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

Li-Jun Jiang (✉ jianglijun2005@163.com)

The Second Hospital of Hebei Medical University <https://orcid.org/0000-0002-5747-1116>

Zan-Hua Rong

The Second Hospital of Hebei Medical University <https://orcid.org/0000-0001-8056-5009>

Xue Zhao

The Second Hospital of Hebei Medical University

Zhi-Yan Dou

The Second Hospital of Hebei Medical University

Lin Yang

The Second Hospital of Hebei Medical University

Research Article

Keywords: Pediatric, Renal biopsy, Glomerular diseases

Posted Date: December 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-140880/v2>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

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 $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$), proteinuria, haematuria, and proteinuria with haematuria. The glomerular filtration rate was calculated by the swatch formula. NS was defined as proteinuria greater than $50 \text{ mg/kg}\cdot\text{d}$ 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 $\pm$ 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.

Table 2
Relationship between glomerular diseases and sex

Pathological classification	Male	Female	P Value
Primary glomerulonephritis	1073(76.0)	639(64.4)	0.000
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	312(21.1)	336(33.9)	0.000
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	26(1.8)	17(1.7)	0.814
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	497(70.2)	1215(71.7)	0.464
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	177(25.0)	471(27.8)	0.160
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	34(4.8)	9(0.5)	0.000
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;

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

Table 4
Changes of spectrum in glomerulonephritis

Pathological classification	1999-2009	2009-2019	P Value
Primary glomerulonephritis	735(69.7)	977(72.5)	0.131
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	305(28.9)	343(25.4)	0.058
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	15(1.4)	28(2.1)	0.229
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;

Pathological classification	1999-2009	2009-2019	P Value
TBMN	5(0.5)	9(0.7)	0.536
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;			

Clinicopathologic Correlation Of Pediatric Glomerular Diseases

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	Clinical classification					
	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 PM_{2.5} in the air [23]. The highest proportion of MN in our study may be because our region has the highest level of PM_{2.5} 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

MN
membranous glomerulonephritis
MPGN
membranoproliferative glomerulonephritis
MsPGN
mesangial proliferative glomerulonephritis
SGN
sclerosing glomerulonephritis
TBMN
thin basement membrane nephropathy
SLE
systemic lupus erythematosus.

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.

Funding

No funding was received for this study.

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.

Acknowledgement

The authors are grateful to the participating team for their precious work.

Authors' information

Li-Jun Jiang¹, Xue Zhao¹, Zhi-Yan Dou¹, Zan-Hua Rong^{1*}, Lin Yang^{2*}

¹Department of Pediatrics, the Second Hospital of Hebei Medical University, Shijiazhuang 050000, China.

²Department of Nephrology, the Second Hospital of Hebei Medical University, Shijiazhuang 050000, China.

*Corresponding author (Zan-Hua Rong, e-mail: rong22501@163.com; Lin Yang, e-mail: yanglin2943@163.com)

References

1. Harambat J, Van Stralen KJ, Kim JJ, et al. Epidemiology of chronic kidney disease in children. *Pediatr Nephrol.* 2012;27(3):363–73.
2. Greenbaum LA, Warady BA, Furth SL. Current advances in chronic kidney disease in children: growth, cardiovascular, and neurocognitive risk factors. *Semin Nephrol.* 2009;29(4):425–34.
3. Shroff R, Ledermann S. Long-term outcome of chronic dialysis in children. *Pediatr Nephrol.* 2009;24(3):463–74.
4. Lewis MA, Shaw J, Sinha MD, et al. UK Renal Registry 12th Annual Report (December 2009): chapter 14: demography of the UK paediatric renal replacement therapy population in 2008. *Nephron Clin Pract.* 2010;115 suppl 1:c279-88.
5. Hattori S, Yosioka K, Honda M, et al. The 1998 report of the Japanese National Registry data on pediatric end-stage renal disease patients. *Pediatr Nephrol.* 2002;17(6):456–61.
6. Zhou F-D, Zhao M-H, Zou W-Z, et al. The changing spectrum of primary glomerular diseases within 15 years: A survey of 3331 patients in a single Chinese centre. *Nephrol Dial Transplant.* 2009;24(3): 870–6.
7. Vachvanichsanong P, Dissaneewate P, McNeil E. Childhood chronic kidney disease in a developing country. *Pediatr Nephrol.* 2008;23(7):1143–7.
8. Bhimma R, Adhikari M, Asharam K, et al. The spectrum of chronic kidney disease (stages 2–5) in KwaZulu-Natal, South Africa. *Pediatr Nephrol.* 2008;23(10):184–6.

9. Miller ME, Williams JA. Chronic renal failure in Jamaican children—an update (2001–2006). *West Indian Med J*. 2009;58(3):231–4.
10. Arapović A, Vukojević K, Filipović N, et al. Epidemiology of 10-year paediatric renal biopsies in the region of southern Croatia. *BMC Nephrol*. 2020;21(1):65.
11. Mohapatra A, Kakde S, Annapandian VM, et al. Spectrum of biopsy proven renal disease in South Asian children: Two decades at a tropical tertiary care centre. *Nephrology (Carlton)*. 2018;23(11):1013–22.
12. Nie S, He W, Huang T, et al. The Spectrum of Biopsy-Proven Glomerular Diseases among Children in China: A National, Cross-Sectional Survey. *Clin J Am Soc Nephrol*. 2018;13(7):1047–54.
13. Yin X-L, Zou M-S, Zhang Y, et al. Twenty-three-year review of disease patterns from renal biopsies: an experience from a pediatric renal center. *J Nephrol*. 2013;26(4):699–707.
14. Santangelo L, Netti GS, Giordano P, et al. Indications and results of renal biopsy in children: a 36-year experience. *World J Pediatr*. 2018;14(2):127–33.
15. Wenderfer SE, Gaut JP. Glomerular Diseases in Children. *Adv Chronic Kidney Dis*. 2017;24(6):364–71.
16. Jiang M, Xiao Z, Rong L, et al. Twenty-eight-year review of childhood renal diseases from renal biopsy data: A single centre in China. *Nephrology (Carlton)*. 2016;21(12):1003–9.
17. Bakr A, Eid R, Sarhan A, et al. Pathological profile of biopsied Egyptian children with primary nephrotic syndrome: 15-year single center experience. *J Nephrol*. 2014;27(4):419–23.
18. Okpechi IG, Ameh OI, Bello AK, et al. Epidemiology of Histologically Proven Glomerulonephritis in Africa: A Systematic Review and Meta-Analysis. *PLoS One*. 2016;11(3):e0152203.
19. Paripović D, Kostić M, Kruščić D, et al. Indications and results of renal biopsy in children: a 10-year review from a single center in Serbia. *J Nephrol*. 2012;25(6):1054–9.
20. O'Shaughnessy MM, Hogan SL, Poulton CJ, et al. Temporal and Demographic Trends in Glomerular Disease Epidemiology in the Southeastern United States, 1986–2015. *Clin J Am Soc Nephrol*. 2017;12(4):614–23.
21. Sui M, Ye X, Ma J, et al. Epidemiology and risk factors for chronic kidney disease in Chinese patients with biopsy-proven lupus nephritis. *Intern Med J*. 2015;45(11):1167–72.
22. Tang L, Yao J, Kong X, et al. Increasing prevalence of membranous nephropathy in patients with primary glomerular diseases: A cross-sectional study in China. *Nephrology (Carlton)*. 2017;22(2):168–73.
23. Xu X, Wang G, Chen N, et al. Long-Term Exposure to Air Pollution and Increased Risk of Membranous Nephropathy in China. *J Am Soc Nephrol*. 2016;27(12):3739–46.
24. Ding Y, He J, Guo J-P, et al. Gender differences are associated with the clinical features of systemic lupus erythematosus. *Chin Med J(Engl)*. 2012;125(14):2477–81.
25. Mu Q, Zhang H, Liao X, et al. Control of lupus nephritis by changes of gut microbiota. *Microbiome*. 2017;5(1):73.

26. Wang J, Syrett CM, Kramer MC, et al. Unusual maintenance of X chromosome inactivation predisposes female lymphocytes for increased expression from the inactive X. Proc Natl Acad Sci USA. 2016;113(14):E2029-38.

Figures

Figure 1

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;