The changing spectrum of primary glomerular diseases within 15 years: A survey of 3331 patients in a single Chinese centre

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Abstract

Background. Primary glomerular disease (PGD) is the leading cause of end-stage renal disease (ESRD) in China. With the development of socioeconomic status of Chinese people in the last two decades, PGD in ESRD is intent to decrease. However, whether this affects the spectrum of PGD is not clear. The aim of the current study is to investigate the changing spectrum of PGD in China.

Methods. The records of 5398 consecutive native renal biopsies performed in adults (≥14 years of age) in our centre between 1993 and 2007 were retrospectively analysed. The criteria for renal biopsy and pathologic diagnosis were kept unchanged. The patients were grouped according to a 5-year interval, 1993–97 (period 1), 1998–2002 (period 2) and 2003–07 (period 3). Then they were divided into four groups according to age for stratified analysis: 14–24 years, 25–44 years, 45–59 years and the elderly (≥60 years).

Results. Three thousand, three hundred and thirty-one patients were diagnosed with PGD. PGD remained the most common renal disease, accounting for 65.9%, 57.7% and 63.2% in period 1, 2 and 3, respectively, without any significant difference. The proportion of elder patients increased significantly from 0% in 1993 to 9.1% in 2007 (P < 0.001). Within 1993–97, the leading PGD was IgA nephropathy (50.7%), followed by non-IgA MsPGN (19.9%), membranous nephropathy (MN) (13.3%) and minimal change disease (MCD) (6.3%), while within 2003–07, the most common PGD was still IgAN (58.2%), but followed by MN (14.3%), MCD (13.4%) and non-IgA MsPGN (7.0%). The age-adjusted frequency of IgAN and MCD increased significantly from period 1 to period 3 (P < 0.01 and P < 0.001, respectively), while that of non-IgA MsPGN, EnPGN and MPGN decreased significantly (P < 0.001, P < 0.01 and P < 0.05, respectively). There was no significant change in the age-adjusted frequency of FSGS, MN and CreGN during the study period. However, when patients were stratified by age, a sixfold increase in frequency of FSGS was identified in the 14- to 24-year group (P < 0.01).

Conclusions. The spectrum of primary glomerulonephritis has changed within the last 15 years. The relative frequency of non-IgA MsPGN, EnPGN and MPGN decreased significantly, while that of MCD and IgA nephropathy increased significantly. The relative frequency of FSGS increased significantly in younger patients.

Keywords: focal segmental glomerulosclerosis; IgA nephropathy; minimal change disease; mesangio proliferative glomerulonephritis; primary glomerulonephritis

Introduction

Chronic glomerulonephritis, mainly caused by primary glomerular disease (PGD), is the most common cause of end-stage renal failure (ESRD) in China although showing a downward trend, which accompanies the rise of diabetic nephropathy and hypertensive nephropathy [1,2]. According to the Beijing Dialysis Registration, chronic glomerulonephritis accounted for 53.0% and 47.3% of all patients receiving haemodialysis in 1999 and 2004, respectively [1,2]. With the rapid development in economy and urbanization, especially within recent two decades, a recently performed population study on Beijing citizens revealed that the prevalence of chronic kidney disease (CKD) is 13% and that ageing, diabetes and hypertension are the main causal factors for CKD [3], though PGD still remains the leading cause of ESRD in China [2]. It has been reported that the spectrum of PGD was substantially changed in the world over the past two decades [4–18]. Since 1985, it had been reported that the proportion of membranoproliferative glomerulonephritis (MPGN) decreased in Italy [4], Spain [5], France [6], Tunis [7], the USA [8] and India [9], and the prevalence of post-infectious glomerulonephritis (PIGN) decreased in Singapore [10], France [6], Tunis [7], and Brazil [11] as well, but the prevalence of focal segmental glomerulosclerosis (FSGS) [8,9,11–17] and IgA...
nephropathy (IgAN) [7,8,17,18] increased. The prevalence of minimal change disease (MCD) remained controversial [8,18]. However, following the rapid change of lifestyle and socioeconomic status in Chinese people, whether the spectrum of PGD changed has not been revealed. Therefore, we retrospectively analysed data of all patients who received renal biopsy in one of the largest clinic nephrology centres within the last 15 years.

Patients and methods

Patients

The records of 5714 adult patients (age ≥14 years) with native renal biopsies performed in the 1st hospital of Peking University from 1993 to 2007 were retrospectively analysed. Indications for renal biopsy were as follows: (1) nephrotic syndrome or nephritic range proteinuria, (2) acute nephritic syndrome, (3) rapidly progressive glomerulonephritis syndrome, (4) chronic nephritic syndrome, (5) asymptomatic haematuria with proteinuria and (6) acute renal failure without confirmed diagnosis. The indication of renal biopsy remained unchanged during the whole observation period. Incomplete records (n = 2), inadequate biopsies (less than 10 glomeruli in the specimen for light microscopy when there were no typical findings in immunofluorescence or electron microscopy or absence of a glomerulus in immunofluorescence, n = 250) and repeat biopsies (n = 70) were excluded. Then, 5398 (94.5%) qualified cases were enrolled in this study. Data included demographic data, clinical and renal histopathological diagnoses.

PGD has been classified into nine entities in this study: IgAN, non-IgA mesangiproliferative glomerulonephritis (MsPGN), membranous nephropathy (MN), MCD, FSGS, endocapillary proliferative glomerulonephritis (EnPGN), crescentic glomerulonephritis (CreGN), MPGN and the others; the last category includes rare diseases such as focal glomerulosclerosis, acute or chronic tubulointerstitial nephritis, acute tubular necrosis and unclassified nephropathies.

The main clinical syndromes observed in patients at the time of the renal biopsy were reported. Nephrotic-range proteinuria (NS) was defined as proteinuria ≥3.5 g/day with or without hypoalbuminaemia. Acute nephritic syndrome was defined as haematuria, RBC casts and proteinuria (<3.5 g/day), which persist <3 months. Rapidly progressive glomerulonephritis (RPGN) syndrome was defined as acute nephritic syndrome with acute deteriorated renal function such as a twofold increase in serum creatinine concentration or a decrease in creatinine clearance by 50%. Chronic nephritic syndrome was defined as proteinuria (1–3.5 g/day) and haematuria that persisted for at least 3 months. Asymptomatic urinary abnormality was defined as proteinuria (<1.0 g/day) and haematuria found by routine check-up, without oedema, hypertension and abnormal renal function.

Biopsy samples were previously obtained using a Trucut biopsy needle before 1994, and using a spring-loaded biopsy gun since 1994. The number of glomeruli in each renal specimen was increased significantly during the study periods (15.5 ± 7.6, 25.6 ± 12.2 and 26.7 ± 11.8 in period 1, 2 and 3, respectively, P < 0.001).

Renal biopsy specimens were forwarded to two pathologists. They were examined by light, immunofluorescence and electron microscopy. In light microscopy, they were fixed in 10% buffered formaldehyde, embedded in paraffin, and 2- to 3-µm sections were stained with haematoxylin and eosin, PAS and periodic acid-silver methenamine (PAM). In immunofluorescence examination, the specimens for immunofluorescence were embedded in OCT compound (Miles Laboratories, Elkhart, IN, USA) and frozen in an acetone–dry ice mixture. The frozen sections were cut into 2–3 µm on a cryostat and stored at −80 °C until use. These sections were rinsed in 0.01 mol/l phosphate-buffered saline (PBS), pH 7.4, fixed in absolute acetone for 10 min, and incubated for 30 min at room temperature with fluorescein-isothiocyanate-conjugated rabbit antihuman IgG, IgA, IgM, C1q, C3, C4 or fibrinogen antisera (Dakopatts, Copenhagen, Denmark). The stained sections were rinsed by PBS and examined under a fluorescence photomicroscope (Zeiss Axiosphot, Oberkochen, Germany). In electron microscopy, the specimens for electron microscopy were fixed by 2.5% glutaraldehyde, followed by osmium tetroxide and embedded in Epon 812. Ultrathin sections stained with tannic acid and lead citrate were examined using a Hitachi H-600 electron microscope. Electron microscopy was performed on 3185 (95.6%) biopsy specimens from the PGD patients. The pathologic diagnostic criteria have been stable during the studied 15 years. When new entities were recognized or new diagnostic criteria appeared, we updated the previous diagnoses one by one according to the new criteria. For example, when fibrillar glomerulonephritis, immunotactoid glomerulopathy, fibronectin glomerulopathy and collagen III glomerulopathy were first recognized in China in 1998, we retrospectively reviewed and updated the diagnoses of our renal biopsies obtained between January 1993 and December 1998. We also updated diagnoses of FSGS in patients admitted between January 1993 and December 2002, according to new classification criteria for FSGS [19]. Differences in results between the two pathologists were resolved by re-reviewing the biopsy slides and coming to a consensus.

The patients were grouped into three periods according to a 5-year interval: 1993–97 (period 1), 1998–2002 (period 2) and 2003–07 (period 3). Further analysis was performed by dividing patients into four groups according to different ages at the time of renal biopsy (14–24 years, 25–44 years, 45–59 years and ≥60 years, respectively).

Statistical analysis

Each year, data were stored on a database file (Excel 2003). All the statistics were analysed by SPSS software (SPSS 11.0, Chicago, IL, USA). The percentage and mean ± standard error of the mean were used to describe
Table 1. Frequencies of primary glomerular disease in different periods

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>No. of biopsies</td>
<td>898</td>
<td>1943</td>
<td>2557</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of PGD (%)</td>
<td>592 (65.9)</td>
<td>1122 (57.7)</td>
<td>1617 (63.2)</td>
<td>0.002</td>
<td>0.962</td>
</tr>
</tbody>
</table>

PGD: primary glomerular disease.

Table 2. Sex difference among different primary glomerular diseases

<table>
<thead>
<tr>
<th>Pathologic diagnosis</th>
<th>n</th>
<th>Male, N (%)</th>
<th>Female, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCD</td>
<td>364</td>
<td>237 (64.6)</td>
<td>129 (35.4)</td>
</tr>
<tr>
<td>MsPGN</td>
<td>371</td>
<td>188 (50.7)</td>
<td>183 (49.3)</td>
</tr>
<tr>
<td>MN</td>
<td>500</td>
<td>286 (57.2)</td>
<td>214 (42.8)</td>
</tr>
<tr>
<td>MPGN</td>
<td>35</td>
<td>22 (62.9)</td>
<td>13 (37.1)</td>
</tr>
<tr>
<td>IgAN</td>
<td>1809</td>
<td>965 (53.3)</td>
<td>844 (46.7)</td>
</tr>
<tr>
<td>CreGN</td>
<td>88</td>
<td>51 (58.0)</td>
<td>37 (42.0)</td>
</tr>
<tr>
<td>EnPGN</td>
<td>38</td>
<td>23 (60.5)</td>
<td>15 (39.5)</td>
</tr>
<tr>
<td>FSGS</td>
<td>110</td>
<td>71 (64.5)</td>
<td>39 (35.5)</td>
</tr>
</tbody>
</table>

MCD, minimal change disease; MsPGN, non-IgA mesangio proliferative glomerulonephritis; MN, membranous nephropathy; MPGN, membranoproliferative glomerulonephritis; IgAN, IgA nephropathy; CreGN, crescentic glomerulonephritis; EnPGN, endocapillary proliferative glomerulonephritis; FSGS, focal segmental glomerulosclerosis.

Results

Demographic features of patients with PGD

From January 1993 to December 2007, 5398 qualified renal biopsies were identified, and 3331 (61.7%) patients were diagnosed as PGD. As shown in Table 1, there was no significant change in the prevalence of PGD during the last 15 years, and it remained the most common renal disease in patients receiving renal biopsies in our centre, accounting for 65.9%, 57.7% and 63.2% in the three periods, respectively (P > 0.05). As shown in Table 2, there was a male predominance in each kind of PGD. The male to female ratio was 1.44:1, 1.25:1 and 1.20:1 in period 1, 2 and 3 (χ² = 4.753, P > 0.05), respectively. There was a significant increase in the mean age upon renal biopsy, which was 32.6 ± 12.4 years, 34.4 ± 13.5 years and 35.8 ± 13.6 years in period 1, 2 and 3 (P < 0.001), respectively. As shown in Figure 1, the proportion of elderly patients (≥60 years old) increased significantly, from 0% in 1993 to 9.1% in 2007 (χ² = 13.480, P = 0.0001).

Clinical syndromes of PGD

The most common clinical presentation of PGD was NS, followed by chronic nephritic syndrome, asymptomatic urinary abnormality, acute nephritic syndrome and RPGN (Figure 2). There was no significant difference in proportion of NS and RPGN (P > 0.05). However, there was a significant decrease in proportion of acute nephritic syndrome (P < 0.01). Although significant changes in proportion of chronic nephritic syndrome (P < 0.05) and asymptomatic urinary abnormality (P < 0.05) were also noticed, they occurred only in period 2.

The disease spectrum of PGD in total

In the 3331 patients with PGD, the leading cause was IgA nephropathy (54.3%), followed by MN (15.0%), non-IgA MsPGN (11.1%) and MCD (10.9%).

The clinicopathologic correlations of PGD

As shown in Table 3, the most common cause of NS was MN (29.5%), followed by MCD (25.3%) and IgA nephropathy (20.0%). The most common cause of RPGN syndrome was
Table 3. The clinicopathological correlations of primary glomerular diseases

<table>
<thead>
<tr>
<th>Histopathologic diagnosis</th>
<th>NS, N (%)</th>
<th>CGN, N(%)</th>
<th>AUA, N(%)</th>
<th>AGN, N(%)</th>
<th>RPGN, N(%)</th>
</tr>
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<tbody>
<tr>
<td>IgAN</td>
<td>320 (20.0)</td>
<td>813 (76.8)</td>
<td>428 (83.4)</td>
<td>207 (79.6)</td>
<td>41 (32.5)</td>
</tr>
<tr>
<td>MN</td>
<td>406 (29.5)</td>
<td>84 (7.9)</td>
<td>7 (1.4)</td>
<td>3 (1.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>MsPGN</td>
<td>175 (12.7)</td>
<td>103 (9.7)</td>
<td>71 (13.8)</td>
<td>21 (8.1)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>MCD</td>
<td>348 (25.3)</td>
<td>12 (1.1)</td>
<td>2 (0.4)</td>
<td>2 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>FSGS</td>
<td>82 (6.0)</td>
<td>24 (2.3)</td>
<td>3 (0.6)</td>
<td>1 (0.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>CreGN</td>
<td>3 (0.2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>EnPGN</td>
<td>9 (0.7)</td>
<td>2 (0.2)</td>
<td>1 (0.2)</td>
<td>22 (8.5)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>MPGN</td>
<td>21 (1.5)</td>
<td>12 (1.1)</td>
<td>1 (0.2)</td>
<td>1 (0.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Others</td>
<td>10 (0.7)</td>
<td>6 (0.6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>1374 (100.0)</td>
<td>1058 (100.0)</td>
<td>513 (100.0)</td>
<td>260 (100.0)</td>
<td>126 (100.0)</td>
</tr>
</tbody>
</table>

NS, nephrotic-range proteinuria; CGN, chronic nephritis syndrome; AUA, asymptomatic urinary abnormality; AGN, acute nephritis syndrome; RPGN, rapidly progressive glomerulonephritis syndrome; MCD, minimal change disease; MsPGN, non-IgA mesangio proliferative glomerulonephritis; MN, membranous nephropathy; MPGN membranoproliferative glomerulonephritis; IgAN IgA nephropathy; CreGN, crescentic glomerulonephritis; EnPGN, endocapillary proliferative glomerulonephritis; FSGS, focal segmental glomerulosclerosis.

The changing spectrum of primary GN

The disease spectrum of PGD in different periods

As indicated in Figure 3, the most common PGD was IgA nephropathy (50.7%), followed by non-IgA MsPGN (19.9%), MN (13.3%) and MCD (6.3%) in 1993–97, while the most common PGD was still IgAN (58.2%) followed by MN (14.3%), MCD (13.4%) and non-IgA MsPGN (7.0%) in 2003–07. The age-adjusted proportion of IgAN and MCD increased significantly from periods 1 to 3 ($P < 0.01$ and $P < 0.001$, respectively), while that of non-IgA MsPGN, EnPGN and MPGN decreased significantly from periods 1 to 3 ($P < 0.001$, $P < 0.01$, $P < 0.05$, respectively). There was no significant difference in the age-adjusted proportion of FSGS, MN and CreGN.

The spectrum of PGD after age stratification

When stratified by age, there were 798, 1814, 522 and 197 patients with renal biopsy in the 14–24 years, 25–44 years, 45–59 years and elderly groups, respectively. As shown in Table 4, a similar changing trend of MCD, IgAN, non-IgA MsPGN, EnPGN, MN, and CreGN was noted in the subgroup analysis. However, a significant (sixfold) increase in the proportion of FSGS was identified in the 14–24 years group ($P < 0.01$). It was 1.2% in 1993–97 and increased to 7.5% in 2003–07 in this subgroup, while the significant trend of increase was not statistically confirmed among the other groups. There was no significant difference in the proportion of males (100.0%, 80.0% and 74.1% in period 1, 2 and 3, respectively, $\chi^2 = 0.641$, $P = 0.423$) and that of nephrotic range proteinuria (50.0%, 80.0% and 85.2%, in period 1, 2 and 3, respectively, $\chi^2 = 1.579$, $P = 0.209$) in the youngest group FSGS patients.

Discussion

In the current study, we analysed the clinical and pathological data of 3331 cases of PGD, diagnosed between 1993 and 2007, in a single renal centre in Northern China. The number of renal biopsies performed increased dramatically from 898 to 2557 in period 1 compared to period 3. The main reasons for this increasing number included the following: (1) the number of beds in our ward was expanded twice during periods 2 and 3, respectively; (2) the referral population increased during the observation period because renal biopsy could not be performed in many local hospitals and (3) with the improvement in economic status of Chinese people, the number of patients who could pay for renal biopsy increased slightly. Anyway, the indications for renal biopsy and the diagnosis criteria remained much the same during the study period, and the referral pattern was largely unchanged as well. It was shown that PGD, with a male predominance, was still the most common disease among patients receiving renal biopsy in China, accounting for 63.3% of renal biopsy patients. However, our study indicated that the change in the disease spectrum of PGD in Chinese people also occurred within the

![Fig. 3. Age-adjusted prevalence of various primary glomerular diseases. $^*P < 0.05$, $^{**}P < 0.01$ and $^{***}P < 0.001$. MCD, minimal change disease; MsPGN, non-IgA mesangio proliferative glomerulonephritis; MN, membranous nephropathy; MPGN membranoproliferative glomerulonephritis; IgAN IgA nephropathy; CreGN, crescentic glomerulonephritis; EnPGN, endocapillary proliferative glomerulonephritis; FSGS, focal segmental glomerulosclerosis.](image-url)
With improvement in standards of living, better public health and the early effective antibiotic treatment of pharyngeal infections, it has been reported that the proportion of MPGN and EnPGN or post-streptococcal acute glomerulonephritis declined in many countries other than China. In 1985, Barbiano di Belgioioso et al. [4] reviewed 1548 renal biopsies from patients with primary glomerulonephritis examined at three nephrology units in Milan from 1972 to 1983. It was found that the proportion of MPGN decreased significantly from 21% in 1972–75 to 6% in 1980–83. Afterwards, the declining proportion of MPGN was reported in Spain [5], Tunis [7], the USA [8] and India [9]. In addition, the decrease in proportion of EnPGN had been noted in Tunis [7] and Brazil [11] as well. But, a paradoxical trend in the proportion of post-infectious glomerulonephritis (PIGN) was reported in India by Narasimhan et al. [9] in 2006. They found that the proportion of PIGN increased from 8.9% in 1971–85 to 12.3% in 1986–2002 ($P = 0.002$). They speculated that this paradoxical increase in PIGN might be related to some changes in biopsy policy during the later period. Our current study confirmed that there was a significant decline in MPGN and EnPGN. The proportion of EnPGN declined from 2.5% in 1993–97 to 0.5% in 2003–07 ($P < 0.001$), while that of MPGN decreased from 1.5% in 1993–97 to 0.7% in 2003–07 ($P < 0.05$).

IgA nephropathy is one of the most common forms of glomerulonephritis worldwide. As shown in Figure 4, there is a marked regional difference in frequency of IgA nephropathy among PGD patients. It occurs with greatest frequency in Asian countries, accounting for 45–58.2% of PGD [18,20,21], while with modest frequency in the USA [16] and Europe [22,23] and with lower frequency in Brazil [24]. The variation in the frequency of IgA nephropathy was explained by different policies in screening kidney diseases and different renal biopsy practices. Many patients with IgA nephropathy, especially those with asymptomatic haematuria and/or proteinuria, are detected on routine urine screening. Prevalence may therefore appear to be higher in countries with an active urine-testing programme and a low threshold for the performance of renal biopsy in patients with isolated asymptomatic haematuria, such as Japan [20], where testing is routinely performed in schools and in the workplace. However, the indication for renal biopsy seems to be controlled on routine urine screening. Prevalence may therefore appear to be higher in countries with an active urine-testing programme and a low threshold for the performance of renal biopsy in patients with isolated asymptomatic haematuria, such as Japan [20], where testing is routinely performed in schools and in the workplace. However, the indication for renal biopsy seems to be comparable among some countries. For example, in reports from Brazil [24], Czech Republic [23], Japan [20]...
and Singapore [18], the frequencies of nephrotic syndrome were 42.0%, 39.3%, 49.5% and 34.0%, respectively. In our current study, nephrotic-range proteinuria was presented in more than 40% of patients and 12.2% of patients had asymptomatic urinary abnormality. Therefore, it is unlikely that the regional differences in the proportion of IgA nephropathy are mainly explained by the difference in renal biopsy policy; instead, the difference might be associated with racial difference. This was supported by Simon’s study [25]. The authors prospectively observed the histological diagnoses of 898 PGD patients diagnosed between 1976 and 2002 in a western region of France. They found that the incidence of IgA nephropathy remained the same throughout the three periods: 28, 28 and 26 per million inhabitants during 1976–85, 1986–95 and 1996–2002.

However, a steady increase in the incidence or proportion of IgA nephropathy of PGD has been reported in the USA [17,26], Tunis [7] and Singapore [18]. In 1999, Woo et al. [18] reported that the proportion of IgA nephropathy in PGN increased from 42% in 1975–86 to 45% in 1987–97 in Singapore ($P < 0.05$). Ben Maiz et al. [7] also found that the proportion of IgA nephropathy in biopsy-proven GN patients in adults increased from 0.9% in 1975–85 to 12.9% in 1995–2005 at the Kidney Unit of Charles Nicolle Hospital in Tunis ($P < 0.0001$). In addition, it was shown that the incidence of IgA nephropathy increased from 0.7/100 000 person-years in 1974–83 to 2.1/100 000 person-years in 1994–2003 in Olmated county, MN, USA [17]. Our study indicated that the frequency of IgA nephropathy in PGD increased from 50.7% in 1993–97 to 58.2% in 2003–07 ($P < 0.01$). These studies suggested, therefore, the changing frequency of IgA nephropathy might be hardly explained solely by the race differences, but some environmental factors should be suspected.

Following an initial observation by D’Agati [12] in the USA, there have been a number of published reports suggesting a significant increase in the proportion of idiopathic FSGS in the 1980s, 1990s as well as 2000s in the USA [8,13–16], Brazil [11] and India [9]. In Chicago, Hass et al. reported the changing proportion of FSGS in renal biopsy patients and nephrotic syndrome patients in 1995 and 1997, respectively. Among all biopsies, the proportion of FSGS increased from 0.0% during the period from 1994 to 1979 to 12.2% during the period from 1987 to 1993 [13]. In 1997, they did the second analysis on the proportion of FSGS in nephrotic syndrome patients [8]. The authors surveyed 1000 consecutive biopsies from 1976 to 1979 and 1000 consecutive biopsies performed from 1995 to 1997 for unexplained aetiologies of nephrotic syndrome in adults; they found that FSGS was the most common cause, accounting for 35% of all cases and over 50% of cases among blacks [8]. In a rural area in Massachusetts, Braden et al. reviewed the relative frequency of FSGS among adult patients with 2 g or greater daily urinary protein excretion, which increased from 13.7% during 1975–1979 to 25% during 1990 to 1994 [15]. Stratified analysis showed a significant increase in the frequency of FSGS in both blacks and Hispanics, and the relative frequency of FSGS increased slightly in whites but did not reach statistical significance. Two reports in the new century showed that the increase trend in the proportion of FSGS continues and the increase has occurred among both white and black and Hispanic patients [16,17].

Conversely, this trend of increase in the occurrence of FSGS has never been proven in China. We found that the relative frequency of FSGS increased slightly from 2.7% in 1993–97 to 3.8% in 2003–07 but did not reach statistical significance. However, when patients were stratified by age, a significant (sixfold) increase in relative frequency of FSGS was found in the youngest (14–24 years) patients ($P = 0.001$). The cause of this increased incidence of FSGS is uncertain. We found no significant changes in the clinical characteristics of patients with FSGS in the youngest patients, including gender and proportion of nephritic-range proteinuria. Therefore, it is unlikely that the increase in FSGS in younger patients was due to changes in the policy for biopsy. The increase trend found in different regions and different races indicated that some environmental factors might play a role in the pathogenesis of FSGS.

Even though this study was performed at one hospital with stable biopsy and diagnosis criteria, there are several limitations. First, it is not a randomized population study. Secondly, detection bias might have occurred since the referral patients in this study were not from the population screened for proteinuria or microscopic haematuria. Finally, this is an observation study with no evidence to understand the influence factor(s) for the changing spectrum. So the spectrum information should be explained with caution of bias.

In conclusion, primary GN is continuously the leading cause of renal biopsy, but the spectrum of primary glomerulonephritis is changing in China. IgA nephropathy and MCD are increasing and IgA nephropathy is the leading histopathological pattern, while non-IgA MsPGN, EnPGN and MPGN are decreasing. The frequency of FSGS has been increased in younger patients.

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