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Characteristics of pediatric inpatients with primary and secondary hypertension

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ABSTRACT

Importance: Extensive population-based studies have explored the prevalence of primary hypertension (HTN) in children and adolescents. However, there is little published data on the characteristics of different types of pediatric HTN and the causes of secondary HTN.

Objective: To investigate the characteristics of different types of pediatric HTN and the causes of secondary HTN in a hospital setting.

Methods: The study cohort comprised pediatric inpatients (<18 years of age) discharged with a diagnosis of HTN from Beijing Children's Hospital during 2015–2020. Pediatric patients with HTN were allocated to secondary and primary HTN groups on the basis of comprehensive analyses of their diagnoses, family history of HTN, and findings on physical examination, as documented in their medical records. The Mann–Whitney U test, χ^2 and Fisher's exact test were used to assess differences in characteristics of patients with different HTN types and causes of secondary HTN.

Results: Data of 1470 inpatients with HTN from 18 clinical departments were included in the analysis. Among them, 458 (31.2%) had primary HTN, and 1012 (68.8%) had secondary HTN. Compared with patients had primary HTN, children with secondary HTN were younger and had lower body mass indexes and longer lengths of stay. Moreover, children with primary HTN had mostly been managed by the Endocrinology and Cardiology Departments, 75.8% of them having obesity-related comorbidities. In contrast, most patients with secondary HTN had been managed by the Nephrology Department, renal diseases being the leading cause of their HTN (46.3%).

Interpretation: Secondary HTN is more common than primary HTN in pediatric clinical settings, renal diseases being the leading cause of secondary HTN.

KEYWORDS
Hypertension, Pediatric, Secondary hypertension

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INTRODUCTION

Hypertension (HTN) in children and adolescents has become a major public health problem, the prevalence being 3%–4%.[1,2] Pediatric HTN is classified as secondary when an underlying cause for the high blood pressure (BP) has been identified, and primary when there is no identifiable cause.[3,4] In recent years, with the prevalence of obesity in children and adolescents, primary HTN has been increasingly reported by population-based studies.[5,6] However, there is little published clinical data on pediatric HTN, the characteristics of different types of HTN and causes of secondary HTN.

In the present study, we extracted data from hospitalization records from multiple clinical departments with the aim of investigating the characteristics of different types of pediatric HTN and the causes of secondary HTN in an inpatient setting.

METHODS

Ethical approval

This study was approved by the Institutional Review Board and Ethics Committee of Beijing Children's Hospital (2021-E-012-R). Since this was a retrospective study and the data analyses were performed anonymously, informed written consent was waived.

Patients

Beijing Children's Hospital, also known as the National Center for Children's Health, is a comprehensive tertiary pediatric hospital, which receives over 70 000 inpatients nationwide every year. In this retrospective study, medical records of all patients hospitalized in Beijing Children's Hospital during August 2015–January 2020 were reviewed. Among the 360 010 discharges, 3782 (1.1%) records of 1557 patients with HTN diagnoses were identified. Otherwise, eligible patients with missing data on diagnostic tests or those who had been admitted to the Pediatric Intensive Care Unit (PICU) were excluded from the study. Finally, data of 1470 inpatients with HTN from 18 clinical departments were included for analysis.

Data collection

The age, sex, length of stay, discharge diagnosis and corresponding International Classification of Diseases version 10 (ICD-10) code were retrieved from the home pages of the patients' medical records. Additionally, information on body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) and family history of HTN were extracted from the admission progress notes. When the records for readmitted patients were incomplete, data from their first admissions were included in the analysis.

Definitions

A diagnosis of HTN was made if a child or adolescent had auscultatory-confirmed SBP/DBP readings ≥95th percentile according to Chinese reference standards on three or more separate occasions.[7] Patients were classified into three groups: primary, secondary and unclear type of HTN on the basis of data in discharge summaries. The ICD-10 codes for the above are I10xx01, I15.901 and I10xx02, respectively. The medical records of patients in the unclear type of HTN group were further searched by two researchers for possible causes of secondary HTN (Table S1),[8,9] and reclassified as primary or secondary HTN. Any disagreement was resolved by discussion with a panel of clinical experts. A flow chart of the classification process is displayed in Figure S1.

Readmission was defined as any hospitalization during the study period. Family history of HTN was defined as a patient having at least one parent or grandparent with hospital-confirmed HTN. Dyslipidemia was defined as having any of the following diagnoses: hypercholesterolemia, hypertriglyceridemia, low concentrations of high-density lipoprotein, or high concentrations of low-density lipoprotein.

Statistical analysis

Continuous variables are expressed as median with interquartile range, and categorical variables as frequency with percentage. Differences in characteristics between primary and secondary HTN were compared using the Mann–Whitney *U* test for continuous variables and the χ^2 or Fisher's exact test for categorical variables. Before comparisons, BMI *Z*-scores were calculated according to the sex- and age-specific BMI cut-off values recommended by the World Health Organization[10,11] and BP values were transformed into *Z*-scores by sex, age, and height using Chinese reference standards.[12] All analyses were performed using SPSS version 25.0. Two-sided $P < 0.05$ was considered to denote statistical significance.

RESULTS

Characteristics of the study patients

Descriptive information for the included patients is provided in Table 1. Among the 1470 pediatric patients, 883 (60.1%) were boys and 587 (39.9%) girls, the mean age being 10.3 ± 4.0 years. Primary HTN was diagnosed in 458 (31.2%) children and secondary HTN in 1012 (68.8%). Compared with patients had primary HTN, children with secondary HTN were younger (0–11 years), had higher *Z*-scores for DBP, longer length of stay and higher re-admission rates (all $P < 0.05$). However, patients with primary HTN had higher BMIs and proportion of family history of HTN than did those with secondary HTN (all $P < 0.05$).

TABLE 1 Characteristics of included pediatric inpatients with hypertension

Characteristics	All (n = 1470)	Primary HTN (n = 458)	Secondary HTN (n = 1012)	P
Male	885 (60.1)	348 (76.0)	535 (52.9)	<0.001
Age (years)				<0.001
0–2	94 (6.4)	0 (0)	94 (9.3)	
3–5	163 (11.1)	2 (0.4)	161 (15.9)	
6–11	592 (40.3)	156 (34.1)	436 (43.1)	
12–17	621 (42.2)	300 (65.5)	321 (31.7)	
BMI z-score[†]	2.3 (0.4, 4.5)	4.2 (2.7, 5.9)	0.9 (−0.3, 2.5)	<0.001
SBP z-score	2.1 (0.9, 3.1)	2.3 (1.3, 3.1)	2.0 (0.6, 3.2)	0.018
DBP z-score	1.7 (0.5, 3.1)	1.3 (0.5, 2.5)	1.9 (0.5, 3.4)	<0.001
Length of stay (days)	12 (8, 18)	10 (8, 13)	14 (9, 22)	<0.001
Readmission	444 (30.2)	28 (6.1)	416 (41.1)	<0.001
Family history of HTN[‡]	383 (36.0)	288 (65.8)	95 (15.2)	<0.001

Data are shown as n (%) or median (Q1, Q3). [†]Available for 919 patients. [‡]Available for 1065 patients. HTN, hypertension; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

The proportions of primary and secondary HTN in each department are presented in Figure 1. Most of children hospitalized in the Endocrinology and Cardiology Departments were diagnosed with primary HTN (89.0% and 64.8%, respectively), whereas those hospitalized in the Nephrology or Rheumatology and Immunology Departments were mostly had secondary HTN (94.7% and 98.1%, respectively).

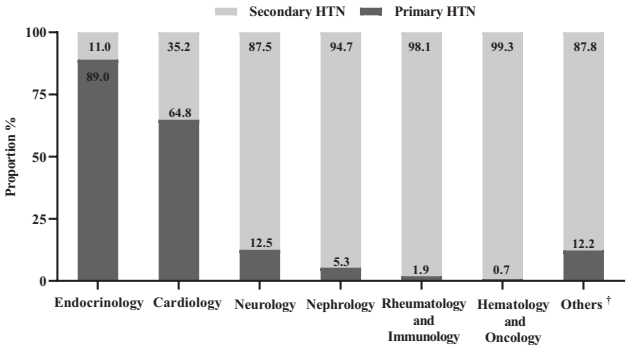

FIGURE 1 Proportions of primary and secondary hypertension by departments. $P < 0.05$ for the comparisons of proportion between primary and secondary HTN by departments. [†]Others including Orthopedics, General Surgery, Dermatology, Neonatology, Otolaryngology, Urology, Gastroenterology, Internal Medicine, Infectious Diseases, Respiratory Medicine, Oral Surgery, and Thoracic Surgery department.

Comorbidities in patients with primary HTN

The major comorbidities among patients with primary HTN and their age and sex distributions are shown in Table 2. Comorbidities were documented in 369 children with primary HTN (80.6%), the commonest ones being obesity (75.8%), followed by non-alcoholic fatty liver disease (NAFLD, 57.4%), dyslipidemia (24.5%), diabetes (15.1%) and obstructive sleep apnea syndrome (OSAS, 15.1%). Compared with boys, girls with primary HTN were more likely to combine with dyslipidemia (22.1% *vs*. 31.8%, $P < 0.05$) and diabetes (11.8% *vs*. 25.5%, $P < 0.05$). Additionally, three or more major comorbidities were documented in 156 (34.1%) patients, and the commonest comorbidity cluster was obesity combined with NAFLD and dyslipidemia (10.7%). However, there was no sex- or age-related difference among the comorbidity clusters (all $P > 0.05$).

Causes of secondary HTN

The common causes of secondary HTN and their age and sex distributions are shown in Table 3. Renal diseases, including renal parenchymal disease (81.2%) and renovascular problems (18.8%), were the most common underlying causes, accounting for 46.3% of cases of secondary HTN. In contrast, neurologic disorders were the least common causes of secondary HTN (1.8%). Moreover, hematologic and tumor-related causes were more common in boys than in girls (11.4% *vs*. 6.7%, $P < 0.05$), whereas rheumatic autoimmune diseases were dominated by girls ($P < 0.05$). Rheumatic autoimmune, hematologic and tumor and cardiovascular diseases were more commonly detected in children with secondary HTN under five years old (all $P < 0.05$).

DISCUSSION

In this study, we comprehensively analyzed the characteristics of patients with different types of HTN in a pediatric clinical setting. Compared with other studies of pediatric inpatients with HTN (Table S2), ours was much larger, including patients from all the clinical departments. Similar to previous studies,[13-15] we found secondary HTN to be the commonest subtype of HTN, accounting for 68.8% of our hospitalized children. However, another tertiary pediatric hospital in Beijing has reported a greater proportion of primary than secondary HTN (78% *vs*. 24%).[16] This discrepancy may be attributable to the higher proportions of children with obesity (68.1% *vs*. 26.5%)

TABLE 2 Age and sex distributions among children with primary hypertension according to major comorbidities

Variables	All (*n* = 458)	Sex		*P*	Age (years)†			*P*
		Male (*n* = 348)	Female (*n* = 110)		3–5 (*n* = 2)	6–11 (*n* = 156)	12–17 (*n* = 300)	
Major comorbidities								
Obesity	347 (75.8)	264 (75.9)	83 (75.5)	0.931	1 (50.0)	126 (80.8)	220 (73.3)	0.149
NAFLD	263 (57.4)	203 (58.3)	60 (54.5)	0.484	1 (50.0)	86 (55.1)	176 (58.7)	0.752
Dyslipidemia	112 (24.5)	77 (22.1)	35 (31.8)	0.039	0 (0)	36 (23.1)	76 (25.3)	0.627
Diabetes	69 (15.1)	41 (11.8)	28 (25.5)	0.001	0 (0)	18 (11.5)	51 (17.0)	0.253
OSAS	69 (15.1)	55 (15.8)	14 (12.7)	0.432	1 (50.0)	24 (15.4)	44 (14.7)	0.376
Major comorbidity clusters				0.395				0.194
0	89 (19.4)	65 (18.7)	24 (21.8)		1 (50.0)	26 (16.7)	62 (20.7)	
1	93 (20.3)	76 (21.8)	17 (15.5)		0 (0)	34 (21.8)	59 (19.7)	
2	120 (26.2)	93 (26.7)	27 (24.5)		0 (0)	51 (32.7)	69 (23.0)	
≥3	156 (34.1)	114 (32.8)	42 (38.2)		1 (50.0)	45 (28.8)	110 (36.7)	

Data are shown as *n* (%). †There were no patients with primary HTN in the 0–2 years group, only three age groups were included in the comparisons. NAFLD, non-alcoholic fatty liver disease; OSAS, obstructive sleep apnea syndrome.

TABLE 3 Age and sex distributions of causes of secondary hypertension in pediatric patients

Causes	All (*n* = 1012)	Sex		*P*	Age (years)				*P*
		Male (*n* = 535)	Female (*n* = 477)		0–2 (*n* = 94)	3–5 (*n* = 161)	6–11 (*n* = 436)	12–17 (*n* = 321)	
Renal	469 (46.3)	256 (47.9)	213 (44.7)	0.309	31 (33.0)	49 (30.4)	217 (49.8)	172 (53.6)	<0.001
Rheumatic autoimmune	205 (20.3)	85 (15.9)	120 (25.2)	<0.001	11 (11.7)	44 (27.3)	88 (20.2)	62 (19.3)	0.024
Hematologic and tumor	93 (9.2)2	61 (11.4)	32 (6.7)2	0.010	9 (9.6)2	29 (18.0)	37 (8.5)2	18 (5.6)2	<0.001
Cardiovascular	75 (7.4)2	40 (8.4)2	35 (6.5)2	0.264	14 (14.9)	9 (5.6)	26 (6.0)2	26 (8.1)2	0.019
Endocrine	27 (2.7)2	17 (3.2)2	10 (2.1)2	0.289	5 (5.3)2	4 (2.5)	11 (2.5)2	7 (2.2)2	0.408
Neurologic	18 (1.8)2	13 (2.4)2	5 (1.0)2	0.098	1 (1.1)2	2 (1.2)	7 (1.6)2	8 (2.5)2	0.671
Others†	125 (12.4)	68 (12.7)	57 (11.9)	0.714	23 (24.5)	24 (14.9)	50 (11.5)	28 (8.7)2	<0.001

Data are shown as *n* (%). † Others included medications, toxicity and infection.

and aged over six years (93.5% *vs*. 82.5%) in their study than in ours. Of interest, we found a five-fold increase in the total number of pediatric inpatients with HTN compared with that found in the same center 12 years ago (2003–2007).[13] This alarming trend emphasizes the importance of prevention of HTN among Chinese children and adolescents.[17,18]

As a result of the recent obesity epidemic, obesity and obesity-related diseases have become common comorbidities of primary HTN.[19,20] In our study cohort, 75.8% of children with primary HTN had a diagnosis of obesity, which is a much higher proportion than that reported by several population-based studies (14%–40%).[21,22] Additionally, NAFLD, dyslipidemia, diabetes and OSAS coexisted with primary HTN in 57.4%, 24.5%, 15.1% and 15.1%, respectively, of pediatric inpatients. Of note, although diabetes and OSAS have been identified as causes of secondary HTN in adults, the underlying mechanism has yet to be defined.[23,24] Therefore, diabetes and OSAS are listed as comorbidities of pediatric HTN in both Chinese and USA clinical guidelines.[25,26] The interactions and causal relationship of these conditions with HTN in children require further investigation.

Admission bias has resulted in the reporting of distinct causes of secondary HTN by other researchers. In our study, rheumatic autoimmune diseases were one of the most common causes of secondary HTN, second only to renal diseases. A large body of evidence has shown that chronic inflammation and immune-mediated mechanisms are involved in the pathogenesis of HTN in patients with systemic autoimmune diseases.[27,28] However, few studies have reported the autoimmune-related HTN in pediatric patients, which suggests a need for more attention and risk assessment in these patients.

The strengths of our study include its large sample size and that data were collected from multiple departments. However, the present study does have several limitations. First, it was conducted in a single center; thus, the admission bias could not be avoided. Second, we could not assess long-term changes in the proportions of different HTN subtypes because of the short duration of the study.

In conclusion, secondary HTN is more common than primary HTN in the pediatric clinical setting, renal diseases being the leading cause. Further multicenter studies are warranted to investigate the proportion of different subtypes of HTN and long-term changes in proportion in Chinese children and adolescents.

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CONFLICT OF INTEREST

None to declare.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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