Original Research Article

HISTOPATHOLOGICAL PATTERN OF NEPHROTIC SYNDROME IN ILE-IFE, SOUTHWESTERN NIGERIA. A 16-YEAR RETROSPECTIVE REVIEW.

Abstract

BACKGROUND.

Nephrotic syndrome is one of the major ways in which kidney disease presents clinically the world over. Where biopsies are carried out, the microscopic appearances observed in the affected patients vary according to age, gender, race and geographical location.1 In most cases, the vital information obtained from the histological assessment of these patients is pivotal to instituting effective management of their diseases.

In this study, we set out to describe the spectrum of microscopic findings in renal biopsies from a retrospective cohort of such patients in our hospital.

METHODOLOGY.

Archival formalin-fixed-paraffin-embedded renal biopsy tissue blocks were subjected to routine Heamatoxylin&Eosin(H&E), Jones Methelamine Silver (JMS), Masson's Trichrome (MT) and Periodic Acid Schiff stains (PAS) as well as immunoperoxidase stains for IgG, IgM, IgA and C3. The slides were viewed using binocular light microscope.

RESULTS.

A total of 73 cases were reviewed with a male to female ratio of 1.7:1 and mean age of 20.2 years SD of 11.6). Overall, focal segmental glomerulosclerosis (FSGS) (48.3%) was the most frequent histological pattern observed. FSGS and minimal change disease were the commonest histological patterns seen in children while FSGS and membranous glomerulonephritis were the

most common patterns in adult population. There were four cases of IgA nephropathy on immunoperoxidase stain. The previous diagnosis was changed in 13 cases, with use of immunostaining which was not carried out albinitio.

CONCLUSION

This study shows that FSGS is the most common histopathological finding among patients with the nephrotic syndrome in our hospital irrespective of age or gender. correct typos addition, we found that the use of immunoperoxidase in assessment of renal biopsy is important in making a more accurate and clinically relevant diagnosis.

Use the same subheading as proposed by the journal.

Include key words.

INTRODUCTION.

The nephrotic syndrome is the most common manifestation of glomerular diseases. It is a complex clinical condition that is characterized by massive proteinuria, hypoalbumineamia, hypercholesteroleamia and generalized oedema.[2]Establishing the histopathological basis of this syndrome in the individual case is most desirable for proper management and follow-up subsequently

For a full evaluation of renal disease, clinical data and serological tests, need to be combined with a complete assessment of renal biopsy using light microcopy, immunofluorescence and electron microscopy. While this standard approach is the routine practice in the developed countries of the world, it however still remains a challenge in many of the developing countries (Nigeria inclusive). Up until recently we have depended solely on the use ofHeamatoxylin& Eosin, JMS, PAS, and MTand these come with all their diagnostic limitations.[3]This study therefore is aimed at evaluating renal biopsy specimens of patients who presented with nephrotic syndrome in our centre over a period of 16 years using light microscopy with the aid of Heamatoxylin& Eosin, ,special histochemical stains and immunoperoxidase stains, since use of immunofluorescence and electron microscopy for paraffin embedded sections are not routinely available in the Nigeria yet. I suggest formulating this sentence since PE sections are not used for

EM.This will enable us to improve on the diagnostic characterization and documentation of the histological basis of nephrotic syndrome in our centre.

Electron microscopy is **a mainstay in the analysis of renal biopsies**, where it is typically employed in a correlative fashion along with light and immunofluorescence microscopy.

METHODOLOGY

STUDY DESIGN

This was a16-year retrospective histological descriptive cross-sectional study of renal biopsies obtained from patients who presented with nephrotic syndrome in the Renal Unit of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria, between January 2002 and December 2017).

CASE SELECTION AND INCLUSION CRITERIA

All renal biopsies of nephrotic syndrome patients received at the Morbid Anatomy Department O.A.U.T.H.C, Ile-Ife from January 2002 to December 2017, excluding the instances where the biopsy tissue was used updefine how many,were recruited for the study. The clinical and demographic information of the individual patient was collected from the accession register as wellas data from the original consultation request cards of the patients. The slides of the cases were retrieved for review of previous diagnosis. Fresh 3micrometer sections were cut from archival tissue blocks and stained with H and E, Periodic Acid Schiff, Jones silver methenamine, and the Masson's trichrome stains.

Immunoperoxidase stains using IgG, IgM, IgA, and C3 antibodies after antigen retrievalwhat was used for antigen retrieval were also applied. Appropriate positive and negative tissue controls were used for each of the stains applied.

All the slides were reviewed using a standard compound binocular light microscope and findings were grouped into standard recognized groups of causes of nephrotic syndrome.

EXCLUSION CRITERIA

All renal biopsy specimens from non-nephrotic patients and cases whose tissue blockshas beenused up or with inadequate tissue samples were excluded from the study.

DATA ANALYSIS

The results were presented using simple descriptive statistical analysis, frequency tables and charts. Statistical analysis was carried out using Windows ver.20 (SPSS).Change – the program is SPSS.

RESULTS

General patient characteristics.

There were 73 patients with the nephrotic syndrome between 2012 and 2017 who had biopsy carried out on them. Of these 73cases,typos 46 were males and 27 were females (male to female ratio 1.7 to 1). The mean age was 20.8 ± 12.4years, the ages rangingfrom 5 to 56years. I wonder how many were excluded?

Most of the patients were children below the age of 16years and focal segmental glomerulosclerosis (FSGS) was the most predominant pattern I suggest to do 2 different analyses – one on children, one on adults. I want authors to define whether nephrotic syndrome in children is cured ex iuvantibus by steroids and biopsy performed only if steroid resistant or the the biopsy is done to each nephrotic sy child patient – most of the guidelines suggest not to perform biopsy right away since MCD is usually steroid sensitive in this case it is a bias

Excepting IgA Nephropathy and post-infectious GN, which occurred more commonly among females, all the histological abnormalities were commoner among males.Figure 1depicts the range of histopathological abnormalities that we found.

HISTOPATHOLOGICAL ABNORMALITIES

Morphological patterns

Focal segmental glomerulosclerosis(FSGS) was the most common histological abnormality across all age groups in this study accounting for 42.5% of the cases(31cases). Minimal change

disease in children and membranous glomerulopathy in adults, respectively, were the next most common. Membranous glomerulonephritisI suggest to use same nomenclature was responsible for 16cases (21.9%). There were 13cases of minimal change disease(17.8%), 6cases of membranoproliferative glomerulonephritis(8.2%), 4cases of IgA(5.5%) Nephropathy, 2cases of Diabetic nephropathy (2.7%) and I case of Postinfectious glomerulonephritis(1.4%). Table 1

Immunoperoxidase Staining Patterns

The immunoperoxidase staining was positive in 60cases and negative in 13cases. These immunoperoxidase-negative were the cases of minimal change disease.

Review of Initial diagnosis

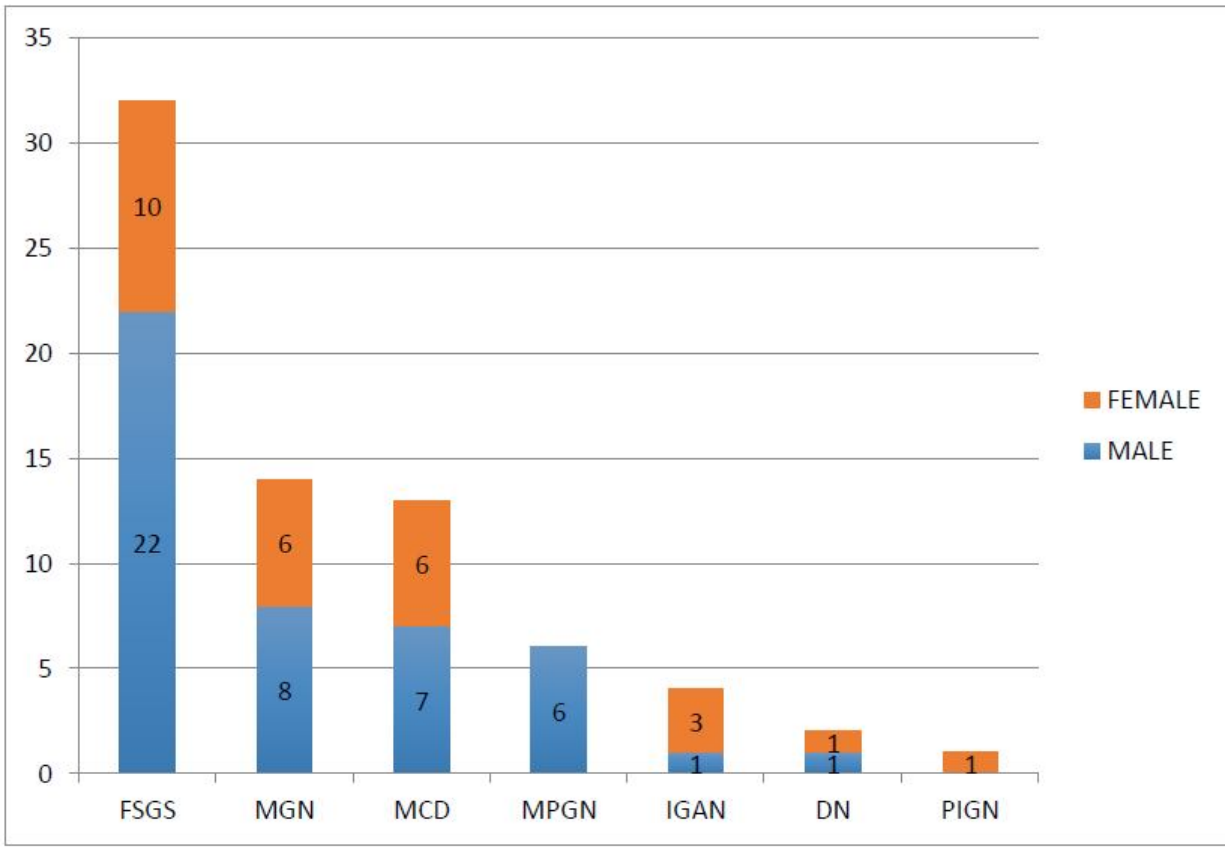
The initial diagnosis was changed in 11cases after special stains and immunoperoxidase were applied. Initially, eight (8) of these 11cases had been diagnosed as minimal change disease, 1 as FSGS, 1 as MPGN and 1 as MSPGNuse full words before abbreviationsrespectively. Six(6) of the initial minimal change disease group were subsequently re-designated as membranous glomerulonephritis and 2 as IgA nephropathy. The cases that had been diagnosed asMSPGN and MPGN were re-designated as IgA nephropathy, because of the striking IgA staining on immunoperoxidase. The initialcase of FSGS had to be changed to Membranous glomerulonephritis. Table1.

Table1. Showing the various frequencies of morphological patterns found in renal biopsies of the Nephrotic syndrome cases seen at the O.A.U.T.H.C using routine and immunoperoxidase stains.

Histological patterns	**Frequency(n/%)routine stains**	**Frequency(n/%)immuno stains**

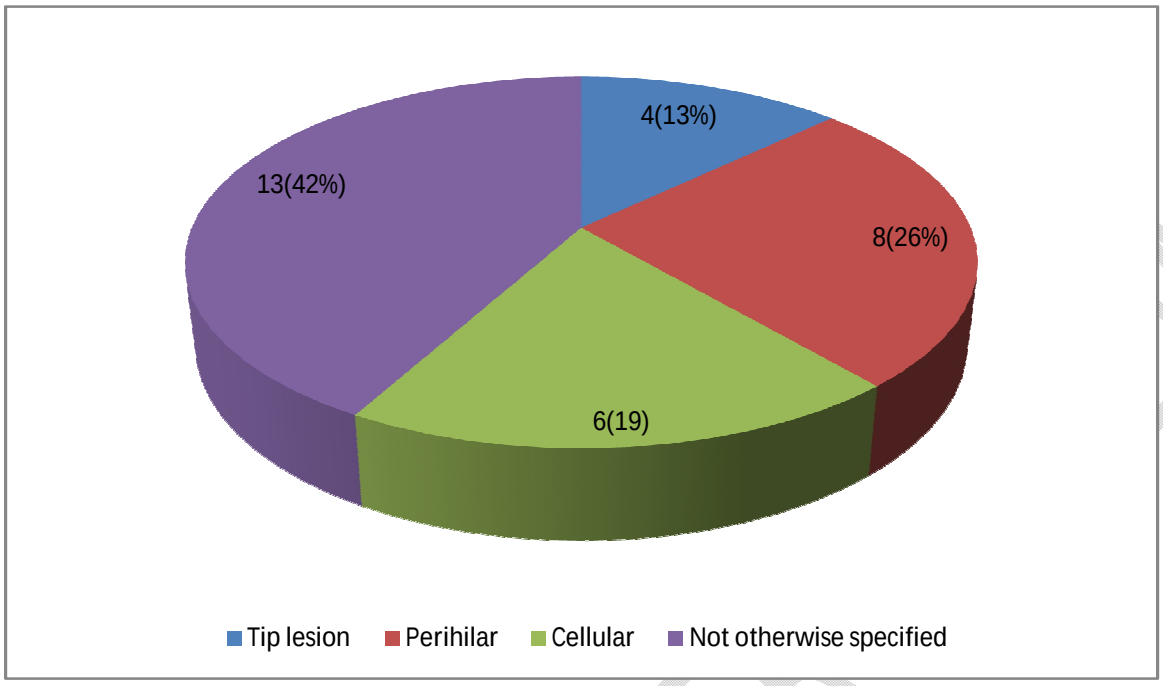
FSGS	32(43.8%)	31(42.5%)
MGN	9(12.3%)	16(21.9%)
MCD	21(28.8%)	13(17.8%)
MPGN	7(9.6%)	6(8.2%)
IGAN	0(0%)	4(5.5%)
DN	2(2.7%)	2(2.7%)
MSGN	1(1.4%)	0(0%)
PIGN	1(1.4%)	1(1.4%)
Total	73(100%)	73(100%)

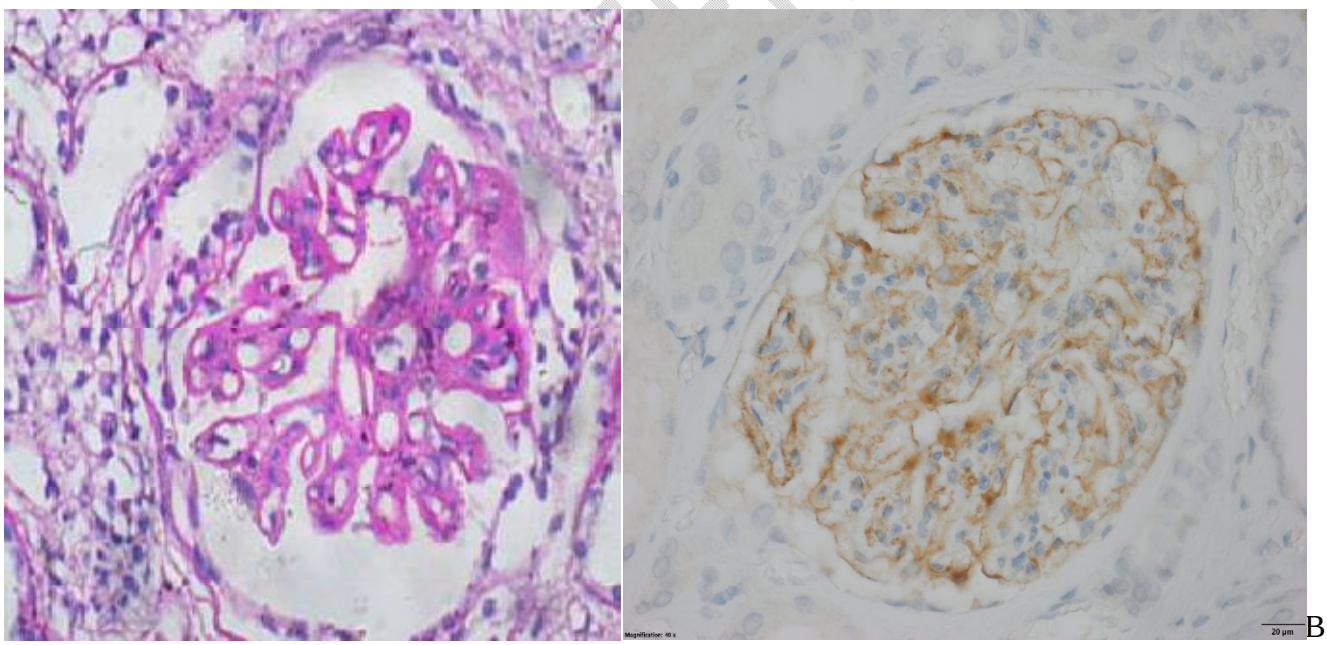
Figure 1.Genderdistribution of the various morphological patterns in nephrotic syndrome patients in O.A.U.T.H.C.



DN, Diabetic Nephropathy; MGN, Membranous glomerulopathy; FSGS, Focal segmental glomerulosclerosis; MCD, Minimal change disease; IGAN, IgA Nephropathy; MPGN, Membranoproliferative glomerulonephritis; PIGN, Postinfectious glomerulonephritis

Figure 2. Subtypes of Focal segmental glomerulosclerosis in nephrotic syndrome patients at the O.A.U.T.H.C.





A B

Figure 3 & 4 – is this one picture or 2(A) Photomicrographs of glomeruli showing thickened glomerular basement Membrane in a 23years old. (PAS stain x 400) B) Granular IgG staining along the glomerular basement membrane in membranous glomerulopathy. (IgG Immunoperoxidase stain x 100)

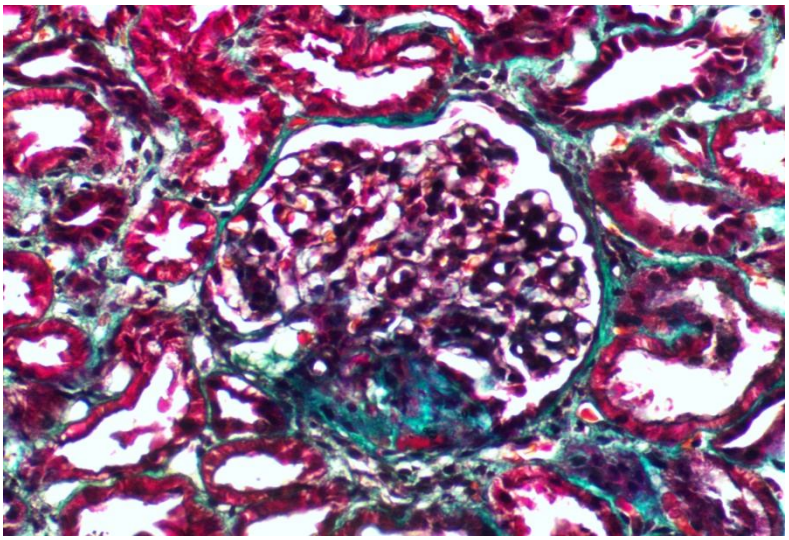


Figure5. Photomicrograph shows area of segmental (Black arrow) sclerosis in a glomerulus in a case of FSGS in a 12-year old boy. (Masson's Trichrome x 100).

DISCUSSION

Nephrotic syndrome is the most common indication for renal biopsy worldwide[5]. It is a major indication for renal biopsy in our center within the study period and accounted for 58.5% of the cases of renal diseases where biopsies were carried outreference or give related results in the results section. This is similar to studies done by Obiagu et al[6], Patricia et al[7] and Okpechi etal[8]in which nephrotic syndrome was the most common indication for renal biopsies. Our findings is however at variance with what Ibrahim et al in Egypt reported in which isolated sub-nephrotic proteinuria constituted the major indication for renal biopsy.[4] This difference may be attributable to the variation in each hospital's renal biopsy protocol. We observed that nephrotic syndrome was commoner in males than in females across all the age groups and this is in agreement with what has been previously reported [9,10,11]Umuiezudike et al[12] in a prospective study of 30 cases in a Lagos clinic however recorded equal prevalence in both genders and this may be because of theirsmaller sample size.

Most of the patients in our study were below 16 yearsin whom focal segmental glomerulosclerosis and minimal change disease constituted the major histological patterns. Focal segmental glomerulosclerosis was seen in 40.5% of 37 children in this study.Several local studies in Nigeria recorded similar findings[13,14,15]Doe et al[16] in Ghana also reported Focal segmental glomerulosclerosis and minimal change disease as the main histological patterns in their cohort of children with nephrotic syndrome, especially in those associated with steroid resistance. In contrast to our study however, they reported no case of membranous or membranoproliferative glomerulonephritis, and this may be because of their small sample size. They only analyzed 13cases.In contrast to our work however, previous work on nephrotic syndrome in adults by Oviasu et al in South-south Nigeria documented minimal change and proliferative glomerulonephritis each accounting for 33.3% as the leading causes of nephrotic syndrome.[17]Obiorah et al[18] in Port Harcourt also, in a study of nineteen childhood and adult cases of nephrotic syndrome, reported membranoproliferative glomerulonephritis as the most common basis of nephrotic syndrome. It is to be noted however, that many of these Nigerian studies examined smaller cohort than we did and that they only employed routine and special stains. That may well explain the differences in our findings.

Minimal change disease is the second most commonly associated morphological finding in children and third commonest histological pattern in adults with nephrotic syndrome in our series. This is in agreement with obtains in other studies both locally and globally. Asinobi et al[13] in Ibadan reported minimal change disease as the third commonest histological pattern associated withnephrotic syndrome in their patients.

Chijoke etal[9] in a clinicopathological study of nephrotic syndrome in adults in North–Central Nigeria reported minimal change disease as the least commonly associated histological pattern (5.3%).

This is however contrary to the finding by Rico et al[19] who in a Colombian paediatric population with nephrotic syndrome, reported minimal change disease as the most common histological pattern observed in children with nephrotic syndrome followed by FSGS and membranous glomerulopathy. The difference from our finding could be due to regional variation in renal biopsy indications. Although Bornilla-Fellix et al[20] had noted a change in the trend of morphological patterns in the renal biopsy of children with nephrotic syndrome in the American

population, they still reported minimal change disease as the most common cause of nephrotic syndrome, the essential difference being an increase in the reported incidence of FSGS particularly in the African-American paediatric population.

IgA nephropathy(IgAN) is recognized to typically present with haematuria, but could be a basis of nephrotic syndrome in the rare cases. We found four cases of IgA nephropathy on immunoperoxidase stain. These cases are characterized by endocapillary proliferation and segmental glomerulosclerosis in some of the glomeruli. Leal et al[21] in a study of 17 cases of IgAN presenting with nephrotic syndrome suggested that these are cases of IgAN with coexistent minimal change disease.

I suggest to discuss importance of immunoperoxidase staining in final diagnosis and also comment on electrone microscopy which was lacking in this case.

CONCLUSION

This study, while underscoring the need for improving the infrastructural repertoire for the tissue diagnosis of the nephrotic syndrome and other renal diseases in resource-limited settings such as ours, provides important preliminary data to guide local nephrologists and provide the basis for further studies on the aetiopathogenesis of the disease in Tropical Africa.

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