



Clinical follow-up study of 166 cases of children with hypertension

Zhenquan Wang, Yiping Shao, Jiahui Jin, Xing Rong, Huixian Qiu, Rongzhou Wu, Maoping Chu

Children's Heart Center, The Second Affiliated Hospital and Yuying Children's Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China

Contributions: (I) Conception and design: Z Wang, Y Shao; (II) Administrative support: R Wu, M Chu; (III) Provision of study materials or patients: X Rong, H Qiu, M Chu; (IV) Collection and assembly of data: Y Shao, Z Wang; (V) Data analysis and interpretation: Z Wang, Y Shao, J Jin; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Maoping Chu. Children's Heart Center, The Second Affiliated Hospital and Yuying Children's Hospital, Wenzhou Medical University, No. 109 Xueyuan Xi Road, Wenzhou, Zhejiang 325027, China. Email: chmping@hotmail.com.

Background: Childhood hypertension is a challenge for pediatricians to discover and diagnose. We sought to analyze its clinical characteristics and related risk factors in patients at a single center.

Methods: From 2009 to 2019, 166 children with hypertension were retrospectively analyzed, and their clinical manifestations and relevant laboratory data were collected for statistical analysis.

Results: A total of 120 males and 46 females were included in this study. Males were more common than females ($P=0.012$), and 86.7% were from rural areas. Hypertension appeared in all age groups, but most of them were puberty (52.4%). Most primary hypertension cases (57/91) had no obvious clinical symptoms, and BMI (OR 1.085, 95% CI: 1.004–1.173, $P=0.038$) and a family history of hypertension (OR 5.605, 95% CI: 2.229–14.092, $P<0.001$) were the risk factors. In the 75 secondary hypertension cases, renal hypertension (62.7%) was the main cause and headache and dizziness were the most common symptoms, and the serum urea is a risk factor (OR 1.524, 95% CI: 1.037–2.239, $P=0.032$).

Conclusions: BMI and a family history of hypertension were associated with primary hypertension. The serum urea was related to secondary hypertension. Emphasis on family history, strengthening family health management and education and publicity of hypertension, were important for diagnosis and detection of children with hypertension.

Keywords: Childhood hypertension; regional distribution; sex; risk factors

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Introduction

Hypertension has long been perceived as a disease of adults, rarely seen in children and adolescents, though recent reports reveal it has become a major public health problem in children worldwide (1). The prevalence of hypertension in children and adolescents reaches 3% to 6%, while the total prevalence of obese adolescents has increased nearly five times, reaching about 30% (2). Equally concerning, hypertension is a lifelong disease; childhood hypertension is one of the most important risk factors for cardiovascular disease in adulthood, causing damage to target organs and worsening with age (3). Although the prevalence of hypertension in children is increasing, many children with

hypertension are misdiagnosed or not diagnosed.

Numerous studies have confirmed that elevated blood pressure in childhood is associated with increased risk of hypertension and metabolic diseases in adults (4). As the time frame of hypertension diagnosis could influence outcome of children in terms of growth development and prognosis, it is critical to make an early diagnosis and draw up treatment and management measures as soon as possible. This study sought to analyze the epidemiological distribution of hypertension in children in Wenzhou, China, determine its clinical characteristics, evaluate the possible risk factors related to its incidence, and evaluate whether these characteristics can provide clinical guidance. We present the following article in accordance with the

STROBE reporting checklist (available at <https://dx.doi.org/10.21037/tp-20-446>).

Methods

Participants

From 2009 to 2019, 166 children (0 < age < 18) were diagnosed with hypertension in Yuying Children's Hospital, the Second Affiliated Hospital of Wenzhou Medical University. These patients were divided into two groups: primary hypertension group (91 cases) and secondary hypertension group (75 cases).

Methods

This is a retrospective study. The following data were collected for each patient: (I) epidemiological and clinical characteristics including age, gender, regional distribution, height, weight, body mass index (BMI); (II) related laboratory indicators: urinary protein, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol; and (III) data from special examinations such as echocardiography, electrocardiogram, or abdominal echocardiography.

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of The Second Affiliated Hospital and Yuying Children's Hospital (LCKY2018-79). Individual consent for this retrospective analysis was waived.

Inclusion criteria

On the basis of the clinical practice guidelines for children with hypertension developed by the American Academy of Pediatrics in 2017 (1) and the updated Chinese hypertension diagnosis guidelines (5), patients were included if they had hypertension, defined in children aged 1–13 years as average clinic measured SBP and/or DBP \geq 95th percentile (on the basis of age, sex and height percentile); and in children over 13 years old as \geq 130/80 mmHg. Patients with white coat hypertension (WCH, it refers to the scenario in which BPs are elevated in the office but normal outside the office) (6), transient hypertension, or postoperative hypertension were excluded from the analysis.

Follow-up process

Long-term outpatient follow-up after discharge is

recommended for all children. For various reasons, children who are unable to follow-up with our clinic are advised to visit local community hospitals or health clinics regularly. At the same time, we conducted an online survey for all children on the status and results of follow-up visits. If the condition changes, it is recommended to go to our hospital for further treatment.

Statistical analysis

IBM SPSS Statistics® version 22.0 software (Armonk, NY, USA) was used for these analyses. In the data, continuous variables were described as mean \pm standard deviation or median; categorical variables were percentages of the number of cases. In the univariate analysis, the chi-square test and Mann-Whitney U test were used to screen for related factors of the two groups, and logistic regression analysis was used to determine risk factors for primary and secondary hypertension. Differences with $P < 0.05$ were considered statistically significant.

Results

Age and gender distribution characteristics of children with hypertension

As *Figure 1* depicts, from 2009 to 2019, our centers diagnosed hypertension in 166 children, including 120 males and 46 females. There were more males than females in both primary hypertension (M:F ratio = 4.06:1) and secondary hypertension (M: F = 1.68:1) ($P = 0.012$). As shown in *Table 1* and *Figure 2*, the age of the children ranged from 3 months to 17 years, with a median age of 13 years. The distribution of primary hypertension or secondary hypertension is mainly puberty (59.3% and 44.0%, respectively). And 39.2% (65/166) of the total population were pubertal males. Most of the children with primary hypertension had a family history of hypertension (53.8% *vs.* 16.0%, $P < 0.001$). And most primary hypertension was found after a health examination (53.8% *vs.* 10.7%, $P < 0.001$).

Regional distribution characteristics of children with hypertension

The Second Affiliated Hospital of Wenzhou Medical University, serving the central city and beyond. Only 13.3% of the children came from Wenzhou central city, with the

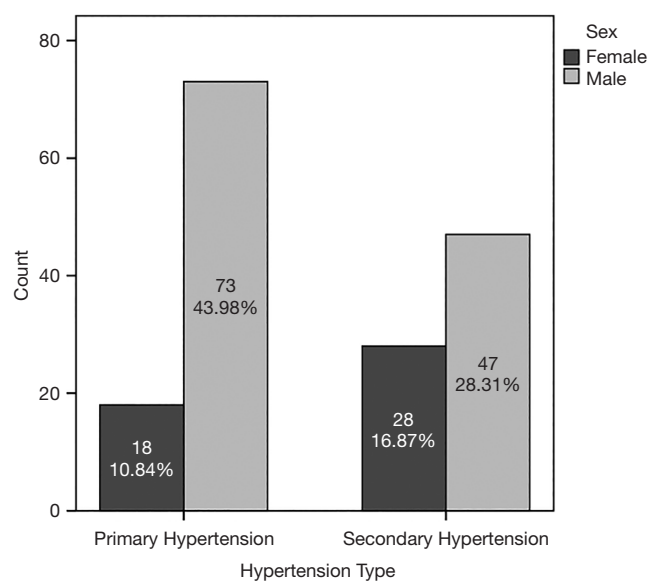


Figure 1 Comparison of sex between primary hypertension and secondary hypertension.

majority (86.7%) coming from rural areas in Wenzhou (71.7%) and outside Wenzhou (15.0%). This distribution is shown in *Figure 3*.

Clinical characteristics and special examination of children with hypertension

Clinical manifestations of children with primary hypertension

At the routine physical examination, 50/91 (54.9%) children with primary hypertension were asymptomatic. Among the symptomatic children, the most common clinical symptoms were dizziness or headache (36/40), which was generally most noticeable after getting up in the morning. There were 11 cases with chest tightness (2 cases) and palpitation (10 cases). And other symptoms are less common, such as blurred vision (2 cases) and syncope (1 case).

Clinical manifestation in children with secondary hypertension

Only 15/75 (20.0%) children with secondary hypertension were asymptomatic. Headaches and/or dizziness (28 cases) were the most common symptoms in 61 of children with secondary hypertension. Digestive system symptoms (24 cases) include abdominal pain and vomiting; secondly, 15 cases of convulsion and 5 cases of edema; 1 patient had cardiovascular system involvement including increased

heart rate, chest tightness.

Etiology of secondary hypertension in children

As shown in *Figure 4*, in 75 cases of secondary hypertension, renal hypertension was the primary cause, mainly related to kidney diseases such as glomerulonephritis and chronic renal failure, accounted for 62.7%. Hypertension induced by connective tissue disease was the secondary cause (12.0%). Secondly, endocrine hypertension, accounted for 10.7%, cardiovascular hypertension about 9.3%, and the remainder included neurosystemic hypertension (2.70%) and drug-induced hypertension (2.70%).

Follow up of children with primary and secondary hypertension

Subsequently, all 166 cases of children diagnosed with hypertension were followed up, as shown in *Table 2*. In primary hypertension, 29 children kept their blood pressure within the normal range after discharge from hospital, 25 of whom were not taking antihypertensive drugs, and in 4 who were. However, there were also 28 children with poorly controlled blood pressure, 12 of whom were taking antihypertensive drugs, and 16 of them did not take medication. Among those with secondary hypertension, 25 children had controlled blood pressure, of whom 15 were not taking antihypertensive drugs, and 10 took antihypertensive drugs to lower their blood pressure. However, 10 children failed to control their blood pressure even after taking antihypertensive drugs. Finally, 63 cases did not receive regular monitoring and follow-up (33 cases of primary hypertension and 30 cases of secondary hypertension). Ten children were lost to contact.

Comparison of different indices of childhood hypertension

As shown in *Table 3*, the BMI of children with primary hypertension was significantly higher than in those with secondary hypertension (23.2 ± 5.52 vs. 20.5 ± 6.48 , $P=0.004$), while triglycerides (1.14 vs. 1.38 mmol/L, $P=0.026$), total cholesterol (4.01 vs. 4.43 mmol/L, $P=0.001$), low-density lipoprotein cholesterol (2.15 vs. 2.56 mmol/L, $P=0.002$) and serum urea (4.06 vs. 4.79 mmol/L, $P<0.001$) were significantly lower in those with secondary hypertension. Logistic analysis was performed for the correlation between primary hypertension and secondary hypertension (*Table 4*). The results showed that male (OR 2.416, 95% CI: 1.204–4.848, $P=0.013$), age (OR 1.093, 95% CI: 1.006–1.187,

Table 1 General information of children

	Primary hypertension	Secondary hypertension	P value
Total count	91	75	166
Sex			0.012
Male	73 (80.2%)	47 (62.7%)	
Female	18 (19.8%)	28 (37.3%)	
Age distribution			0.151
Infancy (<1 y)	0	1 (1.3%)	
Early childhood (1–3 y)	3 (3.3%)	7 (9.3%)	
Preschool (4–6 y)	4 (4.4%)	5 (6.7%)	
School age (7–12 y)	30 (33.0%)	29 (38.7%)	
Puberty (≥13 y)	54 (59.3%)	33 (44.0%)	
Health examination	49 (53.8%)	8 (10.7%)	<0.001
Family history of hypertension	49 (53.8%)	12 (16.0%)	<0.001

Data are presented as N (%).

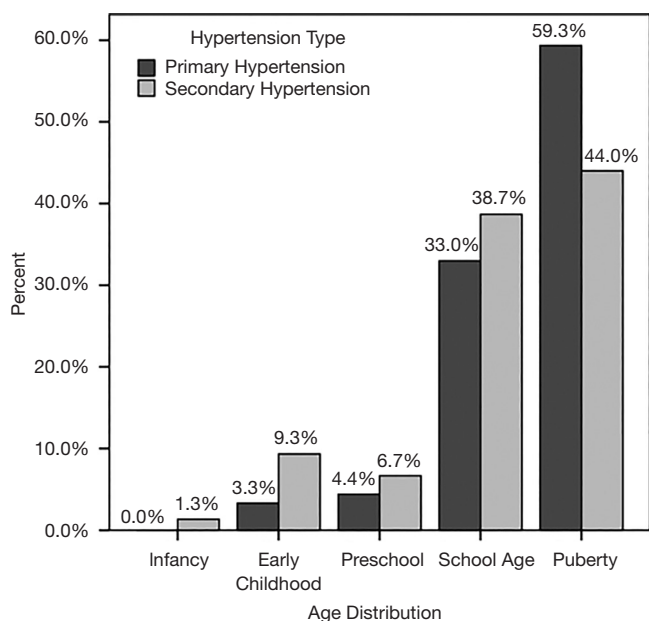


Figure 2 Comparison of age distribution between primary hypertension and secondary hypertension.

P=0.035), BMI (OR 1.083, 95% CI: 1.024–1.145, P=0.005) and a family history of hypertension (OR 6.125, 95% CI: 2.916–12.867, P<0.001) were risk factors for primary hypertension. When we adjusted for confounding factors, such as age, sex, BMI (OR 1.085, 95% CI: 1.004–1.173, P=0.038) and a family history (OR 5.605, 95% CI:

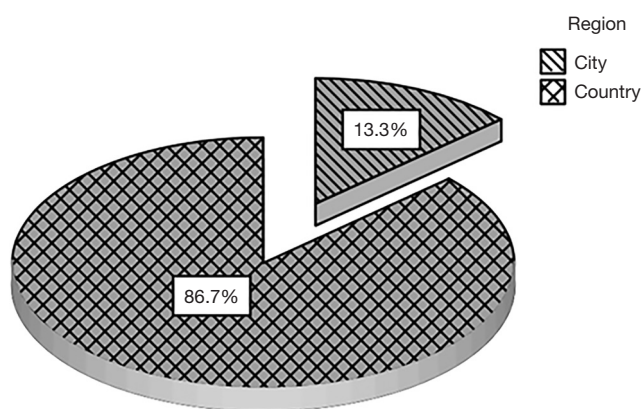


Figure 3 Characteristics of regional distribution.

2.229–14.092, P<0.001) remained the risk factor for primary hypertension. We also analyzed the risk factors for secondary hypertension, and the results showed that total cholesterol (OR 2.123, 95% CI: 1.393–3.236, P<0.001), low density lipoprotein cholesterol (OR 2.156, 95% CI: 1.312–3.544, P=0.002), serum urea (OR 1.438, 95% CI: 1.163–1.779, P=0.001) and creatinine (OR 1.008, 95% CI: 1.001–1.015, P=0.023) were risk factors for secondary hypertension. And after adjusting for confounders such as age and sex, as shown in Table 5, serum urea is still a risk factor for secondary hypertension (OR 1.524, 95% CI: 1.037–2.239, P=0.032).

Discussion

In this study, we analyzed the epidemiological distribution of hypertension in children, determined its clinical characteristics, evaluated the possible risk factors related to its incidence. In this study, we found primary hypertension to be more common than secondary hypertension in children, and renal diseases were the most common in secondary hypertension. A family history of hypertension and increased BMI were related to primary hypertension, and elevated LDL-C and serum urea were associated with secondary hypertension. For children with elevated blood pressure or hypertension, the history and family history should be inquired carefully, and blood pressure should be checked regularly.

Hypertension is classified into two types: primary and secondary, according to the etiology. Primary hypertension refers to disease with elevated blood pressure for which the cause is unknown; while the cause of secondary hypertension is clear, hypertension is only one of the clinical manifestations of an underlying disease. Previous studies (7) have suggested that secondary hypertension is the main cause of hypertension in children and adolescents. However, in 2017, the American Academy of Pediatrics “Clinical Practice Guidelines For Screening And Management Of Hypertension In Children And Adolescents” found that primary hypertension was becoming more prevalent than secondary hypertension (3). Our 10-year retrospective study found 91 cases of primary hypertension versus 75 cases of secondary hypertension, consistent with the American Academy of Pediatrics findings. With the increasing rate of obesity in children, primary hypertension has become one of the most common diseases in children (8,9).

In our study, hypertension more commonly affected male patients than female patients, regardless of whether it was primary or secondary hypertension, showing significant differences between sex. These differences, consistent with reports in adult patients (10), may be related to differences in living habits, lifestyle, diet, and environmental and other factors between men and women. In addition, as reported in other studies (11), the distribution of hypertension skewed toward adolescents, and the overall trend of the number of patients increased with age (12). The increase in the number of adolescent patients with hypertension is not only related to the period of rapid growth and development, but also to sex hormones, growth hormones and cortisol, making adolescent children more likely than other age groups to present with hypertension (4,13).

Health education is very crucial to discover and follow

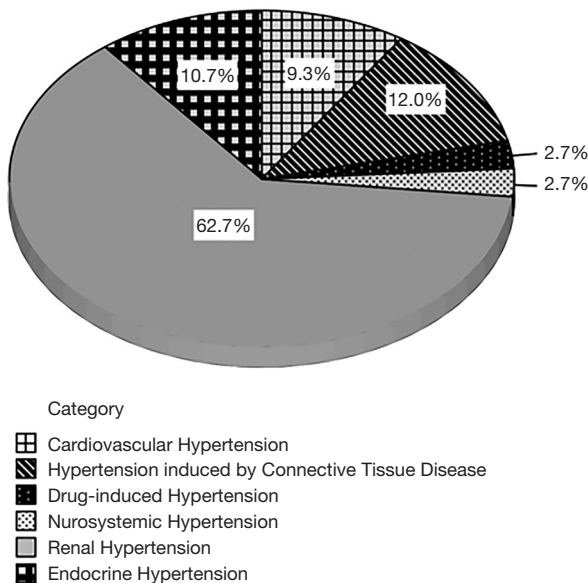


Figure 4 Characteristic of etiology of secondary hypertension.

Table 2 Follow up of children with primary and secondary hypertension

	Follow-up		
	Primary hypertension (N)	Secondary hypertension (N)	Total count
Good blood pressure control, no antihypertensive drugs	25	15	40
Good blood pressure control is OK, take antihypertensive drugs	4	10	14
Poor blood pressure control, take antihypertensive drugs	12	10	22
Poor blood pressure control, no antihypertensive drugs	16	1	17
No monitoring	33	30	63
Loss to follow-up	2	8	10

Table 3 comparison of different indexes between primary and secondary hypertension

	Primary hypertension	Secondary hypertension	P value
Age (year old)	13.0 (12.0–14.0)	12.0 (9.0–15.0)	0.091
BMI	23.2±5.52	20.5±6.48	0.004
Triglyceride (mmol/L)	1.14 (0.835–1.73)	1.38 (0.97–2.18)	0.026
Total cholesterol (mmol/L)	4.01 (3.53–4.58)	4.43 (3.98–5.40)	0.001
High density lipoprotein cholesterol (mmol/L)	1.13 (0.99–1.29)	1.16 (0.94–1.44)	0.576
Low density lipoprotein cholesterol (mmol/L)	2.15 (1.85–2.64)	2.56 (2.15–3.22)	0.002
Serum urea (mmol/L)	4.06 (3.49–4.61)	4.79 (3.52–8.18)	<0.001
Creatinine (μmol/L)	53.2 (42.9–63.7)	55.0 (34.3–123)	0.681
Urea/creatinine ratio	0.08 (0.06–0.09)	0.08 (0.06–0.12)	0.325
Uric acid	408 (346–484)	368 (273–456)	0.094

Data are presented as mean ± SD or median (Q1–Q3). BMI, body mass index.

Table 4 Multiple regression analysis of primary hypertension

	Non-adjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value
Sex (Male)	2.416 (1.204–4.848)	0.013	1.684 (0.606–4.683)	0.318
Age (year old)	1.093 (1.006–1.187)	0.035	1.027 (0.904–1.167)	0.682
BMI	1.083 (1.024–1.145)	0.005	1.085 (1.004–1.173)	0.038
Family history of hypertension	6.125 (2.916–12.867)	<0.001	5.605 (2.229–14.092)	<0.001
Total cholesterol (mmol/L)	0.471 (0.309–0.718)	<0.001	0.487 (0.190–1.246)	0.133
Low density lipoprotein cholesterol (mmol/L)	0.464 (0.282–0.762)	0.002	1.119 (0.335–3.734)	0.855

Statistic: odds ratio (95% confidence interval)/OR (95% CI). BMI, body mass index.

Table 5 Multiple regression analysis of secondary hypertension

	Non-adjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value
Sex (Male)	0.414 (0.206–0.830)	0.013	0.539 (0.201–1.446)	0.220
Age (year old)	0.915 (0.843–0.994)	0.035	0.863 (0.742–1.004)	0.056
Total cholesterol (mmol/L)	2.123 (1.393–3.236)	<0.001	1.228 (0.458–3.295)	0.683
Low density lipoprotein cholesterol (mmol/L)	2.156 (1.312–3.544)	0.002	1.717 (0.479–6.150)	0.406
serum urea (mmol/L)	1.438 (1.163–1.779)	0.001	1.524 (1.037–2.239)	0.032
Creatinine (μmol/L)	1.008 (1.001–1.015)	0.023	1.006 (0.981–1.031)	0.630

Statistic: odds ratio (95% confidence interval)/OR (95% CI).

up hypertension. Firstly, in this study, we found that most (86.7%) of the children with hypertension came from less-developed rural areas, while only 13.3% came from central cities. This is consistent with some findings reported in the literature (14,15). The lack of knowledge and education and the significant differences in cultural practices, living habits, living environments, and sources of information between urban and rural areas, these may be the reasons why there are more patients in rural areas than in urban areas (16).

Secondly, most of the children with primary hypertension (50/91) had no obvious symptoms and manifestations. Among these children, most of symptoms are mild or sporadic and can often be overlooked. This is also one of the reasons for the low rates of awareness and treatment of hypertension in children. On the one hand, children with hypertension have no obvious clinical signs in the early stage when it has not yet caused structural changes in the body organs (17). On the other hand, it also shows that society and families pay insufficient attention to the problem of hypertension in children, and lack of knowledge and education about hypertension in children. Thirdly, it is also indirectly supported by the phenomenon that abnormal blood pressure in 50 asymptomatic children was detected through a health examination in a medical institution rather than through home health monitoring. At last, we found that 76/166 patients had poor follow-up compliance after discharge, including casual withdrawal of medication, without monitoring of blood pressure changes, and irregular follow-up. These outcomes may be related to the following factors: asymptomatic hypertension, lack of attention to health knowledge, insufficient health education and publicity of hypertension. The above highlights the importance of health education and publicity. These views are similar to those reported in the literature (18). All of above showed the lack of knowledge, health education and publicity may be the risk factors of hypertension in children. The task of preventing hypertension is still very difficult (18).

From our study, BMI and a family history of hypertension were risk factors of primary hypertension. In parallel with increasing BMI, the prevalence of hypertension has been reported increased among children. Although BMI is the main factor responsible for increasing rate of hypertension among adolescent, genetic, and family history, susceptibility should not be ignored (19). Of course, previous studies also have found that preterm birth, birth by cesarean section, and family history of hypertension are risk factors for primary hypertension in children (20,21). Unfortunately, the birth history of these children has not been investigated

in this study. And further investigation could be carried out in the later period. Furthermore, after controlling for confounding factors, we found that serum urea is a risk factors for secondary hypertension in this study. Renal diseases are the most common secondary hypertension in children (22). High blood pressure is an important factors of impaired kidney function and kidney damage. Long-term hypertension affects renal function, which leads to serum urea filtration and reabsorption dysfunction (23). Elevated urea is a danger signal of kidney damage which could cause hypertension.

There are also limitations in this study. First, our study sample size is small, and the time span is long. Although we conducted active follow-up, some cases were nonetheless lost to follow-up, leading to unsatisfactory results of our follow-up, for example, only 54.2% of the cases entered the follow-up results. In addition, our study was limited to the Wenzhou region and may not be broadly applicable, as we were limited in our ability to deeply investigate the birth history, growth and development history, families' specific economic situation, lifestyle habits, physical exercise or mental health, all of which may affect blood pressure results.

To sum up, it is difficult for pediatricians to diagnose and observe the therapeutic effect of primary hypertension in children. First, the clinical symptom is mild or asymptomatic; in addition, awareness of hypertension is not enough. We believe that all of individuals, families and medical community should pay attention to children's hypertension. Social and medical institutions should actively promote the establishment of children's health management systems and improve family monitoring and follow-up systems.

Most children with hypertension have no obvious symptoms or manifestations, making it difficult to diagnose. However, the increase in incidence rate of hypertension in children shows the importance of enhancing our education and awareness of children's hypertension and strengthening family management, monitoring and health education. Our findings also show the importance of taking steps toward early discovery of primary hypertension and detection of secondary hypertension. BMI and A family history of hypertension were associated with primary hypertension. The serum urea was related to secondary hypertension. Emphasis on family history, strengthening family health management and education and publicity of hypertension, were important for diagnosis and detection of children with hypertension.

Conclusions

In this study, we found primary hypertension to be more common than secondary hypertension in children, and renal diseases were the most common in secondary hypertension. BMI and a family history of hypertension were related to primary hypertension. And serum urea was a risk factor for secondary hypertension. For children with elevated blood pressure or hypertension, the family history should be carefully inquired, the root cause should be traced, and a careful physical examination should be performed. Strengthening health knowledge, health education and publicity of hypertension are also critical for children hypertension.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/tp-20-446>

Data Sharing Statement: Available at <http://dx.doi.org/10.21037/tp-20-446>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tp-20-446>). 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. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of The Second Affiliated Hospital and Yuying Children's Hospital (LCKY2018-79). Individual consent for this retrospective analysis was waived.

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