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Hypertension in 172 Chinese Children: An 8-Year Retrospective Study

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Background: We evaluated children with hypertension and compared those with essential and secondary (including renal and non-renal) hypertension.

Methods: This retrospective study analyzed data from hypertensive children (age, 0-18 years) referred for treatment between January 2008 and December 2015. Demographic factors, causative factors, and medical treatments were evaluated. Treatment failure was defined as a systolic or diastolic blood pressure ≥95th percentile for age, gender, and height on three separate occasions, despite treatment. All patients not meeting the failure criteria were considered to have controlled hypertension. The control rate was defined as the proportion of patients with controlled blood pressure.

Results: Among 172 consecutive patients, 28% had essential hypertension and 72% had secondary hypertension. As compared with children with secondary hypertension, those with essential hypertension had a higher frequency of family history of hypertension (P<0.001), a higher body mass index (BMI) (P =0.001), lower frequency of proteinuria (P=0.003), lower uric acid (P=0.04), and lower triglyceride (P= 0.048). The medications used in the controlled group were similar to those used in the uncontrolled group. Angiotensin-converting enzyme inhibitors (ACEIs) were only used in nephrogenic patients, and a higher rate of ACEI use seemed to increase control rates. Control rates did not significantly differ by age, number of drugs, or cause of hypertension.

Conclusions: As compared with children with secondary hypertension, those with essential hypertension were more likely to have a family history of hypertension and had a higher BMI, lower frequency of proteinuria, and lower uric acid and triglyceride concentrations. Treatment guidelines for essential and secondary hypertension should be established for children of all ages.

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Key words: hypertension, essential, hypertension, secondary, children, etiology, medication

Introduction

Hypertension is believed to affect 30% of adults[1]. High blood pressure (BP) in childhood, although less common, is an independent risk factor for hypertension later in life[2–5]. Childhood hypertension is associated with significant damage to arteries, the heart, and other organs[6,7] and is often undetected, unrecognized, and untreated[8–11].

The exact prevalence of childhood hypertension is unknown because BP screening is not systematic in children, but with the increasing prevalence of childhood obesity, hypertension is becoming a concern[12]. The prevalence of childhood hypertension was 2.2% among Swiss children aged 10 to 14 years, and the same group had an obesity prevalence of 14%[13]. The global prevalence of hypertension in children is estimated to range from 1% to 5%[14,15], but diagnosis is complicated. Because of diurnal fluctuations and changes in physical activity and emotional stress, BP varies widely during the day in children and adults.

A child should be calm and rested before BP is measured; however, measurement is difficult in young children and crying infants[16]. Furthermore, BP norms in

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childhood are influenced by height, age, and gender, making it impossible to apply a single BP level in the diagnosis of pediatric hypertension[17,18]. In children, the definition of hypertension is entirely based on BP frequency-distribution curves[5]. Thus, BP must be measured according to a standard protocol and repeated several times before a referral is made for further evaluation of hypertension[19–21].

Chronic kidney disease (CKD) affects 15 to 75 children per million worldwide[22]. Although pediatric CKD is rare, associated hypertension is common, and 70% of children with CKD are hypertensive[23,24]. Even in children with CKD, diagnosing hypertension is a challenge, and treating this hypertension is an additional challenge[25–27].

Because of the lack of evidence and consensus, the present study aimed to examine children with hypertension from the Children's Hospital of Fudan University and to compare differences between those with essential and secondary (including renal and non-renal) hypertension.

Materials and Methods

Study Design and Patients

This retrospective chart review analyzed data from all children referred to the Children's Hospital of Fudan University between January 1, 2008 and December 31, 2015. The inclusion criteria were age 0 to 18 years and a diagnosis of hypertension (average BP ≥95th percentile for gender, age, and height) on three separate occasions[17]. BPs for boys and girls, by age and height percentile, were previously reported[17], as shown in **Table 1, 2**. Children were excluded if they had received a diagnosis of white coat hypertension (BP ≥95th percentile when measured in a physician's office or clinic and an average BP <90th percentile when measured outside of a clinical setting[17]) or had missing data. Hypertension was classified as essential and secondary. All cases were reviewed and classified by a cardiovascular specialist. This study was approved by the Ethics Committee of Children's Hospital of Fudan University.

Data Collection

Data collected from medical charts included demographic factors (age, gender, weight, height, and family history), clinical symptoms (dizziness and nausea), laboratory tests (creatinine, uric acid, triglyceride, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), and findings of electrocardiography, echocardiography, and renal ultrasound examinations.

BP Measurement

BP was measured with a standard clinical sphygmomanometer in all children. Child-specific BP cuffs of different sizes (including neonate-sized) were used, and the cuffs were available for parents who wished to buy them for use at home. BP measurements were taken by trained nurses at least 5 minutes after resting. With the arm and heart positioned at the same height, BP was measured for the left and right arms and averaged. Hypertension was diagnosed when the average systolic BP or diastolic BP was ≥95th percentile for gender, age, and height on three separate occasions[17]. Essential hypertension was diagnosed when BP was ≥95th percentile on three separate occasions in the absence of secondary causes of hypertension and with no concurrent use of medication with the potential to raise BP. Secondary hypertension was diagnosed by extensive evaluation, the first steps of which were a thorough history and physical examination. Laboratory tests were then performed, including blood tests, a urine test, renal ultrasound, and echocardiography. Additional examinations were conducted for some children and under some conditions.

BP control was analyzed. According to the BP reference standards for children, the uncontrolled group was defined as a systolic or diastolic BP ≥95th percentile for age, gender, and height on three separate occasions, despite treatment[28,29]. Patients not meeting the criteria for treatment failure were classified as controlled. The control rate was the proportion of patients in the controlled groups.

Statistical Analysis

Descriptive results were compared between groups, in accordance with the distribution of variables. Continuous variables were expressed as mean (±SD) and compared with the Student t-test. Categorical variables were expressed as frequencies and percentages and compared with the chi-square or Fisher exact test. The Fisher exact test was used when more than 20% of the cells had an expected frequency of <5 observations; otherwise, the chi-square test was used. All analyses were performed with Stata 10 (StataCorp LP, College Station, TX, USA). A P value of <0.05 was considered to indicate statistical significance.

Results

Characteristics of Patients

A total of 172 consecutive patients aged 0 to 18 years (median, 9.3 years) were included; 28% had an unknown cause of hypertension (essential hypertension) and 72%

Table 1 Blood pressure for boys, by age and height percentile[17]

Age (years)	BP percentile	SBP, mmHg							DBP, mmHg						
		Percentile of height							Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	104	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	107	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	86	85	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	85	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	107	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91

Table 1 Blood pressure for boys, by age and height percentile[17] (continued)

Age (years)	BP percentile	SBP, mmHg							DBP, mmHg						
		Percentile of height							Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2 Blood pressure for girls, by age and height percentile[17]

Age (years)	BP percentile	SBP, mmHg							DBP, mmHg						
		Percentile of height							Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	57	58	58	59	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	62	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81

Table 2 Blood pressure for girls, by age and height percentile[17] (continued)

Age (years)	BP percentile	SBP, mmHg							DBP, mmHg						
		Percentile of height							Percentile of height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	74	74	74	75	76	77	77
	90th	114	114	116	117	118	119	120	78	78	78	79	80	81	81
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 3 Characteristics of children with essential and secondary hypertension

Characteristics	Essential hypertension (n=48)	Secondary hypertension (n=124)	P
Family history, n (%)	31 (65)	14 (11)	<0.001
Male, n (%)	35 (73)	78 (63)	0.957
Age (years)	9.1±4.4	7.5±4.2	0.907
Body mass index (kg/m^2)	20.9±6.3	16.1±4.3	0.001
Glomerular filtration rate (mL/min)	157.0±36.5	137.5±172.6	0.543
Dizziness, n (%)	16 (33)	31 (25)	0.730
Nausea, n (%)	14 (29)	32 (26)	0.098
Abnormal electrocardiogram, n (%)	20 (42)	58 (47)	0.241
Abnormal ultrasonic cardiogram, n (%)	16 (33)	43 (35)	0.897
Abnormal renal ultrasonogram, n (%)	19 (40)	71 (57)	0.478
Proteinuria, n (%)	1 (2)	50 (40)	0.003
Uric acid (μmol/L)	316.3±123.4	339.7±147.2	0.041
Triglyceride (mmol/L)	1.2±0.6	2.1±1.4	0.048
Total cholesterol (mmol/L)	4.7±0.9	5.1±2.3	0.796
High-density lipoprotein cholesterol (mmol/L)	135.2±16.3	148.5±38.6	0.914
Low-density lipoprotein cholesterol (mmol/L)	85.0±13.4	101.6±33.5	0.932

Table 4 Causes of secondary hypertension (n=124)

Causes	n (%)	Median age at diagnosis, (range)	Male, n (%)
Renal	68 (55)	8.1 (0.7-17.4)	41 (60)
Cardiac	16 (13)	9.7 (4.7-13.8)	10 (63)
Endocrine	15 (12)	12.0 (6.5-18.1)	10 (67)
Neurological	13 (11)	6.0 (1.9-11.0)	8 (62)
Autoimmune	12 (10)	7.0 (1.3-11.7)	9 (75)

Table 5 Causes of hypertension, by age group

Causes	Infancy (<1 year) (n=13)	Preschool (1-5 years) (n=46)	Preteen (6-12 years) (n=88)	Teen (13-18 years) (n=25)	P
Essential, n (%)	4 (31)	6 (13)	29 (33)	9 (36)	0.071
Secondary, n (%)	9 (69)	40 (87)	59 (67)	16 (64)	0.071
Renal	6 (46)	24 (52)	25 (28)	13 (52)	0.027
Cardiac	0 (0)	3 (7)	12 (14)	1 (4)	0.116
Endocrine	3 (23)	4 (9)	6 (7)	2 (8)	0.524
Neurological	0 (0)	6 (13)	7 (8)	0 (0)	0.271
Autoimmune	0 (0)	3 (7)	9 (10)	0 (0)	0.172

had secondary hypertension. Among those with secondary hypertension, 45% had renal hypertension and 55% had non-renal hypertension. **Table 3** shows the characteristics of patients with essential and secondary hypertension. As compared with children with secondary hypertension, those with essential hypertension were more likely to have a family history of hypertension (P<0.001) and had a higher body mass index (BMI) (P=0.001), lower frequency of proteinuria (P=0.003), and lower uric acid (P=0.041) and triglyceride levels (P=0.048).

Causative Factors

Analysis of medical records identified causative factors for secondary hypertension (**Table 4, 5**)[30], namely, renal (nephrotic syndrome, glomerulonephritis, renal artery stenosis, and neurogenic bladder), cardiovascular (congenital heart disease, coarctation of aorta, cardiac valvular diseases, and cardiac insufficiency), endocrine (diabetes, obesity, metabolic syndrome, neuroblastoma, and pheochromocytoma), neurological (mitochondrial encephalopathy and viral encephalitis), and autoimmune (systemic lupus erythematosus, juvenile idiopathic arthri-

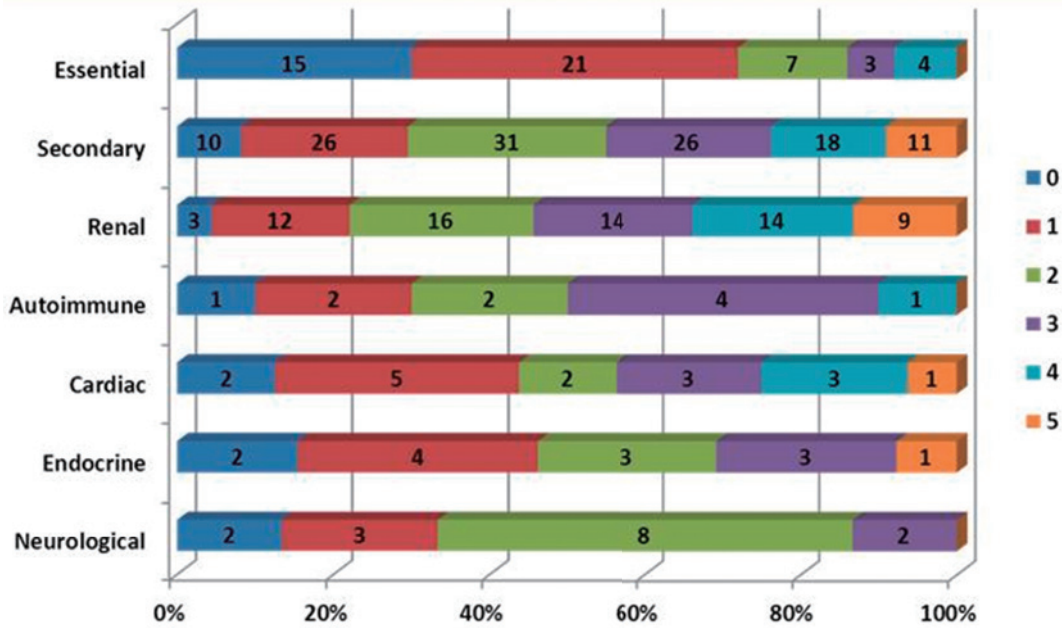

Fig. 1 Number of drugs used to treat hypertension.

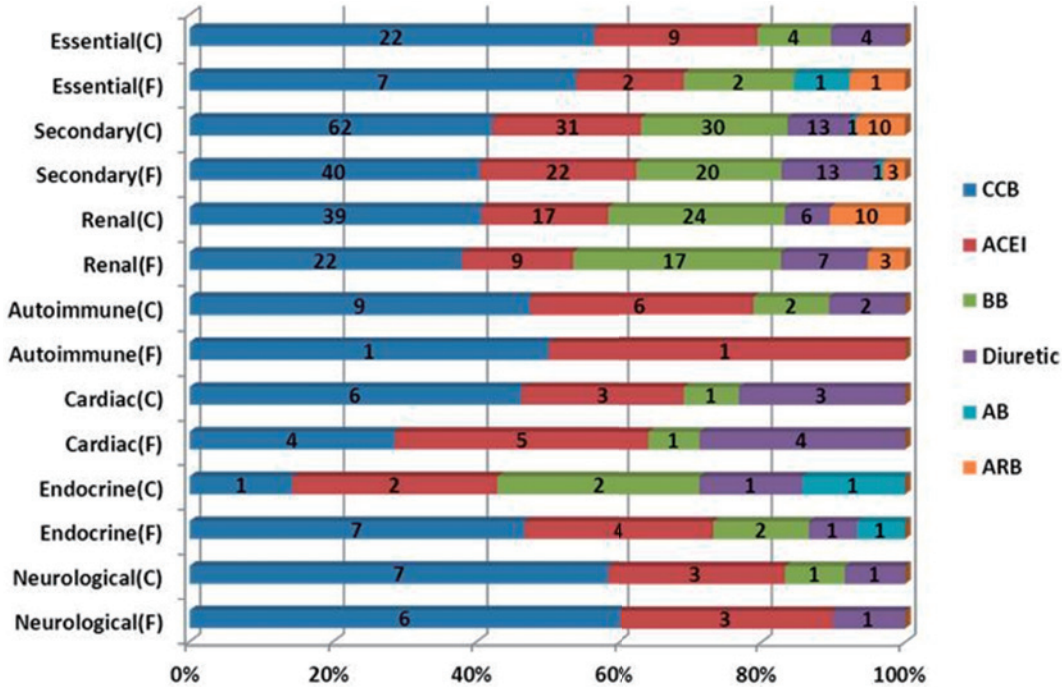

Fig. 2 Drugs prescribed, by cause of hypertension.
C, controlled group; F, uncontrolled group; BB, β-blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; AB, α-blocker.

tis, and rheumatic diseases) hypertension. The proportion of children with renal hypertension was lower in those aged 6 to 12 years than in the other age groups (P=0.027) (**Table 5**).

Hypertension Therapy

The drugs used to treat pediatric hypertension are shown in **Figure 1, 2**. Calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), β-blockers, and diuretics were frequently prescribed, and nifedipine, metoprolol, fosinopril, enalapril, and spironolactone were the most frequently prescribed drugs, in their respective classes, for pediatric hypertension. **Figure 2** shows that the dugs used in the controlled groups were similar to those used in the uncontrolled groups for all

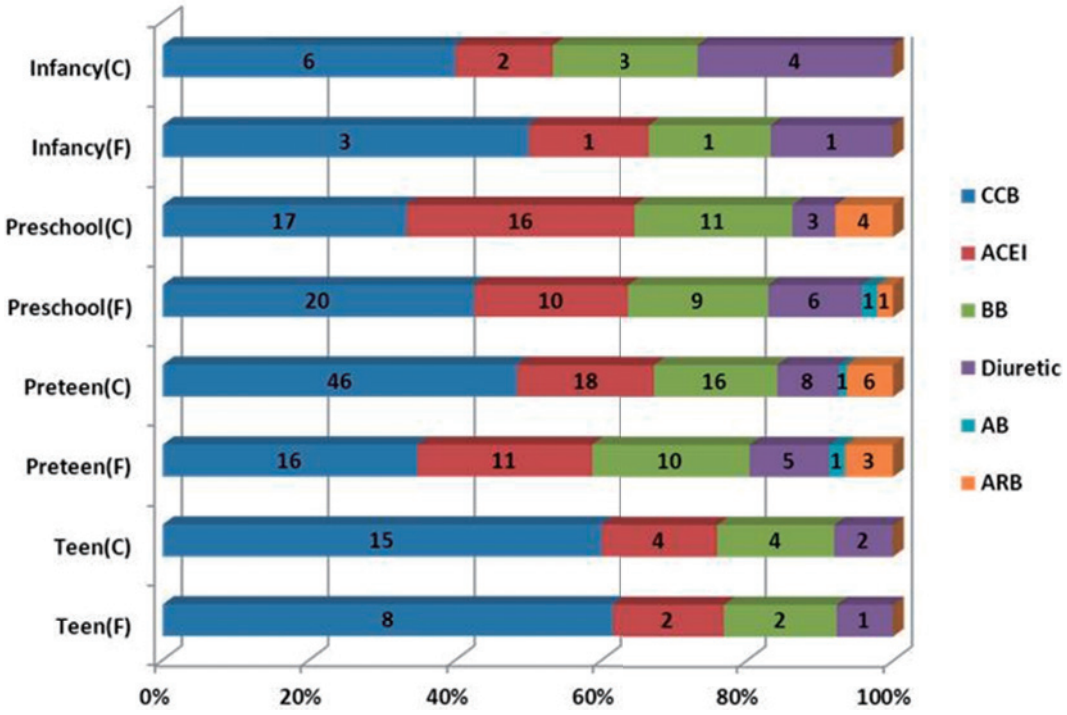

Fig. 3 Class of antihypertensive drugs prescribed, by patient age.
C, controlled group; F, uncontrolled group; BB, β-blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; AB, α-blocker.

causes of hypertension. ACEIs were only prescribed to patients with nephrogenic hypertension, and the rate of ACEI use was positively associated with the control rate.

The most commonly used drugs, by age group, are shown in **Figure 3**. CCBs were most frequently prescribed to teenagers, and angiotensin receptor blockers (ARBs) and α-blockers were only prescribed to the preschool and preteen groups. The proportions were similar in the controlled and uncontrolled groups. ACEIs appeared to be more suitable for children aged 1 to 5 years, and effectiveness was positively associated with ACEI use.

Of the 172 children treated with antihypertensives, BP was classified as controlled for 66.3%. BP control rates, by antihypertensive, are shown in **Table 6**. The control rate did not significantly differ in relation to age, number of drugs prescribed, or cause of hypertension. Control rates were comparable between patients with essential hypertension and those with secondary hypertension. Among patients with secondary hypertension, control rates were much lower for those with endocrine disease than for those with other diseases. Hypertension in infants and teens was not adequately controlled by medication. However, control rates for the non-medication and monotherapy groups were higher than those for the other groups.

Discussion

The prevalence of hypertension in children and adolescents has increased in recent years, and childhood hypertension is an independent risk factor for adult hypertension[2–5]. In addition, development of hypertension early in life is associated with changes in cardiovascular target organs that predict cardiovascular outcomes in adulthood and lead to substantial morbidity and mortality[31–34]. In China, over 2 million deaths were attributed to hypertension in 2010, and management of hypertension, including childhood hypertension, is an important public health concern. Because of the lack of data and consensus, this study examined children with hypertension and compared differences between those with essential and secondary hypertension. Essential hypertension was associated with a family history of hypertension and elevated BMI, while secondary hypertension was associated with increased proteinuria and triglyceride concentration. Disease-specific treatment guidelines should be established for essential and secondary hypertension in children of all ages.

In this study, 28% of the pediatric population had essential hypertension and 72% had secondary hypertension. Flynn[35] reported that secondary hypertension was the main cause of childhood hypertension and that >50% of secondary hypertension cases at tertiary centers were

Table 6 Rates of control of pediatric hypertension, by age, number of components, and cause of hypertension

Variables	Controlled, n (%)	Failed, n (%)	P
Age group			0.118
Infancy (n=13)	7 (54)	6 (46)	
Preschool (n=46)	29 (63)	17 (37)	
Preteen (n=88)	65 (74)	23 (26)	
Teen (n=25)	13 (52)	12 (48)	
Number of components			0.375
0 (n=25)	19 (76)	6 (24)	
1 (n=47)	33 (70)	14 (30)	
2 (n=38)	26 (68)	12 (32)	
3 (n=29)	14 (48)	15 (52)	
4 (n=22)	15 (68)	7 (32)	
5 (n=11)	7 (64)	4 (36)	
Cause of hypertension			0.138
Essential (n=48)	33 (69)	15 (31)	
Secondary (n=124)	81 (65)	43 (35)	
Neurological (n=13)	8 (62)	5 (38)	
Endocrine (n=15)	6 (40)	9 (60)	
Cardiac (n=16)	11 (69)	5 (31)	
Autoimmune (n=12)	11 (92)	1 (8)	
Renal (n=68)	45 (66)	23 (34)	

attributable to renal parenchymal diseases. We found that overweight children with elevated BPs were most likely to receive a diagnosis of essential hypertension, as in previous studies[36,37]. In this study, 65% (31/48) of the patients with essential hypertension had a family history of the disease, highlighting the genetic predisposition to essential hypertension[38,39]. In addition, BMI was higher for children with essential hypertension than for those with secondary hypertension, which confirms previous findings[40,41]. A previous study showed that children with essential hypertension presented at an older age and had a higher frequency of family history of the disease[30], supporting the present study. Unfortunately, data on preterm birth were not available for all patients, so we could not assess the effect of this factor. Gupta-Malhotra et al. reported an association of essential childhood hypertension with preterm birth[30], which warrants further study. As is the case for adult hypertension and in a previous study of childhood hypertension[30], males were predominantly affected, both for essential and secondary hypertension.

The possibility of an underlying disorder should be considered in all children with elevated BPs, even those with an obvious family history and obesity. Young children and children with clinical signs that suggest the presence of systemic conditions associated with hypertension should be examined more extensively. Secondary hypertension was more predominant in preschool children, and the main cause was renal disease. Proteinuria was present in 2% (1/48) of essential hypertension patients and in 40% (50/124) of secondary hypertension patients; thus, patients with proteinuria are possibly more likely to have secondary hypertension. Furthermore, because kidney disease caused by hypertension was the first cause of secondary hypertension, children with elevated BPs should first undergo urinalysis.

Treatment of pediatric hypertension targets the cause, and the goal is to lower BP to within the normal range. Because of the high risks of adult hypertension and morbidity later in life, patients with secondary hypertension require specialist treatment of the underlying cause. Those who need pharmacological treatment could benefit from a consultation with pediatric hypertension specialists. According to guidelines[17], patients with prehypertension and stage 1 hypertension should receive a BMI-based behavioral intervention before drug treatment. Specific methods include regular physical activity and diet control. A diet plan is made by a dietitian. If behavioral interventions fail, drugs are prescribed. Behavior modification is the initial treatment for hypertension. Because of the possible adverse effects of pharmacological therapy, it should be reserved for those who do not benefit from behavior modification. CCBs and ACEIs were the most frequently prescribed drugs for children with essential hypertension. Those with secondary hypertension

were most often treated with CCBs, β-blockers, and ACEIs. The proportion of the present children prescribed ACEIs was much lower than in previous studies[14], especially in the teen group[42]. Future studies should attempt to explain these differences.

Control rates were lower in the infant and teen groups than in the other groups, perhaps because of differences in disease state and physiology, and the lack of BP data for newborns[43]. In this study, ARBs were only prescribed to nephrogenic patients. Greater use of these drugs was associated with better BP control. Herder et al.[44] reported that ARBs are mainly used to treat chronic renal diseases, with or without hypertension, especially in cases refractory to ACEI treatment. Although combination therapy is more effective than monotherapy in controlling hypertension[45], we found that the control rate was higher in the non-medication and monotherapy groups than in the other groups, perhaps because of confounding factors such as resistant hypertension, lifestyle, and nutrition. Unfortunately, these factors could not be assessed in the present study, mainly because data for these variables were not consistently entered on medical charts. Nevertheless, the present study revealed that children with hypertension received a variety of treatments; thus, it is critical to establish disease-specific treatment guidelines for essential hypertension and secondary hypertension in children of all ages.

The limitations of this study include those of any retrospective observational study and the small sample size, which prevented comparison of essential and secondary hypertension and limited the analyses to identification of factors associated with each type of hypertension. Secondly, because there was no control group of children with normal BP, we could not perform multivariate logistic regression analysis to identify the different risk factors for essential and secondary hypertension. Thirdly, the present patient data were collected from several departments, and there may be differences in prescription behavior among the specialties. Fourthly, this study did not focus on control of the primary disease in children with secondary hypertension, and the analysis of drug effects was susceptible to bias. A well-designed prospective study should analyze detailed information, including the clinical and BP characteristics of hypertensive patients, contributors to the disease, and disease management. We expect to gradually expand the present sample size. As the study progresses, accumulating evidence should yield insights into clinical treatment of pediatric hypertension.

As compared with children with secondary hypertension, those with essential hypertension were more likely to have a family history of hypertension and had a higher BMI, a lower frequency of proteinuria, and lower uric acid and triglyceride levels. Treatment guidelines should be established for essential and secondary hypertension in children of all ages.

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Conflict of Interest: The authors declare no conflict of interest.

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