, age, history of HBP, history of diabetes mellitus, and parasite density. as major determinants of CKD.

Table 5. Determinants of CKD in Univariate and Multivariate Analysis (Logistic Regression)

	Univariate				Multivariate			
Variable	**β**	**p**	**OR**	**IC 95%**	**β**	**p**	**OR**	**IC95%**
Onchocerciasis								
No			**1**				**1**	
Yes	0,189	**0,007**	2,8	1,46-6,19	0,164	0,036	4,79	1,748-7,86
Age								
<65years							1	
≥65years	1,653	**0,000**	5,2	2,1-12,99	0,643	0,033	3,902	1,06-8,43
History HBP								
No			1				1	
Yes	1,408	**0,004**	4,1	1,57-10,65	1,19	0,001	3,288	1,615-6,69
History diabète								
No			1				1	
yes	1,944	**0,009**	6,9	1,69-70,19	1,110	0,016	2,541	1,362-7,78
Tabaco								
No			1					
Yes	0,078	0,919	1,1	0,24-4,79				
Alcohol								
No			1					
Yes	0,292	0,646	1,3	0,39-4,66				
Medicinal Plant								
No			1					
Yes	0,616	0,218	1,851	0,69-4,93				
SBP*	-0,025	**0,000**	0,975	0,96-0,99				
DBP*	-0,038	**0,011**	0,962	0,94-0,99				
HBP								
No			1				1	
Yes	1,040	**0,024**	2,8	1,15-6,98	0,440	0,147	1,552	0,86-2,81
BMI*	0,039	0,543	1,04	0,92-1,18				
DM								
No			1					
Yes	0,432	0,575	1,540	0,34-6,96				
Parasit Density								
1-25			1					
26-50	0,647	**0,005**	2,9	1,19-9,28				
>50	0,118	**0,009**	4,1	1,18-7,12				
Constant					1,276	0,000	0,999	

Discussion

In this study, the proportion of farmers and low education levels was significantly higher in onchocerciasis patients compared to healthy subjects. This observation is in agreement with data from the literature which indicate that the low level of education would be related to school absenteeism and agriculture is, with fishing, breeding and hunting, the main activities exposing to contact of the Similium.

In contrast to the prevalence rate of arterial hypertension in adults in sub-Saharan Africa estimated at between 8 and 14% in the past [38], this study found an overall prevalence rate of hypertension in rural areas of 37.7%.

Another observation made in the study population, the frequency of hypertension was high in the 41.4% group of carriers of onchocerciasis than controls 36.4%. This observation is explained by the fact that the microfilariae will cause a production of inflammatory cytokines via

activation of the complement system, coagulation, fibrin derivatives known to induce endothelial dysfunction with oxidative stress and subsequent inflammation. The basis of atherosclerosis and elevation of blood pressure.

The proportion of subjects screened with semi-quantitative proteinuria (15.3%) was lower than that found by Asongayi T. *et al.* 44.4% [23] Tanyigna K.B. et al. who found a frequency of 60% [39] by considering semi-quantitative screening of their studies. When considering both groups of participants (cases versus controls), onchocerciasis appeared to be the main determinant of proteinuria. This observation is consistent with the results of Ngu JL's work. *et al.* who have found an association between proteinuria and onchocerciasis [40].
The frequency of CKD defined by a eGFR <60ml / min / 1.73m^2 is most noticeable in participants already known hypertensive and diabetic also in those who took traditional plants. Moreover, CKD was more found in participants with high SBP, DBP, MAP, and PP and participants with a high parasite density. In the present study, onchocerciasis, important parasite density, age, hypertension, diabetes mellitus emerged as the main determinants of CKD in this medium. Although renal damage related to onchocerciasis has been well studied in experimental pathology with GNMP and GEM as the underlying histological lesion [5,21]. However, an association between onchocerciasis and nephrotic syndrome has been reported in 9 patients in Cameroon [40] with deposits of immune complex onchocerciasis; this observation suggests the possibility of a possible link that must be sought through more elaborate studies. Mechanical damage to glomeruli by microfilariae and immunological damage by immune complexes has been suggested [41,42]. The presence of onchocerciasis and the emerging important parasite density as an independent factor of CKD. The frequency of CKD is almost doubled in cases compared to controls.

Conflits d'intérêt : Aucun.

Références

1. Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, ckardt K-U E, Nahas ME, Jaber BL, Jadoul M, Levin A et al: Chronic kidney disease as a global public health problem: Approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney International 2007, 72:247-225.
2. Sumaili E.K, Krzesinski J-M, Cohen E P., Nseka N. M.: Épidémiologie de la maladie rénale chronique en République démocratique du Congo : une revue synthétique des études de Kinshasa, la capitale. Néphrol et thérapeut 2010, 6 - N° 4:232-239.
3. Stanifer J.W., Maro V., Egger J., Karia F., Thielman N., Turner E.L., Shimbi D., Kilaweh H., Matemu O., Pate U.D.: The Epidemiology of Chronic Kidney Disease in Northern Tanzania: A Population-Based Survey. PLOS ONE/ April 17, 2015.
4. StaniferJ. W. MV E, Karia F.,Thielman N., Turner E.L., Shimbi D., Kilaweh H., MatemuO., Patel U. D.,: The Epidemiology of Chronic Kidney Disease in Northern Tanzania: A Population-Based Survey. PLOS ONE April 17, 2015, 10(4).
5. Pakasa NM. SE: Pathological peculiarities of chronic kidney disease in patient from sub-Saharan Africa. Review of data from the Democratic Republic of the Congo. . Ann Path 2012 Feb., 32(1):40-52.
6. Naicker S.: Challenges for nephrology practice in Sub-Saharan Africa. Nephrol Dial Transplant 2010, 25:649 -650.
7. KDIGO.: Infection-related glomerulonephritis. Kidney International 2012, Supplements 2:200-208.
8. Pakasa NM, Sumaïli EK.: Pathological peculiarities of chronic kidney disease in patient from sub-Saharan Africa. Review of data from the Democratic Republic of the Congo,. AnnPath 2012 Feb, 32(1):40-52.
9. Pakasa NM, Sumaili E.K.: The Nephrotic Syndrome in the Democratic Republic of Congo. N Engl j med march 9, 2006, 354:10.
10. Feehally J.: Ethnicity and renal disease: questions and challenges. Clinical Medicine 2003, 3:578-582.
11. Alebiosu C.O.: Clinical diabetic nephropathy in a tropical African population. WAJM 2003, Vol.22,N°2:132.
12. Bamboye E.L.: ESRD in Subsaharan Africa. . Ethn Dis 2006, 16[Suppl]:2-5-2-9.
13. Ramirez S.P.B., Durai T.T., Hong HSu S.: Paradigms of public-private partnerships in end-stage renal disease care: The National Kidney Foundation Singapore. Kidney Inter 2003, Vol. 63,Supplement 83:101-107.
14. Feehally J.: Ethnicity and renal disease: questions and challenges,. Clinical Medicine 2003, 3:578–582.
15. Pakasa NM., Sumaili E.K.: The Nephrotic Syndrome in the Democratic Republic of Congo. N Engl j med march 9, 2006, 354:10.
16. Sumaili E.K., Krzesinski J-M., Cohen E P., Nseka N. M.: Épidémiologie de la maladie rénale chronique en République démocratique du Congo : une revue

synthétique des études de Kinshasa, la capitale. Néphrol et thérapeut 2010, 6 -N°4:232-239.
17. Bezerra da Silva Junior G., De Francesco Daher E.: Tropical diseases-associated kidney injury. Rev Bras Clin Med São Paulo 2013 abr-jun, 11(2):155-164.
18. Langhammer J, Birk HW, & Zahner H: Renal disease in lymphatic filariasis: evidence for tubular and glomerular disorders at various stages of the infection. . Trop Med and Int Health september 1997, volume2 no9:875-884.
19. Ormerod m A.D., Petersenm J., Husseym J.k., Weirm. J., Edwardm N.: Immune complex glomerulonephritis and chronic anaerobic urinaryinfection-complications of filariasis. . Postgraduate Med J November 1983, 59:730-733.
20. Paganelli R., NGU J. L., Levinsky R.J.: Circulating immune complexes in onchocerciasis. . Clin exp Immunol 1980, 39:570-575.
21. VAN Velthuysen M.-L.F., Florquin S.: Glomerulopathy Associated with Parasitic Infections. clinical microbiology reviews Jan 2000, Vol. 13, No.1:55-66.
22. Ngu J.L. FS: immune complex nephropathy in the tropics. . critical rev in tropical med 1982.
23. Asonganyi T., Seutche N.N, Lando G.: la proteinurie et l'onchocercose. Méd d'Afr Noire 1999:46 12.
24. Rajamanickam A. aBS: Immunomodulation by Filarial Parasites. . INTERNATIONAL TRENDS IN IMMUNITY OCTOBER 2013, 1 (NO.4)
25. KIBUKAMUSOKE J. W.: Nephrotic Syndrome and Chronic Renal Disease in the Tropics. Brit med J Y 1968, 2(33-35).
26. Langharnrner J., Birkl H. -W., Zahner H.: Renal disease in lymphatic filariasis: evidence for tubular and glomerular disorders at various stages of the infection. Trop Med and Int Health september 1997, volume 2 no9 875-884.
27. Duvic C, Nedelec G, Debord T, Herody M, & Didelot F: Important parasitic nephropahies: Update the recent literature. Nephrologie 1999, 20(2):65-74.
28. Levey AS AR, Coresh J, Cohen EP, Collins AJ, ckardt K-U E, Nahas ME, Jaber BL, Jadoul M, Levin A *et al.*,: Chronic kidney disease as a global public health problem: Approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. Kidney International 2007, 72:247-225.
29. Levey A. S., Coresh J., Balk E., Kausz A.T., Levin A., Steffes M.W., Hogg R.J., Perrone R.D., Lau J. , and Eknoyan G.: National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Ann Intern Med 2003, 139:137-147.
30. Varagic J., Susic D., Frolich E.: Heart, aging and hypertension. Curr Opin Cardiol 2001, 16:336-341.
31. Krzesinski J.M., Xhignesse P.: Nouvelles directives en 2007 pour la prise en charge de l'hypertension artérielle. Rev Med Liege 2007, 62(9):566-574.
32. kaur J.: A Comprehensive Review on Metabolic Syndrome. , . Cardiol Res and Pract 2014, Volume 2014:21.
33. Alam M.N., Soni G.P., Jain K.K., Verma S., Panda P.S.: Prevalence and determinants of hypertension in elderly population of Raipur city, Chhattisgarh Int J Res Med Sci 2015 Mar, 3(3):568-573.
34. Capeau J., Bastard J-P., Vigouroux C.: Syndrome métabolique et insulino-résistance : physiopathologie. mt cardio 2006, 2 (2):155-164.
35. Junquero D., Rival Y.: Syndrome métabolique : quelle définition pour quel(s)traitement(s). MEDECINE/SCIENCES 2005, 21:1045-1053.
36. Shankar A., Klein R., Klein B.E.K.: The Association among Smoking, Heavy Drinking, and Chronic Kidney Disease. Am J Epidemiol 2006, 164:263-271.
37. Orth SR., Stockmann A., Conradt C., Ritz E., Ferro M., Kreusser W., Groove. P., and al.: Smoking as a risk factor for end-stage renal failure in men with primary renal disease. Kidney Int 1998, 54(3):926-931.
38. Bourrée P., Djibo N., Bisaro F.: Parasitoses génito-urinaires. Afican journal of urology 2007, 13 N° 3:206-218.
39. Tanyigna K.B., OJA., Amuta E.U., Onwuliri C.O.E., Ujah I.A.O.: Proteinuria and occurrence of onchocerca volvulus micro filariae in skin,urine and blood of onchocerciasis patients after ivermectin treatment in adikpo, benue state, nigeria. . AFR J clin exper m icrobiol 2008, 9(3):119-121.
40. Ngu JL., Chatelanat F., Leke R., Ndumbe P., Youmbissi J.: Nephropathy in Cameroon: evidence for filarial derived immune-complex pathogenesis in some cases. Clin Nephrol 1985(Sep), 24(3):128-134.
41. Burchard G.D., Kubica T., ischendorf F.W., Kruppa T., N.W. B: Analysis of renal function in onchocerciasis patients before and after therapy,. Am J Trop Med Hyg 1999, 60(6):980-986.
42. Duvic C., Nedelec G., Debord T., Herody M., F. D: Important parasitic nephropahies: Update the recent literature. Nephrologie 1999, 20(2):65-74.