SPECTRUM OF NEPHROPATHIES WITH SPECIAL REFERENCE TO PRIMARY GLOMERULOPATHIES

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ABSTRACT

A retrospective study was carried out where histopathology records of Department of Pathology, Armed Forces Medical College, Pune were scrutinised covering a period of 10 years. We came across 325 cases of nephropathies. The sample comprised of 92.6% adults and 7.4% children. 79.7% were males and 20.3% were females. The patient population comprised of 35.1% serving soldiers, 37.8% their family members and 27.1% not related to Armed Forces. The study is based on only light microscopy findings. It was observed that primary glomerular disease was the commonest entity and comprised of 61.5% of all the nephropathies. Acute diffuse proliferative glomerulonephritis was not only the commonest primary glomerulopathy (23.5%) but the commonest nephropathy as well. The other primary glomerulopathies in descending order of frequency were, membranoproliferative glomerulonephritis (22.5%), mesangioproliferative glomerulonephritis (21.5%), chronic glomerulonephritis (9%), minimal change disease (7.5%), membranous glomerulopathy (7%), focal segmental glomerulosclerosis (5%) and crescentic glomerulonephritis (4%). We had only 14 cases (4.3% of all nephropathies) of secondary glomerulopathies, amongst which amyloidosis was the commonest cause. We came across 2 cases (0.6% of all nephropathies) of Alport's syndrome. In the other nephropathies, 22.2% were tubulointerstitial diseases and 5.5% were malignant kidney tumors. In 5.8% renal biopsies, no significant pathology was seen on light microscopy.

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KEY WORDS: Diffuse proliferative glomerulonephritis; Glomerulonephritis; Nephropathy.

Introduction

The evolution of the understanding of medical diseases of the kidney, which dwells predominantly upon glomerulopathies, is one of the most fascinating stories in the history of medicine. It has also been seen since many years that nephropathies as such, contribute significantly to morbidity and mortality in the world as well as in our country. However while discussing the nephropathies, we usually have limited data about the incidence of these disorders in Indian setup. Few centers have published this data in our country [1-4]. But it is felt that more studies are required to be published to get a wider database.

The percutaneous kidney biopsy is considered as the most important investigation to clinch the final diagnosis. The kidney biopsy is gold standard not only for the primary diagnosis but it also gives a fairly accurate idea about the severity of the disease in properly analysed kidney biopsy. The objective assessment of the patients can also be carried out for selection for renal transplantation. If the treating Nephrologist has a fairly accurate idea about the overall incidence of various renal disorders in the population he is treating, he is in a better position to manage the patients.

In view of the above, we carried out a retrospective study in which the histopathology record of 10 years

was scrutinized, to find the nephropathies which were diagnosed during the period. The data was analysed for incidence of various nephropathies. As the primary glomerulopathies were the commonest lesions, a special emphasis was laid on these entities. Although kidney biopsy is not always resorted to for clinching the correct diagnosis in all the cases, analysing the histopathology data was considered the best available method to arrive at reasonably correct conclusions about the incidence of various renal diseases.

Material and Methods

Kidney tissues, either routine percutaneous needle biopsies or the nephrectomy specimens, received in Dept of Pathology of Armed Forces Medical College, Pune for a period of 10 years i.e. from Jan 1989 to Dec 1998 formed the data base of this study. The histopathology records maintained in the department were scrutinised. The details of these cases in form of name, age, sex, individual status either as a serving soldier or their relatives or otherwise; as well as the clinical diagnosis and the histopathological diagnosis offered were noted down. All the interesting kidney biopsies and the cases, in which discordance with clinical profile/clinical diagnosis was observed, were reviewed for confirmation or change of histopathology diagnosis if any. All the cases in which no diagnosis could be offered due to opinion of 'Kidney Tissue Inadequate' or 'No Specific Pathology' were also reviewed.

In our institute, we examine 3 to 4 μ thick paraffin embedded multiple sections of each biopsy, stained with Hematoxyline and Eosin (H & E), Periodic Acid-Schiff (PAS) and combination of PAS and Silver Methenamine (PASM). PAS stain accentuates basement membranes, mesangial matrix and brush borders of

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proximal epithelial cells. PASM permits easy interpretation of lesions of basement membrane. Any other special stain so indicated is also carried out e.g. Maritius Scarlet Blue (MSB) for fibrin; Congo Red stain with polarized light examination for amyloid etc. Immunofluorescence (IF) and electron microscopic (EM) studies are not done routinely.

Results

While examining the histopathology records, we came across 355 kidney tissue reports (303 percutaneous kidney biopsies and 52 nephrectomy specimens) in the study period of 10 years. 30 biopsies, which were considered inadequate due to either paucity (less than five) or absence of glomeruli/or absence of kidney tissue were excluded from the study. Thus 325 cases of kidney tissues formed the basis of study.

Age, sex and individual status:

It was observed that out of these 325 cases, 24 (7.4%) were paediatric patients (less than 12 years) and 301 (92.6%) of adult age group. The youngest patient was of one and a half years, while the oldest individual was 73 years old. It was a male predominant study, as 259 were males (79.7%) and 66 (20.3%) were females. Out of these total 325 cases, 114 (35.1%) were serving soldiers, whereas 211 (64.9%) were either parents or children of the serving soldiers (123 patients-37.8%) or not related to Armed Forces (88 patients-27.1%). Patients in this last group were not only from Maharashtra but also from various states, as even these patients were either civilian defence employees, their relatives or the migrant population from various states of India, who are usually seen accompanying the military personnel.

Incidence of nephropathies:-

It can be observed from Table-1 that out of all the nephropathies, the majority of them were the glomerular diseases. In glomerular diseases primary glomerulopathies were the commonest lesions and were nearly 14 times more common (61.5% against 4.4%) than secondary glomerulopathies, which are seen in the various systemic diseases like diabetes, SLE or amyloidosis. On analysis of the various glomerulopathies it was observed that, acute diffuse proliferative glomerulonephritis (DPGN) which is post infectious in origin, was still the commonest lesion in our setup.

Out of 47 cases, seven (14.9%) were below 12 years of age. In the other primary glomerulopathies, membranoproliferative glomerulonephritis (MPGN) was the second common lesion and mesangioproliferative glomerulonephritis (MesGN) was the third common lesion. In MPGN, five (11.1%) and in MesGN, four (9.3%) were children. Chronic glomerulonephritis (CGN) was the next common glomerulonephritis we came across in our study, however in these 18 cases, not a single paediatric patient was seen. The other glomerulonephritis in descending order of frequency were minimal change disease (MCD), membranous glomerulopathy (MGN), crescentic glomerulonephritis (Crescentic GN) and lastly focal segmental glomerulosclerosis (FSGS). We had two children in MCD group (13.3%) out of total 15 cases, but not a single child was seen in either MGN or FSGS cases. We had two cases of Alport's syndrome in our series, which were confirmed on electron microscopy [5]. Both these patients were adults.

In tubulointerstitial diseases, the interstitial nephritis (IN) was the commonest lesion. Pyelonephritis (PN) and hydronephrosis (HN) were the next common lesions and both these lesions were diagnosed on nephrectomy specimens. Only one patient each in paediatric age group was seen in IN (5.9%) and HN (9.1%) cases. In 18 cases of malignant renal tumors, three (16.7%) were chil-

TABLE 1
Spectrum of nephropathies

Nephropathy	Number of cases	Percentage
A. Glomerular diseases	216	66.5
<i>Primary</i>	<i>200</i>	<i>61.5</i>
DPGN	47	14.5
MesGN	43	13.2
Crescentic GN	08	2.5
MCD	15	4.6
MPGN	45	13.9
MGN	14	4.3
FSGS	10	3.0
CGN	18	5.5
<i>Systemic diseases</i>	<i>14</i>	<i>4.4</i>
Diabetes	03	0.9
SLE	07	2.3
Amyloidosis	04	1.2
<i>Hereditary disorders</i>		
Alport's syndrome	02	0.6
B. Tubuloint diseases	72	22.2
Pyelonephritis	11	3.4
Int nephritis	17	5.2
Hydronephrosis	11	3.4
Nephrolithiasis	05	1.6
Gr nephritis	04	1.2
Other diseases	24	7.4
C. Tumours of kidney	18	5.5
D. Normal on biopsy	19	5.8
Total	325	100.00

Abbreviations : DPGN - Acute diffuse proliferative glomerulonephritis; MesGN - Mesangioproliferative glomerulonephritis; MCD - Minimal change disease, MGN - Membranous glomerulonephritis; MPGN - Membranoproliferative glomerulonephritis; FSGS - Focal segmental glomerulosclerosis; Int Nephritis - Interstitial nephritis, Gr Nephritis - Granulomatous nephritis; Tubuloint. Diseases - Tubulointerstitial diseases; CGN - Chronic glomerulonephritis

dren. Two children had Wilm's tumor and one had renal cell carcinoma (RCC). In adult group 15 were RCC's and one was malignant neuroendocrine tumour.

In our study, 19 cases did not reveal any abnormality on light microscopy. IF or EM could have clinched the diagnosis in these cases but it was not resorted to.

Discussion

Differences were seen in incidence of various nephropathies in our study as compared to the available published data from Western countries as well as from India. We carried out literature review with the help of 'Medline', the compact discs of 'US National Library of Medicine', USA for a period of ten years. In our study, we had observed DPGN as the commonest nephropathy (14.5% as an individual entity of all the nephropathies) as well as the commonest primary glomerulopathy (23.5% of all the primary glomerulopathies) (Table-2). When incidence of DPGN was

TABLE 2

Incidence of primary glomerulopathies in India

	DPGN	MPGN	MesGN	IgA	MCD	CrescenticGN	MGN	FSGS	CGN	Total
Present study	47 (23.5)	45 (22.5)	43 (21.5)	- -	15 (7.5)	08 (4.0)	14 (7.0)	10 (5.0)	18 (9.0)	200 (100)
Jaslok Mumbai	298 (13.3)	314 (14.1)	552 (24.7)	95 (4.3)	479 (21.5)	86 (3.8)	183 (8.2)	86 (3.8)	140 (6.3)	2233 (100)
PGI Chandigarh	(19.0)	(18.0)	(3.0)	(4.0)	(23)	(5.0)	(10.0)	(11.5)	(7.0)	(100)

Note - Figures in the brackets and in bold indicate percentage and top line figures indicate actual number of cases. PGI Chandigarh has not given the actual number of cases. Abbreviations are as for Table 1.

compared with various countries it was observed that, in Netherlands, all European countries, Japan and in Australia, there was a declining rate of incidence of acute post-infectious glomerulonephritis since 1975 [6]. In a French study, virtual disappearance of acute post-streptococcal glomerulonephritis was seen after 1980 [7]. A Russian report stated that, they have not observed a single case of DPGN in recent years [8]. It is well known that socioeconomic conditions have a great bearing on the incidence of infectious diseases. DPGN is known to be post-infectious in nature and in majority of cases it is seen following streptococcal infection. In fact in Armenia, tenfold rise was seen in DPGN in children, following sudden deterioration in socioeconomic conditions [9]. Although some decline has been reported in a South Indian hospital [4], two other Indian studies i.e. from Jaslok hospital, Mumbai (Jaslok series) [1] and from Postgraduate Institute of Medical Education and Research, Chandigarh (PGI series) [2], have shown incidence of DPGN to be 13.3% and 19% respectively (Table-2). Jaslok being a corporate sector hospital, the clientele usually is from higher socioeconomic strata that may probably explain lower percentage of DPGN seen by them. Out of all the cases of DPGN in these studies, majority of them were adults.

MPGN was the second common type of glomerulopathy in our study (Table-2). The incidence seen by us is closer to the incidence seen by PGI, but the Jaslok series had the lowest incidence of 14.1%. A decreasing percentage in MPGN cases was seen in South Indian patients [4]. Moscow Medical Academy [10], France [7] and Brazil [11] have also noted a decreasing incidence of MPGN. If one analyses the etiology of MPGN it will be seen that, here also infection by few bacteria and viruses definitely plays some role [12]. We have not yet reduced the incidence of infectious diseases in our country, which may probably explain the higher percentage of the MPGN cases seen by us as compared to developed countries.

MesGN was our third common primary glomerulopathy and incidence was 13.2%, where as in Jaslok series, the percentage noted was 24.7%, which in fact was their commonest primary glomerulopathy. It is well known that MesGN type of picture can be seen in various conditions like resolving DPGN, IgA nephropathy, SLE, IgM nephropathy or it may be idiopathic in origin [13]. We did not carry out IF for IgA or IgM, hence few of our cases of MesGN may be belonging to these categories. Very high percentage of MesGN was seen in American Indians (83%) [14] and in Bulgaria it was 43% [15]. Kinacid Smith reported incidence of 68% [16] and in Russian study it was found to be the commonest primary glomerulopathy (68%) [8]. In PGI series, incidence of MesGN was found to be just 3%. Wide range of etiology of MesGN may probably explain the variation in its incidence. It may be noted that few authors do not consider it as a morphological entity and do not include it in the classification of glomerulonephritis [17].

MCD incidence of Jaslok and PGI shows much higher percentage as compared to us (Table-2). We had 19 cases, which were reported as 'No Specific Pathology' on light microscopy. As EM studies were not carried out in these cases, we might have missed few MCD cases. Secondly, especially in children, when the nephrologist suspects MCD as the cause of nephrotic syndrome in our setup, a clinical trial of steroids is given initially. The renal biopsy is resorted to, when the child does not respond to a steroid therapy. As, many children of MCD respond very well to steroids, they do not come under the purview of the pathologists. This fact appears to have given a fallacious lower incidence of MCD in children as well as overall low incidence in our study. Even in Jaslok series 60% were found to be adults. However it has been seen in Western countries, that MCD is predominantly a disease of children [18].

The incidence of crescentic GN was similar in our study as compared to both the Indian series. It was

found to be 10% in Sweden [19]. In one study it has demonstrated that, the prognosis of crescentic GN is very poor in children as compared to adults [20]. Crescentic GN represents a heterogeneous group of disorders and has been divided into three types on basis of IF findings. These include anti-GBM linear deposit disease, immune-complex disease and pauci-immune disease. Current literature seems to suggest that the incidence of pauci-immune crescentic GN is increasing [1].

As far as incidence of MGN is concerned, it was found to be almost same in our study as compared to Jaslok and PGI (Table-2). MGN is a disease of adults and we did not have a single child in our 14 cases. Jaslok series had only eight children (4.4%) in their 183 cases. The incidence was found to be 16% in Brazil [11], but in a Russian study, it was just 1.8% [8]. Majority of MGN cases are idiopathic in origin but secondary MGN can occur following drugs like penicillamine and infections like hepatitis, malaria and syphilis. It is also being seen following carcinoma of lung, stomach or breast [21].

We could not diagnose a single case of IgA nephropathy, due to lack of IF facility. It was found to be around four percent in the Jaslok and PGI series. Cruz et al also noted low incidence (8.6%) of IgA nephropathy in Brazil [11], but it was found to be the most common primary glomerular disease in a study carried out in a French region which observed the prevalence of 19% [7]. IgA nephropathy was found to be the commonest primary glomerulopathy along with MCD in Malaysia [22]. It has also been reported that, in South East Asia, Japan, Australia and amongst American Indians, much higher percentage of IgA is seen, as compared to the rest of the world [23].

FSGS was found to be highest in PGI series as compared to us and Jaslok series (Table-2). However incidence was found to be 37.1% of all primary glomerulopathies in Brazil [11]. FSGS was found to be a common cause of nephrotic syndrome in steroid nonresponsive children, in drug addicts and HIV associated nephropathy, as well as in black African population [24].

The incidence of CGN as observed by us was almost similar to two other Indian studies (Table-2). Hardly any study from Western literature quoted so far in this article, have given the exact incidence of the chronic GN in their studies. Khedar et al observed 42% prevalence of hypertension in their 359 patients of primary chronic GN [25]. It is also known that few cases of CGN arise de novo [26].

We had 14 cases of secondary glomerulopathies. It can be seen from Table-3 that lupus nephritis and amyloidosis are more common than diabetic nephropathy in our country. We did not come across a single case of other secondary glomerulopathies like polyarteritis, other vasculitis or hemolytic uraemic syndrome as seen in other Indian studies (included in miscellaneous conditions in Table-3). SLE is particularly more common in China, Malaysia and Singapore, less common in white population as such and least in the black Africans [3]. On the other hand amyloidosis is very important cause of secondary GN in India and that too secondary amyloidosis, in contrast to USA where primary amyloidosis is more common. Amyloidosis surprisingly is rarely encountered in Africa and West Indies [3].

TABLE 3
Incidence of secondary glomerulopathies in India

	Amyloidosis	Lupus nephritis	Diabetic nopathy	Misc	Total
Present study	04 (28.6)	07 (50.0)	03 (21.4)	Nil Nil	14 (100)
Jaslok	142	137	55	17	351
Mumbai	(40.5)	(39.0)	(15.7)	(4.8)	(100)
PGI	208	117	107	102	534
Chandigarh	(39.0)	(21.9)	(20.0)	(19.1)	(100)

Note - Figures in the brackets indicate percentages and top line figures indicate actual number of cases.

Abbreviations - Nopathy - Nephropathy; Misc - Miscellaneous

As far as other nephropathies are concerned, we did not carry out further analysis, as their number in study was very small for any meaningful comparison.

Thus it is apparent that the incidence of various nephropathies varies considerably from country to country. Apart from socioeconomic background, there are racial and ethnic differences. As far as India is concerned, it was seen that in various nephropathies, diseases of glomeruli are the most common nephropathies. DPGN is still the commonest primary glomerulopathy in our country and the commonest renal disease we encounter in the renal pathology. MPGN and MesGN are equally common glomerulopathies we come across. MCD is not only disease of children but is quite common in adults as well. The MGN, FSGS and the CGN are the glomerulopathies, which show incidence of around 7 to 10% in our country. IgA nephropathy and crescentic GN are less than 5%. The secondary glomerulopathies are the less common entities than the primary glomerulopathies but in them amyloidosis is the commonest glomerulopathy.

REFERENCES

1. Chitale A, Khubchandani S. Interpretation of renal biopsies. 1st ed, Mumbai, Jaslok Hospital and Research Centre Publication 1997.
2. Chug KS. Renal disease in India. *Am J Kid Dis* 1998;31:vii-ix.
3. Chug KS. Glomerular diseases in Tropics. *JAPI* 1992;40:215-22.
4. Date A, Jayaseelan L, Brahmadathan KN. Changing pattern of primary glomerulonephritides in a South Indian hospital. *Trans R Soc Trop Med Hyg* 1989;83:419-20.
5. Mani NS, Rai R. Alport's Nephritis (A case report of two cases). *Medical Journal Armed Forces India* 1999;55:61-2.
6. Hoogendoorn D. Acute rheumatism and glomerulonephritis: Current clinical incidence and mortality in the Netherlands. *Ned Tijdschr Geneeskde (Netherlands)* 1989;133:2334-8.
7. Simon P, Ramee MP, Autuly V, Laurelle E, Charasse C, Cam G, Ang KS. Epidemiology of primary glomerular disease in French region. *Kidney Int* 1994;46:192-8.
8. Shulutko BI. The correlation of different forms of primary glomerulonephritis today and their diagnostic criteria. *Ter Arkh (Russia)* 1992;64:40-3.
9. Sarkissian A, Papazian M, Azatian G, Arikians N, Babyloyan A, Leumann E. An epidemic of acute postinfectious glomerulonephritis in Armenia. *Arch Dis Child (England)* 1997;77:342-4.
10. Launavichus A, Vashavskii A. Primary glomerulonephritis: Incidence, dynamics clinical manifestations of morphological types. *Arkh Patol* 1992;54:25-9.
11. Cruz HM, Penna D de O, Saldhana LB, Cruz J, Liuz P, Marcondes M. Histopathology study of primary glomerulonephritis: Retrospective analysis of 197 renal biopsies (1985-1987). *Rev Hosp Clin Fac Sao Paulo, Brazil* 1989;44:94-9.
12. Holley KE, Donadio JV. Membranoproliferative glomerulonephritis. In: Tisher CC, Brenner BM, eds. *Renal Pathology: With clinical and functional correlations*. 2nd ed, Philadelphia, JB Lippincott Company 1994 : 294-329.
13. Chitale A, Khubchandani S. Interpretation of kidney biopsies. 1st ed, Mumbai, Jaslok Hospital and Research Center publication 1997: 58.
14. Hay DE, Hughson MD, Smith SM, Megill DM. Mesangial proliferative glomerulonephritis in Southwestern American Indians 1993;21:486-90.
15. Tiskov I, Nedialkov A, Poichinov D, Minkova V. Clinical laboratory and morphological characteristics of mesangioproliferative glomerulonephritis (Bulgarian) *Vultreshni Bolesi* 1987;26 : 91-5.
16. Kinacid SP, Whitworth JA. *The Kidney: A clinicopathologic study*. 2nd ed, Oxford: Blackwell Scientific Publications 1987:27.
17. Pankewycz OG, Sturgill BC, Bolton WK. Proliferative glomerulonephritis: Postinfectious, noninfectious and crescentic forms. In: Tischer CC, Brenner BM, eds. *Renal Pathology: With clinical and functional correlations*. 2nd ed, Philadelphia, JB Lippincott Company. 1994:222-57.
18. Heptinstall RH. *Pathology of kidney*. 4th ed, Boston, Little Brown and Company 1992:804.
19. Peterson EE, Sundelin B, Heigl Z. Incidence and outcome of pauci-immune necrotizing and crescentic glomerulonephritis in adults. *Clin Nephrol* 1995;43:141-9.
20. Srivastava RN, Moudgil A, Bagga A, Vasudev AS, Bhuyan YN, Sundaram KR. Crescentic glomerulonephritis in children: A review of 43 cases. *Am J Nephrol* 1992;12:155-61.
21. Chitale A, Khubchandani S. Interpretation of kidney biopsies. 1st ed, Mumbai, Jaslok Hospital and Research Center Publications 1998:117.
22. Zainal D, Riduan A, Ismail AM, Norhayati O. Glomerulonephritis in Kelantan, Malaysia. *Southeast J Trop Med Public Health* 1995;26:149-53.
23. Chitale A, Khubchandani S. Interpretation of Kidney biopsies. 1st ed, Mumbai, Jaslok Hospital and Research Center Publications 1997;103.
24. Nadasdy T, Silva FG, Hogg RJ. Minimal change nephrotic syndrome-Focal sclerosis complex (including IgM nephropathy and Diffuse mesangial hypercellularity). In: Tischer CC, Brenner BM, eds. *Renal Pathology: With clinical and functional correlations*. 2nd ed, Philadelphia, JB Lippincott Company 1994:330-89.
25. Khedar MA, Maiz BH, Abderrahim E, Younsi F, Moussa BN, Safar ME, Ayed BH. Hypertension in primary chronic glomerulonephritis analysis of 359 cases. *Nephron* 1993;63:1404.
26. Cotran RS, Kumar V, Robbins S. *Pathologic basis of Disease*. 5th ed, Philadelphia, WB Saunders 1995:927-87.