Changing trends of native renal histopathologic diagnosis in a tertiary health centre in Nigeria

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Abstract

Background: Renal biopsy is an essential tool in investigating renal disease. Over the past few years, several authors have described changes in renal histopathologic diagnosis. Several factors may have contributed to this: including improvements in histopathological techniques, patient's demographic data, presence or absence of underlying disease or malignancy.
Methodology: We reviewed our database of native renal biopsies done between 1968 and 2022 to study the trend in the histological diagnosis of patients with the nephrotic syndrome.
Results: There was a total of 251 biopsy reports for which we had the requisite data which were year of diagnosis and histopathological diagnosis. In the period around 1968, the main histological diagnosis was proliferative glomerulonephritis, followed by membranous glomerulonephritis and miscellaneous. By the period of 1985-2011, membranoproliferative glomerulonephritis (MPGN) predominated as histological diagnosis. From 2012-2022, the pattern changed to focal segmental glomerulonephritis.
Conclusion: There is a changing trend of histopathological diagnosis made from renal biopsy slides. There is a transition to predominance of focal segmental glomerulosclerosis. Whether this reported trend is real or apparent is still unclear.

Évolution des tendances du diagnostic histopathologique rénal natif dans un centre de santé tertiaire au Nigéria

Résumé
Contexte de l'étude : La biopsie rénale est un outil essentiel dans l'investigation des maladies rénales. Au cours des dernières années, plusieurs auteurs ont décrit des changements dans le diagnostic histopathologique rénal. Plusieurs facteurs peuvent y avoir contribué : notamment les améliorations des techniques histopathologiques, les données démographiques des patients, la présence ou l'absence d'une maladie sous-jacente ou d'une tumeur maligne.
Méthode de l'étude : Nous avons examiné notre base de données de biopsies rénales natives réalisées entre 1968 et 2022 pour étudier la tendance du diagnostic histologique des patients atteints du syndrome néphrotique.
Résultats de l'étude : Au total, 251 rapports de biopsie ont été réalisés pour lesquels nous disposions des données requises, à savoir l'année du diagnostic et le diagnostic histopathologique. Vers 1968, le principal diagnostic histologique était la glomérulonéphrite proliférative, suivie de la glomérulonéphrite membraneuse et de divers autres diagnostics. Entre 1985 et 2011, la glomérulonéphrite membranoproliférative (MPGN) prédominait comme diagnostic histologique. De 2012 à 2022, le profil a changé pour devenir une glomérulonéphrite segmentaire focale.
Conclusion : Nous constatons une évolution de la tendance du diagnostic histopathologique réalisé à partir de lames de biopsie rénale. On observe une transition vers une prédominance de la glomérulosclérose segmentaire focale. On ne sait pas encore si cette tendance signalée est réelle ou apparente.

INTRODUCTION

Kidney biopsy is an essential tool in the diagnosis of kidney diseases and, indeed, the gold standard in the diagnosis of glomerular diseases. Furthermore, kidney biopsy guides therapy of glomerular diseases, as well as help to establish the pattern of disease for the purpose of appropriate planning and guidelines in management (1,2). For instance, in the past, it was a common clinical practice to treat children with glomerular disease manifesting as the nephrotic syndrome for minimal change disease without kidney biopsy. But because of disease relapse, increasing steroid resistance, and poor outcome, it became necessary to do a biopsy before treatment. Similarly, in adults membranoproliferative and membranous glomerulopathy were the commonest causes of glomerular disease, but as the years went by, this pattern also began to change (3). Therefore, it is now recommended in guidelines to have a biopsy done before treatment for glomerulopathies.

In addition to the role of kidney biopsy in diagnosis of kidney disease, especially glomerular disorders, kidney biopsy and histological examination also aid determination of severity of kidney disease and prognosis (4). The information provided by histology is important in adopting appropriate management plans. The kidney biopsy and histological examination in diagnosis, severity, and prognosis is not only useful in evaluation of diseases of the native kidney but also useful in the management of diseases affecting transplanted kidneys. Kidney biopsy and histology in patients with kidney allograft dysfunction help in early diagnosis and prompt treatment and subsequently the overall graft survival (5). The role of kidney biopsy and histological examination in the management of glomerular disease cannot be overemphasized. With more sophisticated biopsy protocols, tools, expertise, and availability of precision medicine, it became clear that glomerular diseases were probably undergoing transition. The reasons may be numerous but not certain yet. For instance, infections and infestations played a major role in the pathogenesis of glomerular diseases in the tropics generally, and this was probably the reason for preponderance of 'proliferative glomerulonephritis'. But in the intervening years, novel infections with distinctive pathologies, previously unrecognized genetic mechanisms and genes, and even occupational exposures have made impact on evolution or transitional changes in glomerulopathies (6).

There are reports from around the world about the changing trends in histopathological patterns in patients diagnosed with nephrotic syndrome(7). The reasons are not clear, but these have included refinement of diagnostic tools, improvement in expertise and possible actual changes in the histological patterns. It is important to be aware of these because current guidelines are disease-specific, the treatments rely on precision-medicine, and the outcomes are predictive. For instance, it is now recommended that in people of African descent, apolipoprotein I risk variant gene be screened for before transplantation in focal segmental glomerulosclerosis (FSGS), because of potential for recurrence after transplantation (8). In a recent study from Cote d'Ivoire, the nephrotic syndrome was the indication for kidney biopsy in 64% of cases (9).

It is against this background that we decided to review our biopsy series over the past few decades to know whether there has been a trend in histopathological changes and compare it with what obtains in other regions of the world. We have restricted this to diagnosis of the nephrotic syndrome and other proteinuric states, which are the commonest indications for performing the kidney biopsy, as in other places.

MATERIALS AND METHODS

We reviewed reports of kidney biopsy reports of children and adults from 1968 to 2022, a period of about five decades at the University College Hospital, Ibadan, Nigeria. Only biopsy reports with the nephrotic syndrome or other proteinuric states as diagnosis were reviewed. The data was extracted from signed reports archived in the adult Renal Unit of the Hospital. The adult nephrology unit of the hospital take under care patients above the age of 16 years. The biopsies were usually read and interpreted by consultant pathologists with experience in kidney pathology. Furthermore, being a teaching hospital, the biopsies could be read by a team of a consultant and trainee(s), who together would then sign out the reports. The period of diagnosis and histopathological diagnoses were documented.

Data obtained were entered into Microsoft Excel spread sheet and then exported to the Statistical Package for Social Sciences (SPSS) 20 which was used for the analysis. Categorical variables were presented as frequencies and proportion while continuous variables were presented as means with standard deviations.

RESULTS

There was a total of 251 biopsy reports for which we had the requisite data which were year of diagnosis and histopathological diagnosis. In the period around 1968, the main histological diagnosis was proliferative glomerulonephritis, followed by membranous glomerulonephritis and miscellaneous. By the period of 1985-2011, membranoproliferative glomerulonephritis (MPGN) predominated as histological diagnosis. From 2012-2022, the pattern changed to focal segmental glomerulonephritis (FSGS) as the predominant histological type among patients with nephrotic syndrome. Table 1. In 12 reports, the years of biopsy could not be ascertained and some histological types (proliferative, chronic glomerulonephritis (CGN) and miscellaneous types were no longer reported after year 1985, Table 1.

DISCUSSION

Our findings suggested a change in histological pattern from proliferative glomerulonephritis to FSGS**.** These findings were consistent with what has been reported in some parts of the world, including the United States and India (7,10). For instance, before the 1990s, membranoproliferative glomerulonephritis (MPGN) predominated as histological diagnosis in the United States as was found in our biopsy series. This is similar to findings in India where diffuse proliferative glomerulonephritis (DPGN) was the predominant diagnosis, but by the year 2002, FSGS emerged as the predominant histological diagnosis (10). Table 2. It is to be noted that the change in pattern is also occurring in children. In the Nigerian children, minimal change disease (MCD) accounted for 20.4% and FSGS 39% in a biopsy series (11). A study from India also reported an increase in the diagnosis of FSGS in children and advocated renal biopsy in all children with the nephrotic syndrome (12). A recent systematic review and meta-analysis of primary glomerular disease in Africa found a higher prevalence of MCD than FSGS in children, but noted that ratio of MCD to FSG was less than in previous years. This suggests an increasing prevalence of FSGS (13). The rarity of MCD had previously been reported from our hospital (14). The predominance of MPGN and DPGN in the earlier years suggests high incidence of infectious diseases among the world population (15). Infections were the predominant secondary cause of glomerulonephritis, however, there is an indication that the proportion of secondary glomerulonephritis has reduced (16). This may be due to the increased use of antibiotics and improvement in treatment of diagnosis and treatment of infections generally. In addition, the widespread use of vaccination against common infections may have also contributed to the less roles infections now play as a secondary cause of nephrotic syndrome (17). For instance, in the early sixties and seventies in Nigeria, infections played a significant role in nephropathies. These include hepatitis B(18,19), schistosomiasis, and malaria. Indeed, quartan malaria nephropathy was a common and well recognized entity but has become a rarity (20), whereas it was a common cause of kidney disease in the seventies (21). There is also an uptake in vaccination against hepatitis B and C, which are common causes of secondary glomerulonephritis (22).

The reasons adduced for change in histological pattern include patients' demographics, changing pattern of underlying disease and genetics. There is an increase in the incidence of FSGS in many countries, and especially in the United States among African Americans. The increase in incidence has been attributed to human immunodeficiency virus infection, increase in diabetes mellitus, obesity and hypertension (23). African Americans have higher rates of end stage kidney disease (ESKD) due the APOL1 G1 and G2 risk variants in this population. These risk variants have also been documented in Africa (24,25). But development of kidney disease requires a 'second hit', which may be infection or other environmental factors (26,27). Perhaps, this may explain the increasing prevalence of FSGS around the world, and particularly Africa.

The advent of omics science has improved the ability to identify the aetiology of nephrotic syndrome as primary or secondary (28,29). Previously, diagnostic, prognostic and therapeutic decisions in nephrotic syndrome were largely based upon clinical or histological patterns. This approach of kidney biopsy most often misses the heterogeneity of nephrotic syndrome and its aetiology. Using integrative genomics approach for nephrotic syndrome and its aetiology through the application of bioinformatics and computational methods with comprehensive experimental, molecular and clinical data have been shown to be useful in holistic disease definition (28,29). The prospect of integrative genomics in diagnosis and treatment of nephrotic syndrome offers a new

hope for the application of precision medicine in management of nephrotic syndrome.

This study has explored the trend in histopathological diagnosis over a period in patients with the nephrotic syndrome, but we are unable to compare among such demographics such as sex and age groups. In addition, the number of biopsies is comparatively small as is common in sub-Saharan Africa with limited resources where biopsy rates are low. The lack og electron microscopy and immunofluorescent study is another limitation. The strength of the study is the period which spanned decades, in years.

CONCLUSION

There is a changing trend of histopathological diagnosis made from renal biopsy slides. There is a transition to predominance of focal segmental glomerulosclerosis. Whether this reported trend is real or apparent is still unclear, but possible reasons are the marked reduction in incidence of infectious diseases due to widespread antibiotic use, increase in Non communicable diseases (obesity etc) and vaccination against common infections.

Conflicts of interest: None declared.

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Table 1. Histological diagnosis by period (year)

Period (year)	FSGS	Membranous	Minimal change	Membranoproliferative	Proliferative*	CGN	Miscellaneous	Total
1968 n(%)		14(17.28)	7(8.64)	2(2.47)	35 (43.21)	9 (11.11)	14(17.28)	81
1985-1991 n(%)	9(16.67)	2 (3.70)	3(5.55)	40(74.07)	0	0	0	54
2005-2011 n(%)	14(31.11)	3(6.66)	9(20)	19(42.22)	0	0	0	45
2012-2022 n(%)	37(62.71)	6(10.17)	12(20.34)	4(6.78)	0	0	0	59
Period not available n(%)	8(66.67)	1(8.33)	1(8.33)	2(16.67)	0	0	0	12
Total								**251**

FSGS Focal segmental glomerulosclerosis, CGN chronic glomerulonephritis

Table 2. Distribution of histological subtype by period in the United States and India (7,10)

Country	Period	FSGS	MCD	MPGN	PIGN	PGN	Others CSGN	
USA	Before 1990	23.0%	41.0%	28.0%	-	-	-	
	After 1990	47.0%	25.0%	19.0%	-	-	-	
India	1964-1980	6.5%	20.1%	18.6%	7.5%	36%	30%	6.3%
	1980-1998	9%	23%	18%	10%	19%	31%	7%
	2002-2007	30.6%	14%	17%	24%	2.8%	11%	3.7%