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Local Experiences

Lessons from a Limited Paediatric Renal Registry 1998-2000

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Abstract Since 1998, a limited paediatric renal registry was established by the joint effort of paediatric nephrologists working in 13 public hospitals in Hong Kong. The purpose was to monitor the occurrence of nephrotic syndrome, lupus nephritis, hereditary renal tubular disorders, chronic renal failure, cystic kidney diseases and renal biopsy in children under 15 years of age. The collected data from 1998 to 2000 were analysed and reported. Within the study period, there were about 7 new patients with chronic renal failure each year, and 4-5 patients from the pool of chronic renal failure patients needed to start dialysis treatment or transplantation. There were about 57 new nephrotic patients, 10 lupus nephritis patients per year and 66 patients needed renal biopsies for evaluation. The average incidence of chronic renal failure, endstage renal disease, and nephrotic syndrome were estimated to be respectively 6.2 and 3.8, and 50.5 per million childhood population below 15 years old. The indications and histopathologic findings of renal biopsies by local paediatric nephrologists were reported and were in accordance with overseas practice. This is our first cooperative effort to prospectively obtain epidemiological data on paediatric renal diseases, and it could form a basis to guide us in future planning of service development and academic research.

Key words Chinese; Chronic renal failure; Epidemiology; Glomerulonephritis; Nephrotic syndrome

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Introduction

Accurate epidemiological data are useful to enable health care workers to have a better understanding of a disease and to monitor changing trends of disease characteristics. Knowledge of the disease burden also allows better estimation of workload and resource requirements. Since 1998, the Hong Kong Paediatric Nephrology Society has started to keep a registry of selected renal diseases in children. With the establishment of the Paediatric Surveillance Program by the Hospital Authority in the year 2000, this has become a part of the Surveillance Program. The objective of the registry is to monitor the pattern of occurrence of selected renal diseases in children so as to alert paediatricians of changing trends, to provide incidence data for planning of service provisions or academic research.

Methodology

Six categories of patients were chosen: nephrotic syndrome, lupus nephritis, hereditary renal tubular disorders, chronic renal failure, cystic kidney diseases, and renal biopsies in children under 15 years of age.

Nephrotic syndrome was diagnosed by the presence of generalised oedema, massive proteinuria (with urine protein excretion rate of more than 40 mg/m^2 BSA/hour) plus hypoalbuminemia (with serum albumin concentration of less than 25 g/L) with or without hypercholesterolemia. Systemic lupus erythematosus (SLE) was diagnosed if the clinical features fulfill 4 or more out of 11 criteria of the American College of Rheumatology, and lupus nephritis was diagnosed if there is any urinary abnormalities in a patient with SLE. Chronic renal failure was recognised by a creatinine clearance of less than 25 mL/min/1.73 m^2 as measured by endogenous creatinine clearance or as calculated from body height and serum creatinine concentration according to Schwartz formula (GFR in ml/min/1.73 m^2 = body height in cm X k/Serum Creatinine, where k is 39.8 if patient is younger than 2 years old, 48.6 if patient is between 2 and 12 years old or female of 13 to 21 years old, and 61.9 if patient is male of 13 to 21 years old).

A coordinator was appointed in each paediatric unit of the participating hospitals. The number of participating hospitals were 11 in the year 1998, missing North District Hospital (NDH) and Our Lady of Maryknoll Hospital (OLMH). It was 11 in year 1999 (missing NDH and OLMH) and 13 in year 2000.

Data was collected after the end of each calendar year. For simplicity, only the diagnosis, patient identifier (to prevent duplication of entry), date of presentation, and in the case of renal biopsy, the date of biopsy, their indications and results, were requested for each patient in the above disease categories. No other clinical details were included. The datasheets were compiled to produce descriptive statistics and trends for each disease group.

Results

A summary of the caseloads of each disease group was shown in Table 1.

There are on average 57 new cases of nephrotic syndrome each year (range 43-69). The majority was primary nephrotic syndrome. For the year 2000, secondary nephrotic syndrome accounted for only 8 out of 58 cases (14%), with SLE and HSP being the common causes. Only 2 cases of congenital nephrotic syndrome were reported for the 3-year period.

Lupus nephritis was defined as any child with SLE and any urinary abnormalities. Cases without urine involvement were not included. On average there were 10 cases per year (range 8-13).

A total of 21 children with chronic renal failure, defined as creatinine clearance below 25 ml/min/1.73 m^2 (or GFR as estimated by Schwartz formula) was reported (average incidence 7 per year, range 5-9). Details of endstage renal disease patients were also available from the Central Renal Registry of the Hong Kong Hospital Authority. From 1998 to 2000, the numbers of endstage renal failure patients aged 1 to 15 years were 7, 3, and 3 per year respectively.

The renal cystic disease category involves a heterogeneous group of patients with multicystic dysplastic kidney (4 in 1998, 6 in 1999, and 9 in 2000), autosomal dominant polycystic kidney diseases (3 in 1999 and 2 in 2000), autosomal recessive polycystic kidney diseases (1 in 1999), medullary cystic kidneys (1 in 1998 and 2000), glomerulocystic kidney (1 in 1998), and dysplastic kidney with cysts (1 in 2000). The increasing trend of MCDKD was probably due to increasing use of antenatal ultrasound screening. In general these renal cystic diseases were rare. The hereditary tubular disorders were even rarer with only 6 patients reported in 3 years (2 patients with cystinuria, 1 each with renal tubular acidosis, Bartter's syndrome, Gitelman syndrome, and familial hypercalcemic hypercalciuria).

Table 1 Summary of statistics for limited renal registry 1998-2000

	1998	**1999**	**2000**	**Total**
Nephrotic syndrome	43	69	58	**170**
Lupus nephritis	13	8	9	**30**
Cystic kidney disease	6	10	19	**35**
Hereditary tubulopathy	1	3	2	**6**
Chronic renal failure	5	7	9	**21**
Renal biopsy	71	68	59	**198**
Indications for biopsies				
Evaluation of nephrotic syndrome	22	19	13	**54**
Urinary abnormalities	13	21	19	**53**
Renal impairment/renal failure	6	7	9	**22**
Lupus nephritis	24	8	10	**42**
Henoch-Schönlein nephritis	3	7	7	**17**
Allograft biopsies	3	3	1	**7**

There were a total of 198 renal biopsies in the study period but it showed a decreasing trend from 71 in 1998 to 59 in 2000. Table 2 shows the main indications for renal biopsies and the findings with respect to each indication.

Fifty-four biopsies were performed to evaluate nephrotic syndrome, but not all were new cases presenting within the study period. Histological findings that were significant in guiding treatment were obtained when biopsies were done on account of young age (1 being FSGS), steroid resistance (4 being FSGS, 2 C1q nephropathy), and HBV association (2 being membranous nephropathy). The 26 cases who were biopsied for steroid dependence or frequent relapses yielded mainly MCD (22 cases) and other pathologies (diffuse mesangial proliferation in 1, IgM nephropathy in 2, C1q nephropathy in 1) for which treatment strategy would be the same as MCD.

Fifty-three patients underwent renal biopsy for abnormal urinalysis. Patients who were biopsied for persistent microscopic haematuria alone were mainly found to have Thin Membrane Disease (11), IgA nephropathy (3). However, no definite diagnosis could be made in 4 of the 20 patients biopsied for this indication. Those biopsied for recurrent gross haematuria, or proteinuria with or without haematuria were found to have a variety of lesions some of which may be significant in terms of treatment or prognosis. Twenty-two patients were biopsied for renal failure, among which 15 were due to glomerulonephritis and 5 due to other parenchymal lesions.

Discussion

Disease surveillance have been found to be useful in advancing our knowledge, and various systems of surveillance programs have been set up in the United Kingdom (since 1986), Germany (since 1992), Australia (since 1993), Canada (since 1996), and other countries.[1] In these programs, rare diseases were chosen for monitoring. The present limited renal registry was different in that we monitored not only rare diseases such as tubulopathies, polycystic kidney diseases, and renal failure, but also common conditions such as nephrotic syndrome, lupus nephritis, and common procedures such as renal biopsy.

We can use these data to plan our subspecialty development, to further our knowledge of the incidence of the selected diseases, and to use them as a baseline to plan research projects.

From the limited statistical data, within the study period, there were about 7 new patients with chronic renal failure each year, and 4-5 patients from the pool of chronic renal failure patients needed to start dialysis treatment or transplantation in each year. There were about 57 new nephrotic patients, 10 lupus nephritis patients per year and 66 patients needed renal biopsies for evaluation. These figures were compared to previous surveys to confirm the accuracy and any changing trends.

A study on childhood renal failure in Hong Kong in 1993 showed that the incidence of endstage renal failure was 4.0 per million childhood population (mcp) and the prevalence in 1992 of chronic renal failure and endstage renal failure were 25.4 and 13.1 per mcp respectively.[2] Data from the Census and Statistics Department showed that the mid-year population below 15 years old in the year 2000 was 1,128,100 (data extracted from website *www.info.gov.hk/censtatd/eng/hkstat/*). The current survey thus showed an annual incidence of chronic renal failure of 6.2 per mcp, and that of endstage renal failure of 3.8 per mcp. The former figure was not available in the 1993 survey and the latter figure was in close agreement to the 1993 survey result. Similar renal registries overseas showed that the incidence rates of ESRF in children aged 0-19 years in European countries in the year 2000 ranged from 4.9 to 12.1 per million adjusted population,[3] while the ESRF incidence rates for the United States in the period of 1996 to 1998 were 9.6 (for 0-4 years), 6.9 (for 5-9 years), 14.3 (for 10-14 years), and 28.2 (for 15-19 years) per million childhood population.[4]

Comparing the average reported number of new cases of nephrotic syndrome with the mid-year population in 2000, we estimated that incidence of total nephrotic syndrome was 5.05 per 100,000 childhood population. This was higher than a previous study of childhood idiopathic nephrotic syndrome among public hospitals in Hong Kong from 1991 to 1993. The latter reported a total of 97 children within that 3-year period.[5] This may be because we have included also secondary nephrotic syndrome though this group only accounted for 14% of the total number. Other explanations could be that more patients used the public hospital services (hence included in the survey), or there might be a genuine increase in the incidence. Schlesinger et al in 1968 estimated that the incidence of nephrotic syndrome in children below 16 years old was 2-7 per 100,000 total population in the United States.[6] A more recent population-based cohort study in Yorkshire, United Kingdom reported that the incidence of nephrotic syndrome was 2.3 per 100,000 age-adjusted person years in children 0-15 years of age.[7]

From the available data on the service load, we can better plan the number of tertiary and secondary renal services.

Table 2 Indications and findings of renal biopsies, 1998-2000

	Total cases	**MCD**	**MesPGN**	**FSGS**	**IgMN**	**C1qN**	**Memb. GN**	**DPGN APSGN Postinf GN**	**Other GNs**	**TBMD**	**IgAN**	**Others (RN, CIN, FJN, ATN, Toxic, ATN)**	**No Dx.**
Nephrotic Syndrome	**54**												
Atypical age	8	4		1	3								
Steroid resistant	15	6		4	1	2		1					1
Frequent relapser/ steroid dependence	26	22	1		2	1							
Hepatitis B Virus related	3						2			1			
Nephritic/ nephrotic	2							2					
Abnormal Urinalysis	**53**												
Isolated proteinuria	7			2			1				1	DM 1	2
Proteinuria & haematuria	10		1				2	3		1	1		2
Recurrent gross haematuria	16	1	1	1				1		4	7		1
Persistant microscopic haematuria	20	1	1							11	3		4
Deranged renal function	**22**												
Renal insufficiency/ Chronic renal failure	15			3		1		1	Endstage GN 1; Pauci-immune CGN 1		3	RN 1, CIN 1, FJN 1	2
Acute renal failure	7			1				3	MPGN 1			Toxic 1 ATN 1	
Transplant biopsies	**7**												
Lupus nephritis	**42**												
HSP nephritis	**17**												
Total	**195**	**34**	**4**	**12**	**6**	**4**	**5**	**11**	**3**	**17**	**15**	**6**	**12**

* 3 biopsies performed for monitoring during CSA Px (not included above)

MCD: minimal change disease; MesPGN: mesangial proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; Memb.GN: membranous glomerulonephritis; DPGN: diffuse proliferative glomerulonephritis; ASPGN: acute post-streptococcal GN; TBMD: thin glomerular basement membrane disease; IgAN: IgA nephropathy; C1qN: C1q nephropathy; MPGN: membranoproliferative GN; RN: reflux nephropathy; CIN: chronic interstitial nephritis; FJN: familial juvenile nephronophthisis; ATN: acute tubular necrosis; Toxic: toxic tubulopathy; No dx.: no specific diagnosis

These data may also be the starting point for more academic research. For instance, it may be worthwhile to know more about the demography, steroid response and outcome of the 150 nephrotic patients included in the registry. The approximate incidence also enables us to decide whether clinical trials on treatment options would be feasible.

These data on renal biopsy showed the prevailing practice of local paediatric nephrologists in relation to performing renal biopsies, and showed the spectrum of glomerulonephritis as diagnosed by renal biopsies in the local community. The findings were comparable to those of a previous survey of renal biopsies in 1991 to 1993.[8] It must be pointed out that both studies did not reflect the true incidence because not all patients who presented with urinary abnormalities or nephrotic syndrome underwent renal biopsies. Nevertheless it showed that paediatric nephrologists were doing less biopsies over the years, especially in the evaluation of nephrotic syndrome. In the current survey, most biopsies for steroid dependent or frequently relapsing nephrotic syndrome revealed a renal pathological diagnosis that would not change management. Nevertheless in the previous survey, a significant number of patients with steroid dependence were found to have focal segmental glomerulosclerosis for which the accepted treatment is different from those of Minimal Change Disease or Diffuse Mesangial Proliferation.[8] This is also a controversial issue among North American paediatric nephrologists. In two questionnaire surveys reported by Primack et al in 1994, about 60% of paediatric nephrologists would biopsy children with steroid-responsive (frequently relapsing or steroid dependent) nephrotic syndrome prior to initiating cytotoxic therapy when they are steroid dependent or intolerant. The reasons for biopsy were that findings gave prognostic information and influenced therapy. The other 40% tended not to perform biopsy. However most nephrologists would base further therapy on the histopathologic findings regardless of the previous clinical response to steroids.[9] Thus there is still a role of renal biopsy in guiding therapy in these patients.

Another observation is that patients biopsied for persistent microscopic haematuria were either found to have a diagnosis for which treatment is not necessary (Thin Membrane Disease or IgA nephropathy with mild presentation), or not even a firm diagnosis. This raised doubt on the necessity of doing renal biopsy in this clinical situation. This was in agreement with the findings from the previous survey.[8] Similar clinicopathologic correlation have been reported by Trachtman et al in 1984. Among 76 paediatric patients with isolated haematuria, 56% had abnormal renal pathology with Alport syndrome (9), IgA nephropathy (8), thin glomerular basement membrane (17) and vascular C3 staining (7). The chance of having abnormal findings increased with at least one episode of gross haematuria, or a family history of haematuria in a first degree relative.[10]

For the rare disorders, the incidence may not be accurate if the monitoring period is short. Further monitoring by continuing this renal registry is definitely needed to accurately estimate the incidence of tubulopathies and cystic kidney diseases.

One essential condition of epidemiological survey is to ensure completeness of data and its accuracy. Although the Hospital Authority hospitals capture >90% of all paediatric inpatients, it is still possible that some cases have been attending private paediatricians or adult nephrologists and hence missed in the current database. Nevertheless it is still useful to know the minimal incidence. Further improvement should be possible when the Surveillance Program is extended to the private sector. Also the completeness and accuracy of data collection depends on voluntary submission of each unit's coordinator and it is not possible at present to check it via an independent pathway (e.g. via the Clinical Management System, database from the pathology departments etc.). When the new Clinical Data Analysis and Reporting System became available in the Hospital Authority, it may be possible to check the accuracy of the data collection.

In conclusion, this renal registry is our first effort to obtain epidemiological data on paediatric renal diseases in Hong Kong. It gave a fair idea of the caseload and disease pattern of children with renal diseases managed in the Hospital Authority hospitals. The data was admittedly limited and it can be improved further in terms of scope and data quality. Nevertheless, it could form a basis to guide us in forward planning of service provisions and in conducting academic researches in this area.

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