Hypertension in pediatric patients admitted to inpatient ward at King Abdulaziz University Hospital in Saudi Arabia: Prevalence, causes, and outcomes

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ABSTRACT

Background: The secondary hypertension (HTN) is the predominant form of HTN in pediatrics. Renal diseases and renovascular anomalies are the most commonly reported causes. In this study, we aimed to identify the prevalence, causes, and outcomes of secondary HTN in Saudi Arabia. Methods: A retrospective study was conducted among 3,640 pediatric patients aged between 0 and 18 years, admitted to the pediatric nephrology ward at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. The study has been approved by the ethics review committee of King Abdulaziz University. Results: Prevalence of secondary HTN due to renal disease was (77.0%). Most of the cases were diagnosed with stage 5 renal disease (78.3%). Small kidney size was frequently diagnosed (n = 29, 11.9%), followed by large kidney size (n = 26, 10.7%). One third of the cases (n = 79, 32.4%) were under control, 49 (20.1%) lost follow-up, and 24 (10.1%) deceased. A total of 61 (33.1%) patients progressed to end-stage renal disease and patients were managed by different types of treatments. Conclusion: The prevalence of secondary HTN due to renal disease is considered to be high in pediatric patients admitted to King Abdulaziz University. Several renal diseases in the renal system are associated with secondary HTN mostly attributed to renal malformation. In addition, renal affection, cerebral infarction, bleeding, left ventricular hypertrophy, and valvular lesion are the highest reported complications in our population. Follow-up with ECHO and brain CT is highly recommended in pediatric HTN. Future studies on a larger sample and vigorous follow-up are recommended.

Keywords: Hypertension, pediatric, inpatient, outcomes

Introduction

Hypertension (HTN) is identified as persistent blood pressure values ≥the 95th percentile. Primary HTN has no definite secondary causes but multiple factors such as obesity, insulin resistance, impairment in sodium homeostasis, or renin-angiotensin system may be involved.[1] Secondary HTN, in contrast, is the predominant form of HTN, and the underlying etiology lies behind various secondary causes.[3] In a retrospective review, out of 275 hypertensive children, 57% had secondary HTN due to renal, cardiovascular, autoimmune, endocrine, gastrointestinal, hematological, medication-related or neurovascular causes.[3]

Management guidelines of pediatric HTN were updated in 2017, the disease is recognized by elevated blood pressure >90th percentile; early detection and management measurements are essential to lessen the irreversible changes that could affect the cardiovascular system and renal system.[5,6] Calcium-channel
blockers (CCB) and angiotensin-converting enzyme inhibitors (ACEI) are the most favorable therapy to lower blood pressure in pediatric.\[8\] However, secondary HTN was found to have a better response than primary HTN.\[9\]

The complication of HTN are miscellaneous, HTN could be presented as hypertensive emergency that may involve severe kidney injury, affection of myocardium, and retinopathy.\[10\] In a retrospective study carried out on 246 children with sustained HTN, 35 patients were presented, for the first time, with complications of severe HTN such as congestive heart failure and encephalopathy. The underlying causes of HTN in is this study were attributed to renal, renovascular, or endocrine system disorders.\[11\]

Pediatric population in the Kingdom of Saudi Arabia is highly susceptible to develop either primary or secondary HTN, hence regular screening is highly recommended. In a recent study that aimed outline the prevalence of risk factors of diabetes and HTN among school children in Kingdom of Saudi Arabia, 11.6% had body mass index (BMI) above the normal range and 43% had sedentary lifestyle.\[12\] In a cross-sectional study of 401 adolescents from Jeddah, the prevalence of HTN was 17.2%, pre-HTN was observed in 4.2%, and obesity was reported in 19.2%. In addition, the prevalence of hematuria and proteinuria were 17% and 10.2%, respectively.\[13\] In a recently published article, isolated systolic hypertension (ISH) was the most reported phenotype in obese children (24.3%).\[14\]

However there are no studies assess the prevalence of HTN in pediatric patients admitted to pediatric inpatient ward. Consequently, in our present study, we sought to assess the prevalence, causes, and outcomes of secondary HTN in pediatric patients admitted to King Abdulaziz University Hospital in Jeddah, Saudi Arabia between 2015 and 2019.

**Material and Methods**

**Study setting**

This is a retrospective study, conducted among 3,640 pediatric patients in the pediatric ward at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Patients aged 0–18 years of age were included. The study has been approved by the ethics review committee of King Abdulaziz University June 14, 2017. For the age group (1–13), the American Academy of Pediatrics (AAP) updated guidelines 2017 has been followed to diagnose HTN which is: Normal BP: <90th percentile. Elevated BP: ≥90th percentile to <95th percentile or 120/80 mmHg to <95th percentile or 130/80 to 139/89 mm Hg. Stage 1 HTN: ≥95th percentile to <95th percentile + 12 mmHg. Stage 2 HTN: ≥95th percentile +12 mmHg, or 2140/90 mm Hg. For the ≥13 age group, adolescent same as adults, American Heart Association (AHA) guidelines have eliminated the category of preHTN, categorizing patients as having either Elevated (120–129 and less than 80) or stage I HTN (130–139 or 80–89). While previous guidelines classified 140/90 mm Hg as stage 1 HTN, this level is classified as stage 2 HTN under the new guidelines.\[15\]

**Data collection**

Data were obtained by an electronic questionnaire from pediatric ER, pediatric medical ward, and Pediatric intensive care unit (ICU) files, in the period 2010–2018 at King Abdulaziz University Hospital. The questionnaire included information about gender, age at diagnosis, HTN causes, renal disease stage, blood pressure, HTN urgency, HTN emergency, complication, medical history, laboratory investigation, ultrasound, kidney size, renal disease characteristic, cardiovascular, CT brain, renal CT, medication, past history, and outcomes.

**Data analysis**

Data entry was performed by Microsoft Excel. Descriptive analysis was performed using the SPSS software. Qualitative variables were summarized by calculating the number and percent, whereas the median, 25th and 75th Quartile range were calculated for continuous variables.

**Results**

Out of 3,640 participants, 244 met the criteria for the diagnosis of HTN, 86 patients (35.2%) were female and 158 (64.8%) were male, the mean age was 10 years. Third of the cases (n = 86, 35.2%) were diagnosed at the age between 0 and 2 years, then at the age 6 and 10 years (n = 64, 26.2%).

**Prevalence of secondary HTN and its causes**

The majority of the cases (n = 188, 77.0%) were secondary to kidney disease, then primary cause in (n = 23, 9.4%) cases. Most of the cases were diagnosed with stage 5 renal disease (78.3%). Less than half of the case were HTN urgency (n = 59, 24.2%) and HTN emergency (n = 49, 20.1%). Total of 170 (69.7%) patients did not perform CT brain, 40 (16.4%) had normal CT brain, only 34 (13.9%) had abnormal CT brain and only 4 (1.6%) cases had eye problems. The majority 236 (96.7%) of cases did not have any birth complications. Table 1 summarizes the demographic and baseline characteristic of included patients. Past history of chronic illness is insulted in Figure 1. The majority 286 (77.0%) had “nephrotic syndrome,” followed by 32 (11.4%) “Renal diseases;” and 12 (43%) “Hematological diseases.”

**Renal**

Regarding laboratory and radiological investigations, there was a decrease in serum levels of P, K, and creatinine. While there was an increase in the levels of Calcium (Ca) electrolytes, Magnesium (Mg), glomerular filtration rate (GFR), GFR2, bicarb, and Albumin. On the other hand, the level of PH, RBCs, and protein decreased [Table 2].

Total of 55 (22.5%) did not perform an ultrasound, normal ultrasound was noted in (45.1%), while bi-lateral hydronephrosis in (16.4%) and unilateral hydronephrosis in (6.6%), different findings are presented in Table 3.

Regarding kidney size, total of 56 (22.9%) showed that there is no data about kidney size, 121 (49.6%) had normal kidney size, while
the rest 67 (27.5%) had different findings; small kidney size was frequently diagnosed \((n = 29, 11.9\%)\), followed by large kidney size \((n = 26, 10.7\%)\). Good corticomedullary differentiation was reported in 59% while poor in 13.9%, absence of nephrocalcinosis in 73.8% while it presented in only 2.5%. The majority of cases did not perform micturating cystourethrogram (MCUG) \((n = 209, 85.6\%)\), normal finding in 6.6% while bilateral vesicoureteral reflux was present in 8 cases (3.3%) and unilateral vesicoureteral reflux in 4 cases only. Total of 85.1% did not perform dimercaptosuccinic acid (DMSA) scan, normal finding in 5.7%. Total of 218 (89.6%) did not perform CT renal, 5 (2.0%) had normal CT renal, while only 21 (8.4%) had different findings. Characteristic of renal imaging are presented in Table 4.

**CVS**

The results in Table 5 summarize findings in CVS; there were 157 (65.5%) cases who did not perform ECHO, 52 (21.3%)
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had normal echo, while only 35 (13.2%) had different findings presented in the table; left ventricular hypertrophy in 10 cases followed by valvular lesion in six cases and PDA in two cases.

Brain
The results in Table 6 summarize the findings in the brain; there were 169 (69.3%) patients who did not perform CT brain, 40 (16.4%) had normal finding, while only 35 (14.3%) had different findings; infarction in six cases and bleeding in two cases.

Medication
Only 11 (2.6%) patients did not receive any medications, while the rest received different type of medications; 134 (31.3%) received “ACE inhibitors,” followed by 123 (28.7%) administered “Diuretics (furosemide),” then 106 (24.8%) had “Ca- channel blockers.” Figure 2.

Disease progression and outcomes
One-third of the cases (n = 79, 32.4%) were under control while 49 (20.1%) lost follow-up and 24 (10.1%) deceased. Total of 61 (33.1%) were progressed to end-stage renal disease and patients were managed by different types of treatments; 20 cases were managed by medications, 19 cases were managed by hemodialysis, and 17 cases were managed by peritoneal dialysis [Table 7].

Discussion
There is a lack of knowledge regarding the prevalence of HTN in children of Saudi Arabia. This study findings document the prevalence, causes, and outcomes of HTN in pediatric patients presented in the inpatient ward. Out of 244 included patients, 188 cases had HTN secondary to renal disease with a prevalence of 77.0% while the prevalence of primary HTN was 9.4%. Half of the patients were diagnosed in the first 5 years. Nephrotic syndrome and renal diseases were the most frequent chronic illness that had been reported, which explain the abnormalities in renal imaging and renal function test. However, the reported data

Table 2: Laboratory investigation in included patients

| Variable       | Median | 25th and 75th Quartile range |
|----------------|--------|------------------------------|
| Ca initial     | 2.18   | (2.0,2.3)                    |
| Ca last        | 2.24   | (2.0,2.3)                    |
| P initial      | 1.57   | (1.3,1.9)                    |
| P last         | 1.52   | (1.2,1.8)                    |
| K initial      | 4.20   | (3.8,4.9)                    |
| K last         | 4.0    | (3.6,4.4)                    |
| Ca initial electrolytes | 2.1  | (1.8,2.4)                    |
| Ca last electrolytes | 2.2  | (1.9,2.5)                    |
| Mg initial     | 0.8    | (0.7,0.9)                    |
| Mg last        | 0.9    | (0.7,1.0)                    |
| Alb initial    | 27.0   | (17.0,33.0)                  |
| Alb last       | 31.0   | (23.0,36.0)                  |
| RBCs initial   | 2.0    | (0.9,10.0)                   |
| RBCs last      | 2.0    | (1.0,14.0)                   |
| Protein initial| 2.0    | (1.0,3.0)                    |
| Protein last   | 2.0    | (1.0,3.0)                    |
| Creatinine initial | 53.5 | (28.8,164.0)                |
| Creatinine last | 50.0 | (30.0,269.0)                |
| GFR initial    | 95.7   | (45.1,146.9)                 |
| GFR last       | 197.2  | (102.2,245.2)                |
| PH initial     | 7.33   | (7.2,7.4)                    |
| PH last        | 7.34   | (7.2,7.4)                    |
| Bicarb initial | 23.0   | (18.0,25.6)                  |
| Bicarb last    | 24.0   | (20.8,27.0)                  |
| GFR initial 2  | 7.5    | (2.7,15.3)                   |
| GFR last 2     | 9.1    | (1.4,15.1)                   |

Table 3: Ultrasound finding

| Variable                                | n  | Percentage |
|-----------------------------------------|----|------------|
| Not done                                | 55 | 22.5       |
| Normal                                  | 110| 45.1       |
| ARPKD                                   | 1  | .4         |
| Atrophic left kidney                    | 1  | .4         |
| Bilateral hydronephrosis                | 40 | 16.4       |
| Bilateral atrophy                      | 1  | .4         |
| Bilateral hydroureter                   | 1  | .4         |
| Bilateral minimal fullness of renal pelvis | 1  | .4       |
| Bilateral small echogenic kidney with RT renal cortical cyst | 1 | .4 |
| Bilateral small echogenic kidneys with mild to moderate ascites | 1 | .4 |
| Bilateral small hydrocele               | 1  | .4         |
| Ectopic right kidney                    | 1  | .4         |
| Hypercystic                             | 1  | .4         |
| Hypercystic and multiple cyst on both   | 1  | .4         |
| Increase echogenicity bilateral         | 1  | .4         |
| Increase echogenicity                   | 1  | .4         |
| Increase echogenicity                   | 1  | .4         |
| Increase right renal echogenicity       | 1  | .4         |
| Kidney stones                            | 1  | .4         |
| Left multicycstic kidney                | 1  | .4         |
| Mild prominence of calyceal system      | 1  | .4         |
| Multiple cysts                          | 1  | .4         |
| Polycystic kidney                       | 1  | .4         |
| Severe hydroneuters                     | 1  | .4         |
| Small echogenic kidney                  | 1  | .4         |
| Stable polycystic kidneys               | 1  | .4         |
| Unilateral hydronephrosis               | 16 | 6.6        |

Figure 2: Frequencies of medications used in patients
In another study, underlying causes of HTN in 242 patients were mostly due to renal or renovascular diseases such as renal artery thrombosis, cystic kidney disease, glomerulonephritis, and reflux nephropathy. In another study, underlying causes of secondary HTN in 242 patients were mostly due to chronic glomerulonephritis (49.2%), followed by coarctation of aorta, (53.3%) then obstructive uropathy (15.8%) and reflux nephropathy (12.2%) in contrast to low prevalence of thrombotic arterial disease. Our results are consistent with the current literature; in age group up to 6 years, renal disorders followed by coarctation of the aorta are the most commonly reported causes, followed by the renal parenchymal disease in older age.89.6% was due to renal or renovascular diseases such as renal artery thrombosis, cystic kidney disease, glomerulonephritis, and reflux nephropathy.

### Table 4: Characteristics of renal imaging

| Variable                                             | n  | Percentage |
|------------------------------------------------------|----|------------|
| Kidney size                                           |    |            |
| Normal                                               | 121| 49.6       |
| No data                                              | 56 | 22.9       |
| 5.6 × 3 cm size of the left kidney                   | 1  | .4         |
| A large right sided abdominal mass is identified     | 1  | .4         |
| measuring approximately 6.5 times 7.6 times 8.8 cm   |    |            |
| times in diameter, located in the expected region of |    |            |
| the right adrenal gland                               |    |            |
| Big                                                  | 26 | 10.7       |
| Lt kidney atrophied, Rt kidney enlarged               | 1  | .4         |
| Minimal increase in the size                         | 1  | .4         |
| Relatively increased                                  | 1  | .4         |
| right kidney only                                     | 1  | .4         |
| Right kidneys is small                                | 1  | .4         |
| Rt is small                                           | 1  | .4         |
| Rt. is small, Lt. is big                             | 1  | .4         |
| Small                                                | 29 | 11.9       |
| The right is normal                                   | 1  | .4         |
| The right kidney enlarged                             | 1  | .4         |
| With cyst measures 0.5 cm                             | 1  | .4         |
| Chorionicomedullary differentiation                   |    |            |
| N/A                                                  | 57 | 23.3       |
| Normal                                               | 1  | .4         |
| Cortical thickness                                   | 2  | .8         |
| Cortical thickness of 0.8                             | 1  | .4         |
| Good                                                 | 144| 59.0       |
| good in the right                                    | 2  | .8         |
| increased cortical echogenicity                       | 1  | .4         |
| Irregular outline with multiple diverticulae          | 1  | .4         |
| Mild cortical increase echogenicity with no dilation  | 1  | .4         |
| or stones                                             |    |            |
| Poor                                                 | 34 | 13.9       |
| Nephrocarcinosis                                     |    |            |
| Absent                                               | 180| 73.8       |
| N/A                                                  | 58 | 23.7       |
| Present                                              | 6  | 2.5        |
| MCUG                                                 |    |            |
| Not applicable                                       | 209| 85.6       |
| Normal                                               | 16 | 6.6        |
| bi-lateral vesicoureteral reflux                      | 8  | 3.3        |
| Bladder is distended and elongated                   | 1  | .4         |
| Grade 5 right sided vesicoureteric reflux            | 1  | .4         |
| Grade V                                              | 1  | .4         |
| Neurogenic bladder                                    | 1  | .4         |
| Neurogenic bladder with no vesicoureteric reflux      | 1  | .4         |
| Normal but the patient may have neurogenic bladder   | 1  | .4         |
| Obstruction                                          | 1  | .4         |
| Uni-lateral vesicoureteral reflux                     | 4  | 1.6        |
| DMSA                                                 |    |            |
| Normal                                               | 14 | 5.7        |
| Not applicable                                       | 217| 85.1       |
| bi-lateral scarring                                  | 5  | 2.0        |
| evidence of bilateral renal impairment, wore on the | 1  | .4         |
| left side                                            |    |            |
| no evidence of functioning tissue at the left side on | 1  | .4         |
| the right side                                       |    |            |
| Contd...                                              |    |            |
In our study, 157.4% of patients had left ventricular hypertrophy and valvular lesion. In a cross-sectional study in northern India among 1,085 school children aged from 11 to 17 years, the prevalence of obesity and HTN were 3.7% and 4.9%, respectively. A multicenter study by Narang et al. concluded that age, sex, socioeconomic status, and geographical distribution had an impact on the prevalence of HTN. In 2017, Das Mk et al. reported that the prevalence of HTN raises with BMI and age. More specifically, the prevalence of HTN among underweight was 14.6% compared to 20.6% among normal weight persons. In a cross-sectional study in northern India among 1,085 school children aged from 11 to 17 years, the prevalence of HTN and overweight were 5.9% and 3.5%, respectively. However, Sumboonnanonda et al. found that BMI more than 25 is not reliable to differentiate primary and secondary HTN, since there is no significant difference between them.

Previous studies have revealed that many factors are associated with the high rates of HTN such as age, sex (male) or obesity. In another study of 25,309 children and adolescents aged 7–18 years, the prevalence of obesity and HTN were 3.7% and 4.9%, respectively. A multicenter study by Narang et al. concluded that age, sex, socioeconomic status, and geographical distribution had an impact on the prevalence of HTN. In 2017, Das Mk et al. reported that the prevalence of HTN raises with BMI and age. More specifically, the prevalence of HTN among underweight was 14.6% compared to 20.6% among normal weight persons. In a cross-sectional study in northern India among 1,085 school children aged from 11 to 17 years, the prevalence of HTN and overweight were 5.9% and 3.5%, respectively. However, Sumboonnanonda et al. found that BMI more than 25 is not reliable to differentiate primary and secondary HTN, since there is no significant difference between them.

In general, systemic HTN could affect the cardiovascular system. In our study, left ventricular hypertrophy and valvular lesions were the highest abnormality reported, even with a few event and small prevalence reported. In a cross-section study on hypertensive young patients, 17% had concentric left ventricular hypertrophy. However, Lesiman et al. found a humble relationship between blood pressure variability and left ventricular hypertrophy in primary and secondary HTN; however, secondary HTN was associated with increased sleep period diastolic standard deviation. Further, regular screening for elevated blood pressure and preventable measurement to control weight, reduce salt intake, encourage healthy dietary habits and active lifestyle are all recommended to avoid the complications of pediatric HTN.

The main aim of healthcare practitioners in the management of pediatric secondary HTN is to normalize the blood pressure below the 90th percentile and closely monitor any potential target organ damage. However, there is no preferred antihypertensive medication, but it is recommended to start with the lowest dosage of the antihypertensive medication till target blood pressure is reached. If still target blood pressure is not achieved with the maximum dosage of a single medication, a second medication with complementary action should be added. In our study, the majority of patients were treated by angiotensin-converting enzyme inhibitor (ACEI), since it was found to be a good choice for a child with proteinuria due to renal disease. Also, the highest percentage of patients who progressed to end-stage renal disease were managed by medications. Beside pharmacological therapy, lifestyle modification could be effective to decline the blood pressure. Significant reduction in blood pressure in adolescent was accomplished by maintaining the DASH diet (Dietary Approaches to Stop HTN) versus standard diet.

It is worth mentioning that evidence-based information and statistics about pediatric HTN would help the policymakers and all healthcare practitioners in the effective management of HTN and associated comorbidities. The National Institute of Health (NIH) of the USA has reported that at least once annual evaluation of blood pressure and checking the elements of anthropometry are warranted.

Our study has some limitations: (1) it was carried out as a single-center, (2) participants were only inpatients cases, (3) investigations performed were not sufficient to evaluate and investigate the complications of HTN, and (4) there were some missing data from specific profiles.

**Conclusion**

The prevalence of secondary HTN due to renal disease is considered to be high in pediatric patients admitted to King Abdulaziz University. Several renal diseases in the renal system are associated with secondary HTN mostly attributed to renal malformation. In addition, renal affection, cerebral infarction, bleeding, left ventricular hypertrophy, and valvular lesion are the highest reported complications in our population. Follow-up with ECHO and brain CT is highly recommended in pediatric HTN. Future studies on a larger sample and vigorous follow-up are recommended.

**Recommendations**

- Follow-up extended studies with ECHO, eye examination and brain CT are highly recommended in pediatric HTN.

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**Table 5: CVS finding**

| Variable                                              | n  | Percentage |
|-------------------------------------------------------|----|------------|
| No ECHO                                               | 157| 65.5       |
| Normal                                                | 52 | 21.3       |
| 7 mm fenestrated ASD shunting left to right            | 1  | .4         |
| Cardiomyopathy                                        | 1  | .4         |
| Coarctation of aorta                                  | 1  | .4         |
| Dilated left ventricle and left atrium                 | 1  | .4         |
| IVC thrombus                                          | 1  | .4         |
| Left ventricular dilation                              | 1  | .4         |
| Left ventricular hypertrophy                           | 10 | 4.1        |
| Left ventricular hypertrophy + valvular lesion         | 1  | .4         |
| Mild peripheral pulmonary stenosis                    | 1  | .4         |
| Minimal pericardial effusion and minimal pericardial thickening | 1  | .4         |
| Patent foramen ovale                                  | 1  | .4         |
| PDA                                                   | 2  | .8         |
| Pericardial effusion                                  | 1  | .4         |
| TGA, PDA S/P ARTERIAL switch operation                | 1  | .4         |
| Tof dilated RV + pulmonary atresia/s/p tof repair     | 1  | .4         |
| and tricuspid valve repair and lpa unifocalization     |    |            |
| Valvular lesion                                       | 6  | 2.5        |
| Valvular lesion, TOF                                   | 1  | .4         |
| VSD                                                   | 1  | .4         |
Studies with larger sample and multi-centers approach are recommended.
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