



Effect of hypertension on the long-term prognosis of children with primary focal segmental glomerulosclerosis—a retrospective cohort study

Linlin Huang^{1,2}, Wentao Peng^{1,3}

¹Nursing Department of West China Second Hospital, Sichuan University, Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, Chengdu, China; ²West China School of Nursing, Sichuan University, Chengdu, China; ³Nursing Department, Chengdu Qingbaijiang Maternal and Child Health Hospital, Chengdu, China

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Correspondence to: Wentao Peng, Nursing Department of West China Second Hospital, Sichuan University, Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, No. 20 Section 3 Renmin South Road, Wuhou District, Chengdu, Sichuan 610041, China; Chengdu Qingbaijiang Maternal and Child Health Hospital, No. 87 Qingjiang South Road, Qingbaijiang District, Chengdu, Sichuan 610041, China. Email: scuwlzx@163.com.

Background: Primary focal segmental glomerulosclerosis is a common clinicopathologic syndrome. More than 50% of the patients may have hypertension, which can further deteriorate the renal function of patients. However, the impact of hypertension on the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis is still unclear. The end-stage renal disease greatly increases medical costs and mortality. Studying the related factors of end-stage renal disease is helpful to prevent and treat end-stage renal disease. This study aimed to explore the impact of hypertension on the long-term prognosis of children with primary focal segmental glomerulosclerosis.

Methods: The data of 118 children with primary focal segmental glomerulosclerosis admitted to the Nursing Department of West China Second Hospital from January 2012 to January 2017 were retrospectively collected. The children were divided into a hypertension group (n=48) and a control group (n=70) according to whether they had hypertension. The children were followed up (by clinic visit and telephone interviews) for 5 years to compare the differences in the incidence of end-stage renal disease between the two groups.

Results: Compared with the control group, the proportion of patients with severe renal tubulointerstitial damage in the hypertension group was significantly higher (18.75% vs. 5.71%, $P=0.026$). Moreover, the incidence of end-stage renal disease was markedly higher (33.33% vs. 5.71%, $P<0.001$). Both systolic and diastolic blood pressure had a certain value in predicting the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis ($P<0.001$ and $P=0.025$, respectively), and the predictive value of systolic blood pressure was relatively higher. Multivariate logistic regression analysis showed that hypertension was risk factors for end-stage renal disease in children with primary focal segmental glomerulosclerosis ($P=0.009$, relative risk: 17.022, 95% CI: 2.045–141.723).

Conclusions: Hypertension was a risk factor for poor long-term prognosis in children with primary focal segmental glomerulosclerosis. For primary focal segmental glomerulosclerosis children with hypertension, blood pressure should be actively controlled to prevent the development of end-stage renal disease. Moreover, due to the high incidence of end-stage renal disease, we should monitor the end-stage renal disease during follow-up.

Keywords: Hypertension; primary focal segmental glomerulosclerosis; children; end-stage renal disease

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Introduction

Primary focal segmental glomerulosclerosis is a common clinicopathological syndrome that involves hematuria, albuminuria, edema, hypertension, and abnormal renal function, and lacks specificity. Acute renal failure and albuminuria are common complications (1,2). Spherical sclerosis occurs with the expansion and fusion of segmental sclerosis. At the same time, because of segmental sclerosis, the glomerular filtrate enters into the gap between the Baumann's bursa and parietal epithelial cells, gradually peels off the glomerular pole, and then further peels off the epithelial cells and basement membrane of renal tubules. The lesion invades the downstream nephron along the renal tubules, resulting in focal tubular atrophy, renal interstitial fibrosis, and acute renal injury, which eventually lead to renal failure (3-5). About 50% of patients with primary focal segmental glomerulosclerosis can be accompanied by hypertension, which can further promote the development of end-stage renal disease. However, hypertension is a chronic disease, and some children have poor compliance and cannot control blood pressure well. Moreover, the effect of hypertension on the long-term prognosis of children with primary focal segmental glomerulosclerosis is still unclear. Studying the related factors of end-stage renal disease is helpful to prevent and treat end-stage renal disease. This study aimed to explore the impact of

hypertension on the long-term prognosis of children with primary focal segmental glomerulosclerosis. We present the following article in accordance with the STARD reporting checklist (available at <https://tp.amegroups.com/article/view/10.21037/tp-22-649/rc>).

Methods

General information

The data of 118 children with primary focal segmental glomerulosclerosis admitted to the Nursing Department of West China Second Hospital from January 2012 to January 2017 were retrospectively collected. The children were divided into a hypertension group (n=48) and a control group (n=70) according to whether they had hypertension, and were followed up for 5 years to compare the difference in prognosis between the two groups. The inclusion criteria were as follows: (I) primary focal segmental glomerulosclerosis diagnosed by renal biopsy; (II) aged 3–17 years; and (III) complete clinical medical records. The exclusion criteria were as follows: (I) lost to follow-up; (II) secondary infection; (III) malignant tumor; (IV) solitary kidney; (V) diabetes nephropathy, immunoglobulin A nephropathy, membranous nephropathy, lupus nephritis, purpura nephritis, and other nephropathies; (VI) secondary focal segmental glomerulosclerosis; and (VII) cases in which end-stage renal disease had been diagnosed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Nursing Department of West China Second Hospital (No. 2022KY-0098), and the requirement for the patients' written informed consent for this retrospective clinical study was waived.

Study variables

Clinicopathological features such as age at diagnosis, gender, systolic blood pressure, diastolic blood pressure, hematuria, albuminuria, edema, glomerular filtration rate, and biopsy pathological results were collected retrospectively. The renal biopsy pathological results included the classification of primary focal segmental glomerulosclerosis (non-specific type, apical type, collapsed type, cellular type, and

Highlight box

Key findings

- Hypertension was a risk factor for poor long-term prognosis in children with primary focal segmental glomerulosclerosis.

What is known and what is new?

- More than 50% of primary focal segmental glomerulosclerosis patients may have hypertension, which can further deteriorate the renal function.
- The incidence of end-stage renal disease was associated with hypertension.

What is the implication, and what should change now?

- For primary focal segmental glomerulosclerosis children with hypertension, blood pressure should be actively controlled to prevent the development of end-stage renal disease.

periportal type) (6), the glomerulosclerotic ratio, the degree of tubulointerstitial disease, and the degree of foot process fusion (divided into extensive fusion and segmental fusion by 50%). According to the cumulative area of the cortical lesions, tubulointerstitial lesions were divided into mild disease (<25%), moderate disease (25–50%), and severe disease (>50%).

Treatment

All children were given hormone and/or immunosuppressive therapy. Also, children with hypertension were treated according to the Hypertension Guidelines for Children and Adolescents issued by the United States in 2017 (7).

Follow-up

The children were followed up for more than 5 years to observe the incidence of end-stage renal disease. Follow-up was carried out through outpatient visits and telephone interviews.

Definition

End-stage renal disease in children was defined as a glomerular filtration rate <15 mL/(min·1.73 m²) or necessary renal replacement therapy (dialysis ≥3 months or renal transplantation).

Statistical analysis

SPSS 26.0 software (IBM, USA, Chicago) was used for data analysis. All measurement data conformed to a normal distribution and were expressed as the mean ± standard deviation, and the differences between the two groups were analyzed using an independent sample *t*-test. All counting data were expressed as n (%), and the chi-square test was used to analyze the differences between the two groups. The receiver operating characteristic (ROC) curve was used to analyze the predictive value of systolic and diastolic blood pressure for the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis. The Kaplan-Meier survival estimate was used to analyze the cumulative survival rate, and multivariate logistics regression analysis was applied to explore the risk factors of end-stage renal disease in children with primary focal segmental glomerulosclerosis. *P*<0.05 indicated that the difference was statistically significant.

Results

Comparison of the clinicopathological characteristics between the two groups

Compared with the control group, the proportion of patients with severe renal tubulointerstitial damage (18.75% vs. 5.71%, *P*=0.026) and the incidence of end-stage renal disease (33.33% vs. 5.71%, *P*<0.001) in the hypertension group were significantly higher (Table 1).

The predictive value of systolic blood pressure and diastolic blood pressure on the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis

Systolic and diastolic blood pressure had a certain value in predicting the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis (area under the curve: 0.752, 95% CI: 0.627–0.877, *P*<0.001; area under the curve: 0.659, 95% CI: 0.530–0.788, *P*=0.025), and the predictive value of systolic blood pressure was relatively higher (Table 2 and Figure 1).

Comparison of the incidence of end-stage renal disease in children

Compared with the control group, the cumulative incidence of end-stage renal disease in the hypertensive group was markedly higher (*P*<0.001) (Figure 2).

The risk factors of end-stage renal disease in children with primary focal segmental glomerulosclerosis

Multivariate logistic regression analysis showed that hypertension and severe renal tubulointerstitial disease were risk factors for end-stage renal disease in children with primary focal segmental glomerulosclerosis (*P*=0.009 and *P*<0.001, respectively) (Table 3).

Discussion

Primary focal segmental glomerulosclerosis can occur at any age, but it is more common in children and adolescents. End-stage renal disease caused by primary focal segmental glomerulosclerosis has increased the burden on families and society. The prevention and treatment of end-stage renal disease are key to the treatment of primary focal segmental glomerulosclerosis. Therefore, we designed this study to

Table 1 Comparison of clinicopathological characteristics between the two groups

Variables	Hypertension group (n=48)	Control group (n=70)	t/ χ^2 value	P value
Age at diagnosis (Years)	11.42±4.12	10.90±3.41	0.742	0.459
Gender			0.120	0.729
Male	11 (22.92%)	18 (25.71%)		
Female	37 (77.08%)	52 (74.29%)		
Systolic blood pressure (mmHg)	165.77±14.02	115.27±13.96	19.270	<0.001
Diastolic blood pressure (mmHg)	99.58±14.56	72.21±8.74	12.744	<0.001
Hematuria	25 (52.08%)	34 (48.57%)	0.140	0.708
Albuminuria	25 (52.08%)	39 (55.71%)	0.151	0.697
Edema	30 (62.50%)	32 (45.71%)	0.116	0.734
Glomerular filtration rate [mL/(min·1.73 m ²)]	107.94±19.02	111.51±23.89	0.866	0.388
Pathological type			3.656	0.454
Non-specific type	16 (33.33%)	23 (32.86%)		
Apical type	11 (22.92%)	18 (25.71%)		
Collapsed type	10 (20.83%)	7 (10.00%)		
Cellular type	5 (10.42%)	13 (18.57%)		
Periportal type	6 (12.50%)	9 (12.86%)		
Proportion of glomerulosclerosis (%)	11.08±4.00	11.41±4.95	0.385	0.701
Degree of tubulointerstitial lesion			4.936	0.026
Mild and moderate	39 (81.25%)	66 (94.29%)		
Severe	9 (18.75%)	4 (5.71%)		
End-stage renal disease	16 (33.33%)	4 (5.71%)	15.431	<0.001

Data are presented as n (%) or mean ± standard deviation.

Table 2 The predictive value of blood pressure for the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis

Test result variable(s)	Area under the curve	P value	95% CI	
			Lower bound	Upper bound
Systolic blood pressure	0.752	<0.001	0.627	0.877
Diastolic blood pressure	0.659	0.025	0.530	0.788

identify the risk factors for the development of end-stage renal disease in primary focal segmental glomerulosclerosis children. The results showed that hypertension was a risk factor for the development of end-stage renal disease in primary focal segmental glomerulosclerosis patients.

The pathological characteristics of primary focal segmental glomerulosclerosis involves the focal distribution

of the segmental sclerotic glomeruli, most of which have spherical sclerosis, accompanied by different degrees of podocyte proliferation, segmental endothelial cell and mesangial cell proliferation, renal tubular epithelial cell injury and focal atrophy, renal interstitial focal lymphocyte, monocyte infiltration, and fibrosis (8-10). When primary focal segmental glomerulosclerosis develops further, it can

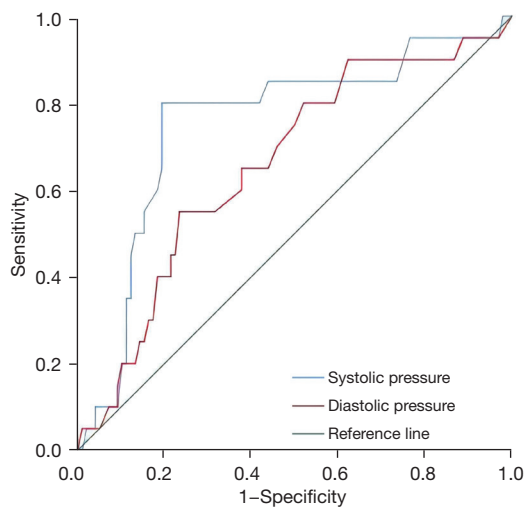


Figure 1 The predictive value of systolic blood pressure and diastolic blood pressure for the development of end-stage renal disease in children with primary focal segmental glomerulosclerosis.

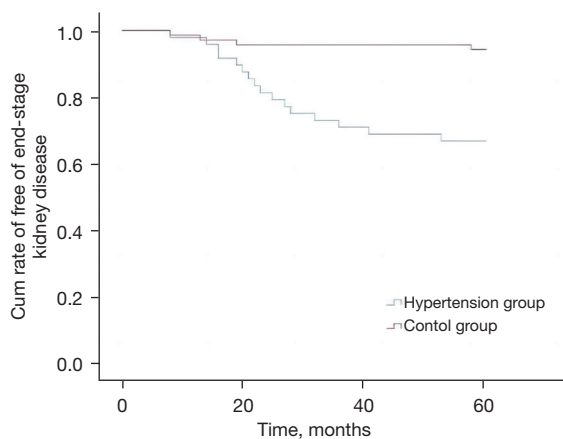


Figure 2 Comparison of the incidence of end-stage renal disease in children.

lead to renal insufficiency and hypertension. The mechanisms of primary focal segmental glomerulosclerosis causing hypertension mainly involve: (I) the activation of the renin-angiotensin system leads to the increase of renin-angiotensin secretion, resulting in hypertension (11-13); and (II) water and sodium retention due to renal insufficiency causes excessive blood volume, which leads to hypertension (14-16). Malignant hypertension can also promote glomerular filtration rate decline, atrophy of renal tubules, and renal interstitial fibrosis, leading to the development of end-stage renal disease and eventually forming a vicious circle (17).

Hypertension can also lead to secondary focal segmental glomerulosclerosis (18). A previous study showed that 41.00% of patients with primary focal segmental glomerulosclerosis were accompanied by hypertension, promoting the development of renal insufficiency (19), which is consistent with the results of this study. The present study showed that 40.68% (48/118) of children with primary focal segmental glomerulosclerosis had hypertension, which was related to the final development of end-stage renal disease. In addition, this study also showed that severe tubulointerstitial disease was a risk factor for end-stage renal disease in children with primary focal segmental glomerulosclerosis ($P < 0.001$). Severe tubulointerstitial disease is a direct manifestation of the severity of primary focal segmental glomerulosclerosis. In patients with severe tubulointerstitial disease, more than 50% of tubulointerstitial lesions occurred and a large number of necrotic tissues were found in the tubulointerstitial. Patients with severe tubulointerstitial disease may eventually develop into end-stage renal disease.

Limitations

This study was a retrospective clinical study, and the number of cases was relatively insufficient.

Table 3 Risk factors of end-stage renal disease in children with primary focal segmental glomerulosclerosis

Variables	B	SE	Wald	P value	Relative risk (95% CI)
Hypertension	2.835	1.081	6.872	0.009	17.022 (2.045–141.723)
Severe renal tubulointerstitial disease	5.628	1.398	16.211	<0.001	278.091 (17.963–4,305.099)
Constant	-12.595	3.542	12.644	<0.001	

SE, standard error.

Conclusions

Predicting the occurrence and development of different diseases has been a hot research topic in recent years, with scholars aiming to predict the prognosis of patients and guide treatment (20-24). The present study found that hypertension was a risk factor for poor long-term prognosis in children with primary focal segmental glomerulosclerosis. Therefore, for children with primary focal segmental glomerulosclerosis with hypertension, blood pressure should be actively controlled to prevent the development of end-stage renal disease in children.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at <https://tp.amegroups.com/article/view/10.21037/tp-22-649/rc>

Data Sharing Statement: Available at <https://tp.amegroups.com/article/view/10.21037/tp-22-649/dss>

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <https://tp.amegroups.com/article/view/10.21037/tp-22-649/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Nursing Department of West China Second Hospital (No. 2022KY-0098), and the requirement for the patients' written informed consent for this retrospective clinical study was waived.

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