The Spectrum of Children's Kidney Diseases—2403 Renal Biopsy-Proven Cases from a Single Centre in China Between 1999 and 2019

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Abstract

Background: This study aimed to investigate the clinical and pathological characteristics and the changes in glomerular diseases in 2403 pediatric renal biopsies from 1999 to 2019.

Methods: Renal biopsies performed on children aged ≤18 years between 1999 and 2019 were analysed at our center. We analysed the clinical and histological characteristics, distribution of pediatric glomerular diseases with various clinical presentations, and changes in the glomerular disease patterns during the study period.

Results: The most common primary glomerular disease was IgA nephropathy (IgAN) (24.3%), followed by minimal change disease (MCD) (15.3%) and membranous glomerulonephritis (MN) (13.1%). Henoch-Schonlein purpura nephritis (HSPN) (18.1%) and lupus nephritis (LN) (7.2%) were the most frequently recorded secondary glomerular diseases. Alport syndrome and thin basement membrane nephropathy (TBMN) were the most common inherited glomerular diseases, accounting for 1.2% and 0.6% of the total glomerular diseases in children, respectively. The number of boys with IgAN, MCD and IgM nephropathy (IgMN) was higher than that of girls, while the number of girls with MN and LN was higher than that of boys. The frequencies of MCD, MN, IgMN and endocapillary proliferative glomerulonephritis (EnPGN) in the 13-18-year-old group were higher than those in the 0-12-year-old group, while the frequencies of IgAN, mesangial proliferative glomerulonephritis (MsPGN) and focal proliferative glomerulonephritis (FPGN) were lower than those in the 0-12-year-old group. The ratio of Alport syndrome and TBMN in the 0-12-year-old group was higher than that in the 13-18-year-old group. The proportion of patients with MCD and MN in 2010-2019 was higher than that in 1999-2009, while the ratio of IgAN, MsPGN, IgMN, EnPGN, membranoproliferative glomerulonephritis (MPGN), HSPN and HBV-associated glomerulonephritis (HBV-GN) decreased. MCD (28.5%) was the most common cause of nephrotic syndrome (NS). In children with haematuria and proteinuria, HSPN (38.8%) and IgAN (36.9%) were more common than other glomerular diseases. IgAN (39.4%) was the most common cause of AKI. Sclerosing glomerulonephritis (SGN) (21.1%) was the main cause of progressive chronic kidney disease (CKD).

Conclusions: Glomerular diseases in children were related to sex and age. From 1999 to 2019, the spectrum of children’s kidney disease in our center changed significantly.

Background

Chronic kidney disease (CKD) has become one of the major diseases threatening global public health [1, 2]. It is a major chronic disease that causes a high medical burden and seriously affects quality of life. If CKD is not diagnosed and treated in time, the mortality of CKD will be significantly increased once it develops into end-stage renal disease (ESRD) [3]. Therefore, how to detect and treat CKD early in children is a clinical problem to be solved.

The aetiology of CKD varies in different regions and ethnic groups. Congenital anomalies of the kidney and urinary tract (CAKUT) are the main causes of CKD in children in developed countries [1, 4, 5], while
glomerular diseases are the main causes in developing countries [6–9]. Glomerular disease is still the main cause of CKD in children in China [6]. The diagnosis and treatment of glomerular diseases mainly depend on renal biopsy. Renal biopsy is an invasive procedure with the risk of haemorrhage and arteriovenous fistula. Therefore, it is very important to study the spectrum of glomerular diseases; the relationship between renal pathology and clinical manifestations; and the relationship between glomerular diseases and age, sex and years. This will correctly diagnose glomerular disease in children without renal biopsy. In China, there are few centers that study glomerular diseases in children.

This study retrospectively analysed the clinical and pathological data of 2403 renal biopsies of children in a single center; clarified the constitution, changes and distribution of kidney diseases; and analysed them according to the patient's sex and age.

Materials And Methods

Inclusion and exclusion criteria

From 1999 to 2019, we selected 2453 children with kidney disease under the age of 18 who underwent renal biopsy. The exclusion criteria were pathological results of renal biopsy with less than 5 glomeruli under a light microscope, incomplete clinical data, or tubulointerstitial disease or renal vascular disease without glomerular lesions. Finally, 50 cases were excluded, and 2403 cases were included in this analysis. The patients and/or parents signed the consent form before renal biopsy. The research was in compliance of the declaration of Helsinki and approved by the ethics committee of the Second Hospital of Hebei Medical University. Before enrollment, written informed consent was provided by patients or their guardians.

Clinical Classification

According to the clinical classification standard of children's glomerular disease formulated by the Chinese Medical Association in 2000, we divided 2403 children into six clinical types: nephrotic syndrome (NS), acute kidney injury (AKI), progressive CKD (defined as eGFR < 60 mL/min/1.73 m²), proteinuria, haematuria, and proteinuria with haematuria. The glomerular filtration rate was calculated by the swatch formula. NS was defined as proteinuria greater than 50 mg/kg·d or greater than 3.5 g/kg and serum albumin less than 30 g/L. Proteinuria that does not meet the criteria for NS is defined as proteinuria.

Indications And Contraindications For Percutaneous Renal Biopsy

The indications for percutaneous renal biopsy include steroid-resistant NS, a part of steroid-dependent and frequently recurrent NS; NS with glomerular haematuria or renal insufficiency or hypertension or low complement; unexplained persistent haematuria and/or proteinuria; unknown AKI or unexplained
progressive CKD; nephrotic proteinuria or NS or gross haematuria or AKI caused by Henoch-Schonlein purpura nephritis (HSPN); and other secondary glomerulonephritides. The contraindications for renal puncture include an isolated kidney, displaced kidney, abnormal renal structure, coagulation disorder, ESRD and renal infection.

Pathological Examination

All pathological tissues were examined by light microscopy and immunofluorescence, and approximately 50% of them were further examined by electron microscopy.

Grouping

According to age, they were divided into two groups: 0-12 years old and 13-18 years old. According to the time of renal puncture, they were divided into two groups: 1999-2009 and 2010-2019. According to sex, they were divided into male and female groups. According to the clinical classification of children's kidney disease, they were divided into 6 groups: NS, AKI, progressive CKD, proteinuria, haematuria and proteinuria with haematuria. The constituent ratios of renal pathology in different sexes, ages and years were compared. The constituent ratio of renal pathology corresponding to different clinical types was compared.

Statistical analysis

Data were expressed as the mean ± SD. The chi-square test was used to analyse the constituent ratio. SPSS 23.0 software was used for statistical analysis. A P value of ≤ 0.05 was considered to be statistically significant.

Results

General information

A total of 2403 renal biopsy specimens were analysed from 1999 to 2019, including 1411 males and 992 females, with a male to female ratio of 1.4:1. The average age at renal biopsy was 13.5 ± 3.4 years old. The youngest was 1 month, 708 cases (29.5%) were 0-12 years old, and 1695 cases (70.5%) were 13-18 years old. From 1999 to 2009, 1055 patients (43.9%) underwent renal biopsy, and 1348 patients (56.1%) underwent renal biopsy from 2010 to 2019. The most common clinical syndrome was NS (50.1%), followed by haematuria and proteinuria (38.3%) (Table 1).
Table 1
Demographic and clinical characteristics of 2403 children who underwent kidney biopsy 1999 to 2019

| Characteristics | Total, n=2403 | Sex  | Male, n=1411 | Female, n=992 |
|-----------------|--------------|------|--------------|---------------|
| Clinical syndrome, n(%) |          |      |              |               |
| Nephrotic syndrome | 1204(50.1)  | 665(47.1) | 539(54.3)    |               |
| Haematuria and proteinuria | 921(38.3)  | 561(39.8) | 360(36.3)    |               |
| AKI              | 104(4.3)    | 68(4.8) | 36(3.6)      |               |
| Haematuria       | 88(3.7)     | 56(4.0) | 32(3.2)      |               |
| Proteinuria      | 67(2.8)     | 47(3.3) | 20(2.0)      |               |
| Progressive CKD | 19(0.9)     | 14(1.0) | 5(0.5)       |               |
| Age, yr, mean(SD) | 13.5(3.4)  | 13.5(3.4) | 13.5(3.3)    |               |
| 0-12, n(%)       | 708(29.5)   | 402(28.5) | 306(30.8)    |               |
| 13-18, n(%)      | 1695(70.5)  | 1009(71.5) | 686(69.2)    |               |
| Time of kidney biopsy, n(%) |          |      |              |               |
| 1999-2009        | 1055(43.9)  | 665(47.1) | 390(39.3)    |               |
| 2010-2019        | 1348(56.1)  | 746(52.9) | 602(60.7)    |               |

Values are numbers(percentage).

In this study, 1712 (71.2%) patients were diagnosed with primary glomerular disease, 648 (27.0%) patients were diagnosed with secondary glomerular disease, and 43 (1.8%) patients were diagnosed with hereditary glomerular disease. The most common primary glomerular disease was IgA nephropathy (IgAN) (24.3%), followed by minimal change disease (MCD) (15.3%) and membranous glomerulonephritis (MN) (13.1%). HSPN (18.1%) and lupus nephritis (LN) (7.2%) were more frequent in secondary glomerular diseases. Alport syndrome and thin basement membrane nephropathy (TBMN) were the most common inherited glomerular diseases, accounting for 1.2% and 0.6% of the total glomerular diseases in children, respectively (Figure 1).

The Relationship Between Glomerular Diseases And Sex

As described in Table 2, the number of boys with IgAN, MCD and IgM nephropathy (IgMN) was significantly higher than that of girls, while the number of girls with MN was significantly higher than that of boys. In secondary glomerular diseases, the number of girls with LN was significantly higher than that
of boys, and there was no significant difference in the proportion of HSPN between the two groups. There was also no significant difference in the proportions of Alport syndrome and TBMN between the two groups.
| Pathological classification | Male    | Female   | P Value |
|-----------------------------|---------|----------|---------|
| **Primary glomerulonephritis** |         |          |         |
| IgAN                        | 382(27.1) | 201(20.3) | 0.000   |
| MCD                         | 259(18.4) | 109(11.0) | 0.000   |
| MN                          | 156(11.1) | 159(16.0) | 0.000   |
| GML                         | 58(4.1)   | 34(3.4)   | 0.390   |
| MsPGN                       | 53(3.8)   | 38(3.8)   | 0.925   |
| IgMN                        | 61(4.3)   | 19(1.9)   | 0.001   |
| FSGS                        | 34(2.4)   | 29(2.9)   | 0.438   |
| EnPGN                       | 35(2.5)   | 28(2.8)   | 0.605   |
| SGN                         | 15(1.1)   | 8(0.8)    | 0.525   |
| MPGN                        | 13(0.9)   | 5(0.5)    | 0.243   |
| FPGN                        | 3(0.2)    | 3(0.3)    | 0.985   |
| C1qN                        | 1(0.1)    | 4(0.4)    | 0.192   |
| CreGN                       | 3(0.2)    | 2(0.2)    | 1.000   |
| **Secondary glomerulonephritis** |         |          |         |
| HSPN                        | 252(17.9) | 182(18.3) | 0.760   |
| LN                          | 34(2.4)   | 139(14.0) | 0.000   |
| HBV-GN                      | 23(1.6)   | 12(1.2)   | 0.397   |
| ANCA-GN                     | 3(0.2)    | 3(0.3)    | 0.985   |
| **Hereditary glomerulonephritis** |         |          |         |
| Alport                      | 19(1.3)   | 10(1.0)   | 0.454   |

Values are numbers (percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;
| Pathological classification | Male  | Female | P Value |
|-----------------------------|-------|--------|---------|
| TBMN                        | 7(0.5)| 7(0.7) | 0.506   |

Values are numbers (percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;

**The Relationship Between Glomerular Diseases And Age**

As shown in Table 3, in primary glomerular diseases, the frequencies of MCD, MN, IgMN and endocapillary proliferative glomerulonephritis (EnPGN) in the 13-18-year-old group were significantly higher than those in the 0-12-year-old group, while the frequencies of IgAN, mesangial proliferative glomerulonephritis (MsPGN) and focal proliferative glomerulonephritis (FPGN) were lower than those in the 0-12-year-old group. There was no significant difference between the two age groups in secondary glomerulonephritis. The ratio of Alport syndrome and TBMN in the 0-12-year-old group was significantly higher than that in the 13-18-year-old group.
# Table 3

Relationship between glomerular diseases and age

| Pathological classification | 0-12 year | 13-18 year | P Value |
|-----------------------------|-----------|------------|---------|
| Primary glomerulonephritis  |           |            |         |
| IgAN                        | 227(32.1) | 356(21.0)  | 0.000   |
| MCD                         | 83(11.7)  | 285(16.8)  | 0.002   |
| MN                          | 50(7.1)   | 265(15.6)  | 0.000   |
| GML                         | 28(4.0)   | 64(3.8)    | 0.835   |
| MsPGN                       | 41(5.8)   | 50(2.9)    | 0.001   |
| IgMN                        | 13(1.8)   | 67(4.0)    | 0.008   |
| FSGS                        | 24(3.4)   | 39(2.3)    | 0.128   |
| EnPGN                       | 11(1.6)   | 52(3.1)    | 0.034   |
| SGN                         | 6(0.8)    | 17(1.0)    | 0.721   |
| MPGN                        | 6(0.8)    | 12(0.7)    | 0.718   |
| FPGN                        | 5(0.7)    | 1(0.1)     | 0.014   |
| C1qN                        | 2(0.3)    | 3(0.2)     | 0.979   |
| CreGN                       | 1(0.1)    | 4(0.2)     | 1.000   |
| Secondary glomerulonephritis|           |            |         |
| HSPN                        | 117(16.5) | 317(18.7)  | 0.206   |
| LN                          | 51(7.2)   | 122(7.2)   | 0.996   |
| HBV-GN                      | 7(1.0)    | 28(1.7)    | 0.216   |
| ANCA-GN                     | 2(0.3)    | 4(0.2)     | 1.000   |
| Hereditary glomerulonephritis|         |            |         |
| Alport                      | 23(3.2)   | 6(0.4)     | 0.000   |

Values are numbers (percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;
## Changes Of Spectrum In Glomerulonephritis

As shown in Table 4, the number of renal biopsies in 2010-2019 was higher than that in 1999-2009. In primary glomerular diseases, the proportion of patients with MCD and MN in 2010-2019 was significantly higher than that in 1999-2009, while the ratios of IgAN, MsPGN, IgMN, EnPGN and membranoproliferative glomerulonephritis (MPGN) decreased. In secondary glomerular diseases, the frequencies of HSPN and HBV-associated glomerulonephritis (HBV-GN) in 2010-2019 were lower than those in 1999-2009. There was no difference in the proportions of patients with Alport syndrome and TBMN between the two groups.

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| Pathological classification | 0-12 year | 13-18 year | P Value |
|----------------------------|-----------|------------|---------|
| TBMN                       | 11(1.6)   | 3(0.2)     | 0.000   |

Values are numbers (percentage).
## Table 4
Changes of spectrum in glomerulonephritis

| Pathological classification          | 1999-2009 | 2009-2019 | P Value |
|--------------------------------------|-----------|-----------|---------|
| **Primary glomerulonephritis**       |           |           |         |
| IgAN                                 | 299(28.3) | 284(21.1) | 0.000   |
| MCD                                  | 142(13.5) | 226(16.8) | 0.026   |
| MN                                   | 64(6.1)   | 251(18.6) | 0.000   |
| GML                                  | 42(4.0)   | 50(3.7)   | 0.730   |
| MsPGN                                | 48(4.5)   | 43(3.2)   | 0.083   |
| IgMN                                 | 48(4.5)   | 32(2.4)   | 0.003   |
| FSGS                                 | 28(2.7)   | 35(2.6)   | 0.930   |
| EnPGN                                | 36(3.4)   | 27(2.0)   | 0.032   |
| SGN                                  | 10(0.9)   | 13(1.0)   | 0.967   |
| MPGN                                 | 14(1.3)   | 4(0.3)    | 0.004   |
| FPGN                                 | 2(0.2)    | 4(0.3)    | 0.912   |
| C1qN                                 | 0(0.0)    | 5(0.4)    | 0.126   |
| CreGN                                | 2(0.2)    | 3(0.2)    | 1.000   |
| **Secondary glomerulonephritis**     |           |           |         |
| HSPN                                 | 217(20.6) | 217 (16.1) | 0.005 |
| LN                                   | 65(6.2)   | 108(8.0)  | 0.082   |
| HBV-GN                               | 22(2.1)   | 13(1.0)   | 0.023   |
| ANCA-GN                              | 1(0.1)    | 5(0.4)    | 0.350   |
| **Hereditary glomerulonephritis**    |           |           |         |
| Alport                               | 10(0.9)   | 19(1.4)   | 0.304   |

Values are numbers (percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;
As shown in Table 5, the constituent ratio of renal pathology corresponding to different clinical types was different. MCD (28.5%) was the most common cause of NS, followed by MN (23.7%), IgAN (14.8%) and LN (9.6%). In children with haematuria and proteinuria, HSPN (38.8%) and IgAN (36.9%) were more frequent than other glomerular diseases. The common causes of proteinuria were glomerular minor lesion (GML) (25.4%), MN (16.4%), focal segmental glomerulosclerosis (FSGS) (14.9%), and IgAN (10.4%). GML (50.0%), IgAN (15.9%), Alport syndrome (11.4%), MsPGN (10.2%) and TBMN (8.0%) were more common in children with haematuria. IgAN (39.4%) was the most common cause of AKI, followed by MCD (21.2%), LN (10.6%) and FSGS (6.7%). Sclerosing glomerulonephritis (SGN) (21.1%) was the main cause of progressive CKD, followed by IgAN (15.8%), Alport syndrome (15.8%) and IgMN (10.5%).
Table 5
Clinicopathologic correlation of pediatric glomerular Diseases

| Pathological type | Clinical classification       | Nephrotic syndrome (n=1204) | Haematuria and proteinuria (n=921) | AKI (n=104) | Haematuria (n=88) | Proteinuria (n=67) | Progressive CKD (n=19) |
|-------------------|-------------------------------|----------------------------|-----------------------------------|-------------|------------------|-----------------|----------------------|
| IgAN (n=583)      |                               | 178 (14.8)                 | 340 (36.9)                        | 41 (39.4)   | 14 (15.9)        | 7 (10.4)        | 3 (15.8)             |
| MCD (n=368)       |                               | 343 (28.5)                 | 2 (0.2)                           | 22 (21.2)   | 0                | 1 (1.5)         | 0                    |
| MN (n=315)        |                               | 285 (23.7)                 | 19 (2.1)                          | 0           | 0                | 11 (16.4)       | 0                    |
| GML (n=92)        |                               | 4 (0.3)                    | 25 (2.7)                          | 1 (1.0)     | 44 (50.0)        | 17 (25.4)       | 1 (5.3)              |
| MsPGN (n=91)      |                               | 36 (3.0)                   | 41 (4.5)                          | 4 (3.8)     | 9 (10.2)         | 1 (1.5)         | 0                    |
| IgMN (n=80)       |                               | 71 (5.9)                   | 2 (0.2)                           | 3 (2.9)     | 0                | 2 (3.0)         | 2 (10.5)             |
| FSGS (n=63)       |                               | 44 (3.7)                   | 1 (0.1)                           | 7 (6.7)     | 0                | 10 (14.9)       | 1 (5.3)              |
| EnPGN (n=63)      |                               | 17 (1.4)                   | 42 (4.6)                          | 3 (2.9)     | 1 (1.1)          | 0               | 0                    |
| SGN (n=23)        |                               | 5 (0.4)                    | 11 (1.2)                          | 0           | 1 (1.1)          | 2 (3.0)         | 4 (21.1)             |
| MPGN (n=18)       |                               | 9 (0.7)                    | 7 (0.8)                           | 1 (1.0)     | 0                | 0               | 1 (5.3)              |
| FPGN (n=6)        |                               | 1 (0.1)                    | 4 (0.4)                           | 0           | 0                | 1 (1.5)         | 0                    |
| C1qN (n=5)        |                               | 4 (0.3)                    | 1 (0.1)                           | 0           | 0                | 0               | 0                    |
| CreGN (n=5)       |                               | 0                          | 0                                 | 4 (3.8)     | 0                | 0               | 1 (5.3)              |
| HSPN (n=434)      |                               | 63 (5.2)                   | 357 (38.8)                        | 5 (4.8)     | 2 (2.3)          | 6 (9.0)         | 1 (5.3)              |
| LN (n=173)        |                               | 115 (9.6)                  | 44 (4.8)                          | 11 (10.6)   | 0                | 2 (3.0)         | 1 (5.3)              |
| HBV-GN (n=35)     |                               | 25 (2.1)                   | 6 (0.7)                           | 0           | 0                | 4 (6.0)         | 0                    |
| ANCA-GN (n=6)     |                               | 0                          | 3 (0.3)                           | 2 (1.9)     | 0                | 0               | 1 (5.3)              |

Values are numbers(percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;
### Pathological type and Clinical classification

| Pathological type | Nephrotic syndrome (n=1204) | Haematuria and proteinuria (n=921) | AKI (n=104) | Haematuria (n=88) | Proteinuria (n=67) | Progressive CKD (n=19) |
|-------------------|-----------------------------|-----------------------------------|-------------|-------------------|-------------------|----------------------|
| Alport (n=29)     | 4 (0.3)                     | 11 (1.2)                          | 0           | 10 (11.4)         | 1 (1.5)           | 3 (15.8)             |
| TBMN (n=14)       | 0                           | 5 (0.5)                           | 0           | 7 (8.0)           | 2 (3.0)           | 0                    |

Values are numbers (percentage).

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;

### Discussion

In our study, we found that the ratio of boys to girls with glomerular disease was 1.4:1, which was roughly the same as the sex ratio of children with glomerular diseases reported earlier [10–12]. Boys were more likely to have IgAN and MCD than girls, which accounted for a larger proportion of glomerular diseases. The glomerular diseases confirmed by biopsies varied with age and sex. In 1999-2019, the spectrum of glomerular disease in children changed.

Of the 2403 patients in this study, 1712 (71.2%) patients were diagnosed with primary glomerular diseases, 648 (27.0%) patients with secondary glomerular diseases, and 43 (1.8%) patients with hereditary glomerular diseases. The proportion of primary glomerular disease and secondary glomerular disease was roughly the same as that of children's glomerular disease previously reported [12–14], but the proportion of hereditary kidney disease was lower. Arapović showed that Alport syndrome accounted for 11.1% of glomerular diseases in children [10]. This difference may be due to different regions and races, because these diseases are caused by genetic abnormalities.

According to renal biopsy, IgAN (24.3%) was the most common primary glomerular disease, followed by MCD (15.3%), MN (13.1%), and FSGS (2.6%). The most common primary glomerular disease in children is MCD. Since most cases of MCD can be diagnosed clinically without renal biopsy, IgAN is the most common glomerular disease diagnosed by renal biopsy. IgAN is also the most common chronic glomerular disease in the world [15]. In a single-center study in China, IgAN was identified as the most common glomerular disease in children [16]. In a cross-sectional study in China, MCD was considered to be the most common glomerular disease in children [12]. In Egypt and South Asia, MCD was reported to be the most common glomerular disease in children [11, 17, 18]. In Croatia and Italy, IgAN was reported to
be the most common glomerular disease in children [10, 14]. In Serbia and the United States, FSGS was reported to be the most common primary glomerular disease in children [19, 20]. The change in glomerular disease spectrum in children from different countries may be due to the different indications for renal biopsy and race.

HSPN (18.1%) was the most common secondary glomerular disease. LN is the most common secondary glomerular disease in children in South Asia [11]. HSPN is more frequent in children, while LN is more frequent in adults [21]. Children are more likely to suffer from HSPN than adults.

It is worth noting that, in this study, the proportion of MN in glomerular diseases increased from 6.1–18.6%, which was much higher than that of children in other countries [11, 17, 19, 20] and higher than that reported by Nie et al., which showed that the proportion of children with membranous nephropathy in China increased from 3–7% [12]. The number of patients with MN in the United States has been decreasing year by year [20]. Idiopathic membranous nephropathy is one of the most common causes of adult NS. In China, MN (43.3%) has become the most common primary glomerular disease, as opposed to IgAN. The prevalence of idiopathic MN in China has increased significantly, especially in young patients in the early stage [22]. Some studies have found that the frequency of MN is associated with long-term exposure to high levels of PM2.5 in the air [23]. The highest proportion of MN in our study may be because our region has the highest level of PM2.5 in the air. In the past 10 years, the incidence of HBV-GN and EnPGN has decreased significantly, which may be due to the widespread use of hepatitis B vaccines in China and timely antibiotic treatment for pharyngitis.

Our study found that boys were more likely to suffer from MCD and IgAN, while girls were more likely to suffer from LN, which was consistent with previous reports [12, 20]. This sex difference may be due to differences in chromosome and sex hormone levels [24]. For example, many genes carried on the X chromosome, such as those encoding FoxP3 and the Toll-like receptors TLR7 and TLR8, are associated with the pathogenesis of autoimmune diseases [26], which may play a very important role in the pathogenesis of systemic lupus erythematosus (SLE).

MCD (28.5%) was the most common cause of NS. The common cause of haematuria was GML (50.0%), followed by IgAN (15.9%). In children with haematuria and proteinuria, HSPN (38.8%) and IgAN (36.9%) were more common than other glomerular diseases. Patients with simple microscopic haematuria can be followed up. If there is proteinuria or gross haematuria, renal biopsy is recommended.

Conclusions

Glomerular diseases in children were related to sex and age. From 1999 to 2019, the spectrum of children's kidney disease in our center changed significantly. This study described the prevalence of renal biopsy in children in central China and provided a reference for a better understanding and prevention of kidney diseases.
Abbreviations

CKD
Chronic kidney disease
CAKUT
congenital anomalies of the kidney and urinary tract
ESRD
end stage renal disease
AKI
acute kidney injury
eGFR
estimated glomerular filtration rate
Alport
Alport syndrome
ANCA-GN
ANCA associated glomerulonephritis
CreGN
crescentic glomerulonephritis
C1qN
C1q nephropathy
EnPGN
endocapillary proliferative glomerulonephritis
FPGN
focal proliferative glomerulonephritis
FSGS
focal segmental glomerulosclerosis
GML
glomerular minor lesion
HBV-GN
HBV associated glomerulonephritis
HSPN
Henoch-Schonlein nephritis
IgAN
IgA nephropathy
IgMN
IgM nephropathy
LN
Lupus nephritis
MCD
minimal change disease
Declarations

Ethics approval and consent to participate

The research was in compliance of the declaration of Helsinki and approved by the ethics committee of the Second Hospital of Hebei Medical University. Before enrollment, written informed consent was provided by patients or their guardians.

Consent for publication

This manuscript is an original article that has not been previously published and will not be submitted to any other journal. All the authors have read this manuscript and agree that the work is ready for submission, and accept responsibility for the manuscript’s contents.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Li-Jun Jiang, Zan-Hua Rong and Lin Yang formed the study concept, conducted the study, analyzed the data, interpreted the results, and drafted the manuscript. Xue Zhao made substantial contribution to the
acquisition of data, and the analysis and interpretation of data. Zhi-Yan Dou contributed to the study design. All co-authors critically reviewed and revised the initial draft and approved the final version of the manuscript.

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Figures

Pathological categories of 2403 cases of pediatric glomerular disease

Alport: Alport syndrome; ANCA-GN: ANCA-associated glomerulonephritis; CreGN: crescentic glomerulonephritis; C1qN: C1q nephropathy; EnPGN: endocapillary proliferative glomerulonephritis; FPGN: focal proliferative glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GML: glomerular minor lesion; HBV-GN: HBV-associated glomerulonephritis; HSPN: Henoch-Schonlein nephritis; IgAN: IgA nephropathy; IgMN: IgM nephropathy; LN: Lupus nephritis; MCD: minimal change disease; MN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MsPGN: mesangial proliferative glomerulonephritis; SGN: sclerosing glomerulonephritis; TBMN: thin basement membrane nephropathy;