



Glomerular Nephropathies: Epidemiological, Therapeutic and Evolutive Profile at the University Hospital of Oujda.

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ABSTRACT

The epidemiological approach to glomerular diseases remains less developed in our country. The aim of our study is to identify the frequency of glomerular nephropathies in our context; and to describe their different demographic, clinical, biological characteristics, as well as their etiological and evolutive profile. We have led a retrospective study at the department of nephrology, University Hospital M^{ed} VI, between 2014 and September 2017. We collected 93 patients, including 51 men. The average age at the diagnosis was of $34,8 \pm 14,8$ years old. The clinical presentation was dominated by the nephrotic syndrome (60.21%), hematuria (26/88%), and hypertension (22.58%). Glomerular nephritis were primitive in 70.96 % of the cases, the minimal change disease, segmental and focal glomerulosclerosis and membranoproliferative glomerulonephritis represented the most common histological types with 18,18%, 42,4% and 24,04% of the cases, their etiologies were dominated by lupus nephropathy, 78,3% of our patients received a symptomatic treatment. The use of corticosteroids in primitive glomerular nephropathy has been proposed in only 53.7 % of the cases, and associates with immune suppressives in 17.9% of cases.

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Introduction

Glomerulopathies represent a pathological entity characterized by a lesion of the function and structure of renal glomerulus, of inflammatory or uninflammatory origins.

Their classification stands on clinical and anatomopathological data, including the lesions observed in optic microscopy and the examination results in immunofluorescence and electronic microscopy.

The two main glomerular signs are proteinuria and hematuria. They can be associated to hypertension and for renal failure. The predominance of one of the signs and its evolutive profile define different clinical presentations: The nephrotic syndrome, the acute nephritis syndrome, the rapidly progressive glomerulonephritis syndrome, the chronic glomerulonephritis syndrome and the relapsing macroscopic hematuria syndrome.

The border between primitive and secondary glomerulonephritis is fragile. A primitive nephropathy could secondarily prove to be an element of a systemic disease.

Renal biopsy is essential for diagnosis. The same histological lesion could be observed in primitive or secondary glomerulopathies.

On the other hand, the evolution in molecular biology have enabled to identify as genetically transmitted nephropathies hitherto called « primitive »

Every clinician should be able to detect the glomerular nephropathy at risk, to identify its signs and symptoms to ask for and interpret the initial explorations, to initiate appropriate treatment, and to refer to specialist coworker since the diagnosis is always based on histological lesions in renal biopsy.

In Morocco, as in other countries, glomerular nephropathies constitute a frequent clinical problem, in both

city practice and hospitals. One of the main difficulties in the determination of their epidemiological situation in our country is the absence of national files.

The objective of our study is to determine the frequency of primitive and secondary glomerular nephropathies, clinical and biological characteristics, as well as their etiological and evolutive profiles

Means and methods

It is a retrospective, analytic, epidemiological study executed at the unit of nephrology in the university, hospital Mohamed VI, Oujda, between 2014 and September 2017.

Inclusion criteria: cases with one of the primitive and secondary glomerular nephropathies diagnosed at the university hospital. Cases of nephropathies diagnosed in the other health facilities but followed at the university hospital of Oujda.

Exclusion criteria: Cases of diabetic nephropathies. Cases with uncompleted clinical or paraclinical information.

In total, we have included 93 cases.

Demographic data (age at the moment of RB, gender, profession, origin and social insurance) were identified, as well as clinical data (medical and surgical, obstetrical antecedents, general signs: asthenia, emaciation, fever, anorexia), the presence of an oedematous syndrome, hypertension, diuresis, and urinary bandelette, extra renal problems: dermatological, rheumatological, cardio-vascular, respiratory, neurological, ENT, ocular and digestive), biological data (proteinuria of 24h (g/24h), urea(g/l), creatinemia (mg/l), glomerular filtration rate (GFR) (ml/min/1,73m²), ECBU, protidemia (g/l), albuminemia (g/l), hematological abnormalities, inflammatory work-up, immunological work-up, infections and neoplastic work-up) and anatomopathological data (final diagnosis after RBP).

We have also analyzed the different adopted therapeutics, the evolution and complications.

The collected data were ceased on SPSS, and EXCEL software.

Results

93 cases were compiled

The average age of patients at the moment of RB was of $34,8 \pm 14,8$ years, with extremes of 9 and 75 years old . We noted a masculine predominance with a sex-ratio (M/W) of 1,2.

The circumstances of discovering the glomerular nephropathies were warred and mostly associated in the same patient. We have found a nephrotic syndrome in 56 cases, that to say 60.21% , a hypertension in 21 cases , that to say 22.58 % , a macroscopic hematuria in 25 cases (26.88%), a renal failure in 16 cases (17/2%) , a leucocyturia in 20 cases (21.5 %).

Concerning antecedents, 14 patients had a hypertension (15.6%), diabetes and medical treatment, at equal rate, among 9.6% of the patients, 6.4 % had tuberculosis antecedents, at equal rate, among 1.9%, and 1.7 % had a hypothyroid son.

The examination of our patients showed some general sings (fever among 6.45%, asthenia among 24.73% , anorexia among 21.5% ,emaciation among 3.22%), rheumatological problèms among 32.25% of patients , dermatological sings among 6.45% and pulmonar signs among 5,34 % and digestive sings among 3.22% of the patients.

For the biological results, the average value of proteinurea was of $4,9 \pm 3,7$ g/24 h with extremes of 0 and 21 g/24h .A nephrotic syndrom was noted among 56 patients (60,21), A non nephrotic proteinurea was found among 29 patients (31,18%), 27 was absent among 8 patients (31.18%).It was absent among 8 patients (8.6 %).

The blood urea rate was normal among 25 patients (26.88 %).

It was superior to 0.45 g/l and extremes of 0.12 and 3.73 g/l. Creatinemia was inferior to 12 mg/ l among 41 patients (44,08 %). It variated between 4,5 and 140 mg/l with an average of 26,38 and a standard deviation of 29,13 mg/l testifying the variability of the found values. The average of clearance of the calculated creatinemia was of $76,45 \pm 53,55$ with extremes of 8,58 x183, 85 ml/min .it was inferior to 60 ml /min among 37 patients (39,78 %) extremes of 11 and 55g/l. A hypoalbuminemia (< 30g/l)was observed in 60,45% of cases with a average of $19,6\% \pm 6,8$ g/l.

The average of protidemia was of $53,75 \pm 14,73$ with extremes of 14,70 and 78g/l. A hypo protidemia (<60g/l) was observed in 66,7 % of cases with an average of $43,19 \pm 10,92$ g/l.

Apart from these abnormalities of the renal work-up, the patients had presented other biological abnormalities :

- Anemia : 42 cases (45,16 %)
- Hyperleukocytosis : 11 cases (11,82 %)
- leukopenia : 3 cases (3,22 %)
- Lymphopenia : 12 cases (12,9 %)
- Thrombopathy : 1 case (1,07 %)
- 38 cases with inflamatory syndrom (40,86 %).

All our patients benefited from a whole immunology work-up including the research for anti -nuclear and anti DNA antibodies in 16,12%

The nephrotic syndrom was the main indication for the renal biopsy puncture in our population (65,2 %) ; the rapidly progressive glomerulonephritis syndrom (RPGN) (8,4 %). The nephritic syndrom in 6,6 % of patients and relapsing macroscopic hematuria in 1,9 %.

The histological diagnosis of glomerular nephropathies showed a focal segmental glomerulosclerosis (FSG) in 32,2% of cases, a lupic nephropathy (LN) in 29% cases, a minimal change disease (MCD) 12,9 % of cases, 8,9% of cases were an IgA glomerulonephritis, 6,4% as membranous nephropathy (MN), and 2,1 % a membrano-proliferative glomerulonephritis (MPGN) .

We have noted a feminine predominance in the MPGN and MCD , as well as for the lupic nephropathy contrasted to the other GN where men were predominant.

The diagnosed glomerulopathies during our study were primitive in 66 cases, that to say 70,96%

The frequency of primitive nephropathies was higher among patients aged b/w 20-29 and 30-39 (41,5 %).

Otherwise, the more the age was advanced , the more the frequency of primitive nephropathies decreased. The male sex was predominant in all primitive nephropathies (54,5%) , except for the MPGN and MGL.

The depicted secondary glomerulopathies were lupic nephropathies (29%) of cases .The average age of our patients was of $32,56 \pm 10,40$ years , with externes between 17 years old and 50y old. We have observed four case of lupic nephropathies that were declared before 20 y old (15%) and two cases declared at the age of 50years (7,8%).

Among men, the average age of the disease occurrence was of 22,4 years with extremes from 17x32 years old ; as opposed to women where it was of 34,86, years with extremes from 17 and 50 years.

The renal biopsy picture was administered for 25 of our patients among a total number of 27 patients having lupic nephropathy, that to say 92,60% .However, the RB was not practised for two admitted patients having a profound thrombopenia. The proliferative glomerulonephritis were the most frequent.

Glomerulonephritis class V of the who was the most frequent, observed among 17 patients, 63% of cases GN class III was observed among 5 patients, 18,5 % of cases.

GN type V were found in 11 , 1 % of cases . GN type II and VI were respectively observed in 7,40% and 3,70% of cases.

The other anatomopathological problems were present in 10 cases : A tubular involvement was noticed among 4 patients (14,8 %). Intestinal involvement also among 4 patients (14,8%) vascularitis among 2 cases (7, 4%)

The majority of our patients (78.3 %) benefited from a symptomatic treatment composed of anti hypertensors, anti-proteinuria, diuretics and anticoagulants.

In primitive GN, the use of corticotherapy was proposed in 53,7% of cases , and corticotherapy associated Immunosuppressors in 17,9 % of cases. For secondary GN, treatment was mainly etiologic .

To present relasing, treatment by synthesis antipaludians (SAP)was also administred for 26 of lupic GN.

Among the 93 elaborated files, we deplored 6 deaths, 10 patients who lost sight, and 77 among them (82 %) benefited from a follow -up over 6 months.

After a retreat of 6 months, the complete remission was obtained in 54 % of cases, and partial one in 32 % therapeutic failure was noted in 14 %

Discussion

The epidemiology of GN is variable in Europe in national and regional files, which is not the case in African countries where there are usually reported cases or mono centric experiences with limited number of diseases .This is essentially due to the lack of epidemiological resources and

expertise in the execution and interpretation of renal biopsy [1,2].

The prevalence of glomerular nephropathies in Morocco is less known because of the absence of national files. The MaReMar study, the first span epidemiological study realized in Morocco, between January 2010 and March 2011, estimates the prevalence of renal chronic disease to 2.9%, whose 32,7% is secondary diabetic nephropathy, and 0,66% to other glomerular nephropathies. In our series, we diagnosed 93 cases of glomerular nephropathies over a 4 year period whose 70,9% are primitive. Studies in France and Italy [3][4], estimated the incidence relating the number of glomerular nephropathies identified by renal biopsy to the population of the enlistment zone and demonstrated that the incidence is twice higher among men rather than women.

The age ratio varies depending on studies. Simon affirms that the annual incidence of GN among elderly people is not significantly different to that of young adults, only the frequency of histological forms is distinct [5]. Also, the incidence of IgA GN is 3 to 4 times higher among young adults rather than elderly people of more than 60 years old. Conversely, the membranous nephropathy is 3 times more frequent among old people.

In our serie, the frequency of the nephrotic syndrome is superior to the ones found in European studies. This high rate can be explained, from one hand to the fact our patients consulted at an advanced stage of the disease where the clinical tolerance is worst. Conversely, western teams who biopsized less symptomatic glomerulopathies with abnormalities are only found in urinary base. In this initiative, abnormalities in the urinary base are systematically searched in different health facilities [1,2,3].

Primitive glomerulopathies

The prevalence of primitive glomerulopathies has been less studied, and the majority of the published studies are European. A review of data revealed incidence rates between 0,2/100000/year and 2,5/100000/year among adults [5,7].

Minimal change disease and focal segmental glomerulosclerosis

This anatomo-clinical entity, also called idiopathic nephrosis, is more frequent among children rather than adults. Some studies relate the incidence of nephrotic syndrome, which produces an overestimation of the disease [8,9], others related the incidence based on the histologic diagnosis [10,11]. The incidence rates among kids vary between 0,23/100000/year and 15,6/100000 with a prevalence of 16 cases for 100000 kids in function of ethnic origins. For adults, the reported rates are between 0,2/100000/year and 0,8/100000/year [12,13]. No tendency of evolution over time has been noticed.

In our study, the frequency of MCD, FSG was respectively of 18,1% and 42,4%. The absence of uniform codification on the clinical and histological scale makes the comparison between studies difficult.

The membranoproliferative GN

The MPGN represented 4,5% of GN in our serie. This frequency is concordant with results by Rivera [7] and Schena [14]. This incidence has clearly been decreased in industrialized countries, and it is interpreted as the consequence of the amelioration of hygiene and systematic ant biotherapy precociously administered in rhino-pharyngeal infections, a treatment that would also enable to decrease the incidence of proliferative endocapillary GN [14,15].

The membranous glomerulopathy

In European countries, the EMG is the second primitive GN in frequency after the IgA nephropathies, with a rate varying around 20% ACCORDING to authors [7,14].

Ben Maiz [16] reports that the incidence of EMG has changed from 8,9% to 11,9% during the two last decades. This increase is in fact particular to adults. However, for kids, he has noted a decrease probably related to the vaccination against Hepatitis B, becoming obligatory in Tunisia since 1995.

In our serie, the frequency of the membranous nephropathy was of 24,2% among the total of primitive GN. It is then in second position after the MCD.

The male predominance in the MCD is noticed by almost all authors [14,17], similarly to our serie.

The IgA GN

The IgA GN, or the Berger disease, is actually the most known chronic primitive GN in the world. In our study, the frequency of IgA GN was of 7,7%. This weak rate of nephropathy could be explained in part by the fact that the immunohistochemical study of the renal biopsy was in current use, and in other part, the abnormalities of urinary sediment were not systematically searched for in different health facilities, and finally, many patients with macroscopic hematuria would consult in urology instead. Yet, we cannot know whether it is an identification problem or a real difference in frequency.

Ben Maiz [16] reports that the incidence of IgA nephropathy has changed from 0,73% to 10%, the elderly population being spared, it is rational to doubt the westernization of lifestyle. This nephropathy is described as a silent ailment systematically depicted in 60 to 68% of cases; whether it is a microscopic hematuria (36%), a proteinuria (60%), a hypertension (10%) or an AKI (2%) [18,19]. The classical recurrent macroscopic hematuria contemporary to a rhino pharyngeal infection is observed in 32% of cases. Two other modes of acute revelation are also described [20], a NS (3%) or an acute NS (4%).

Secondary glomerulopathies

The lupic nephropathies are among nephropathies are among the most frequent and the most severe visceral diseases of disseminated erythematous lupus (DEL). The exact frequency of renal disease during DEL is hard to appreciate. It varies according to clinical and histological criteria.

In our study, the frequency of lupus nephropathies was 29.03%, compared to all glomerular nephropathies. This lower rate than in the literature is explained in part by the fact that lupus disease is multisystemic, patients are followed in other medical specialties. Ben Maiz [16] reports that the incidence of lupus nephropathy increased from 9.8% to 16.1% in adults, raising the suspicion of the role of sun exposure and the increasing use of cosmetics. Lupus mainly affects young women (90% of cases), with an average age of 32 years. Our study found a comparable average age of 32.6 years and the female predominance was also noted.

Renal manifestations of SLE are rarely indicative of the disease. They are nevertheless early, occurring most often during the first years of lupus evolution; however, they may only appear later, several years after the onset of the disease [21,22].

In most cases, renal involvement is characterized by proteinuria of variable abundance and microscopic hematuria, the importance of which, as a rule, reflects the degree of cellular proliferation within the glomerular lesions. Renal

failure, of varying degrees, is present in about 15% of patients during the discovery of nephropathy. [23,24]

Conclusion

The epidemiological approach to glomerular diseases remains less developed in our country. We have noticed that they are usually diagnosed at an advanced stage. The clinical expression was dominated by the nephrotic syndrome and the renal failure. Renal biopsy is an essential tool to the precise diagnosis of the type and etiology of GN. Our histological and etiological results are less different than those in literary data. Evolution, in medium and long term, was dominated by the occurrence of a chronic kidney failure in 26,4% of cases. This should lead us to question the means of early diagnosis and the therapeutic prevention in order to avoid, or at least slower the evolution, taking into account the treatment of patients having kidney failure from a socioeconomic angle.

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