

Original Article**Prevalence of Renal Hypertension In Apparently Healthy Term Newborns.**

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Abstract

Introduction: Neonatal hypertension (HT) is an emerging challenge for neonatologists and pediatricians around the world. The prevalence of renal causes of neonatal hypertension due to congenital renal anomalies and malformations including obstructive uropathy and cystic kidney disease is not well estimated up till now. Early diagnosis of congenital renal anomalies is the corner stone of good prognosis and better outcome.

Aim of the study: To determine the prevalence of neonatal renal hypertension in apparently healthy term neonates discharged in the first 48 h of life from two university hospitals.

Methods: Two thousand apparently healthy appropriate for gestational age (AGA) term newborns had blood pressure (BP) measurements using the oscillometric technique All results of blood pressure were compared to estimated blood pressure values in percentile curves generated by Dionne et al.

Results: There were 29 of 2000 (1.45%) screened newborns diagnosed as having systemic hypertension, our study showed that renal anomalies were the main causes of neonatal systemic hypertension. It represent (93.1 %) of total causes in our study, [with pelviureteric junction (PUJ) Obstruction (31%), polycystic kidney (24.1%), nephrocalcinosis (13.7 %), unilateral renal dysplasia (10.3%), renal hypoplasia (3.4%), unilateral multi cystic kidney (3.4%)]. The remaining cases (6.9%) were due to aortic coarctation. No endocrinal cases was diagnosed in our study.

Conclusion: This study showed that renal anomalies were the most common causes of neonatal systemic hypertension in apparently healthy term newborns. Beside that this study provided normative BP values for healthy full term AGA newborns in the first 48h of life. These values can be used in the evaluation of BP in newborns.

Keywords: Newborn, blood pressure, ultrasonography, neonatal renal hypertension, polycystic kidney disease, pelviureteric obstruction.

Running title: Prevalence of Renal Hypertension In Apparently Healthy Term Newborns.

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geget: The Journal of the Egyptian Society of Pediatric Nephrology and Transplantation (ESPNT)

geget <https://geget.journals.ekb.eg/>

Published by ESPNT <http://espnt.net/>

Cohosted by Egyptian Knowledge Bank <https://www.ekb.eg>

Introduction

Routine BP measurement though a common clinical practice among adult physicians, is not usually observed in the pediatric practice especially in the well newborns. This may be due to the relatively low incidence of hypertension in the pediatric age group [1]. Neonatal hypertension (HT) is an emerging challenge for neonatologists and pediatricians around the world. The first published neonatal BP study at birth was performed by Holland and Young [2] in 1956 by palpating the brachial artery below an inflatable cuff. They compared the average SBP (systolic Blood pressure) at birth of neonates in various conditions, such as abnormal deliveries, abnormal pregnancies (e.g., pre-eclampsia), premature infants and among twins [3].

Blood pressure is a continuous changing variable and the values depend on multiple factors. In neonatal population, these factors include gestational age at birth, postnatal and postmenstrual age, and appropriateness for gestational age (AGA). Other factors which are often neglected include maternal drugs, Apgar scores, maternal HT, mode of delivery, anesthesia used during delivery [4].

Renal congenital anomalies are the common causes of neonatal hypertension and the early diagnosis of them still the corner stone of good prognosis and better outcome [5].

Aim of the study

To determine the prevalence of neonatal renal hypertension in apparently healthy term neonates discharged in the first 48h of life from two university hospitals.

Methods

Study population: This is a prevalence study performed on 2000 apparently healthy term newborns delivered either by cesarean section or spontaneous vertex delivery in two University Hospitals. This study was carried out during the period from January 2019 to the end of November 2019.

Inclusion criteria: All apparently healthy term discharged newborns weighted >2500 g delivered either by cesarean section or spontaneous vaginal delivery. The following newborns were excluded from the study: Any newborn needed neonatal intensive care unit admission, low birth weight (<2500 g) history of maternal illness or drug intake during pregnancy.

The following was done for all newborns:

- a. Informed written consent from the parents of the newborn to participate in the study.
- b. Detailed history was taken from parents especially maternal, medical and obstetric history.
- c. Thorough physical examination was performed including body length, body weight, heart rate, respiratory rate, temperature, gestational age assessment using Ballard score for all newborns as well as complete systemic examination.
- d. Blood pressure was measured according to Standardized protocol for blood pressure measurement in neonates [6]. Within 1st 6 hours after delivery and after 24-48 hour using DINAMAP carescapev100 vital signs monitor made in USA. After an appropriate cuff size was applied on the
- e. right arm we wait 15 min after cuff is placed. Each neonate was calm in supine position during measurement. The

hypertensive newborns have further measurement of blood pressure of both upper and lower limbs for confirmation and detection of coarctation of the aorta.

The monitor (DINAMAP CarescapeV100) is switched on while the cuff inflation and deflation is automatically done by the instrument with subsequent display of the BP values on the screen. All results of blood pressure compared to estimated blood pressure values in percentile curves generated by Dionne et al. [7]. We considered that the newborn is hypertensive and needs follow up if 2nd reading or both 1st and 2nd readings of measuring BP were above 95th percentile.

Investigations were done only for neonates with confirmed hypertension within 48hr after delivery including complete blood count (CBC), C-reactive protein (CRP), serum electrolytes ,thyroid hormone , serum creatinine ,blood urea nitrogen ,arterial blood gas analysis, plain Chest X-ray, abdominopelvic ultrasound, renal Doppler and Echocardiogram. All diagnosed cases are under regular follow up at the Pediatric nephrology clinic in the university hospital.

Statistical analysis

Data were collected and analyzed using IBM SPSS software package version 22.0 (IBM corporation and others, USA). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean \pm standard deviation and median.

Significance of the obtained results was judged at the 5% level. The used tests were: Chi-square for categorical variables (to compare between different groups), Both Fisher's Exact when more than 20% of the cells have expected count less than 5, Mann Whitney test for abnormally quantitative variables, to compare between two studied groups, and Pearson coefficient to correlate between two normally quantitative variables.

Results

This study was carried out on 2000 apparently healthy term newborns. They were classified as normotensive (1971 newborns) and hypertensive (29 newborns).

The normotensive group included 1031 females and 940 males newborns. Of these neonates, 710 neonates were delivered vaginally, and 1261 neonates were delivered by cesarean section (CS).

On the other hand the hypertensive group (N=29) included (13 males and 16 females) 12 of them were delivered by normal vaginal delivery while 16 were delivered by (CS).

All newborns delivered after 36 weeks of gestation and weighed > 2500 – 3900g. All of them were apparently healthy and discharged within 48 hr of delivery.

The clinical data of all studied newborns are summarized in (Table 1). There is a highly significant difference in blood pressure values of SBP (Systolic Blood pressure), DBP (Diastolic Blood pressure), MAP (Mean Arterial Blood Pressure) between hypertensive and normotensive group. Other clinical parameters showed no significant difference.

(Table 2) Shows comparison of blood pressure between males and

females of normotensive and hypertensive newborns.(No significant difference detected). (Table 3) Compares the blood pressure values between newborns delivered vaginally and those delivered by CS of normotensive and hypertensive groups (No significant difference). (Table 4) Arterial blood pressure in the normotensive newborns with distribution according to Body weight.

(Table 5) Shows laboratory values in hypertensive group (all values are within normal ranges) [8]. (Table 6) Shows ultrasound and Doppler

findings of renal anomalies in hypertensive group. (Tables 7) Shows Blood pressure percentile values (norms) in apparently healthy newborns.

All laboratory data of hypertensive apparently normal newborns were normal including serum creatinine* (reflect maternal serum creatinine in the first 48 hr).

Two cases were diagnosed by echocardiography as coarctation of aorta and no endocrinal cases were diagnosed in our study.

Table 1: Clinical data of normotensive and hypertensive apparently healthy newborns

	Normotensive N=1971	Hypertensive N=29	P
Birth weight (gm)	3185 ± 480	3110 ± 335	0.402
Birth length (cm)	48.5 ± 2.1	48.7 ± 1.8	0.6100
HC(cm)	35 ± 1.9	35 ± 1.7	1.000
Weeks of gestations (weeks)	37 ± 2	37 ± 2	1.000
Blood pressure at 0-6 hours			
SBP (mmHg)	63.1 ± 5.4	85.22 ± 2.38	<0.001*
DBP (mmHg)	36.8 ± 4.3	65.45 ± 2.55	<0.001*
MAP (mmHg)	46.4 ± 5.1	74.5 ± 2.3	<0.001*
Blood pressure at 24 - 48 hours			
SBP (mmHg)	65.2 ± 5.4	82.22 ± 2.38	<0.001*
DBP(mmHg)	40.2 ± 4.3	63.45 ± 2.55	<0.001*
MAP(mmHg)	49.4 ± 4.6	71.5 ± 2.3	<0.001*
Gender Male	940 (47%)	13 (0.45 %)	0.759
Female	1031 (51.5%)	16 (0.8%)	
Mode of delivery			
Normal Vaginal Delivery	710 (36%)	12 (52.5%)	0.356
Caesarean Section	1261 (64%)	17 (47.5%)	

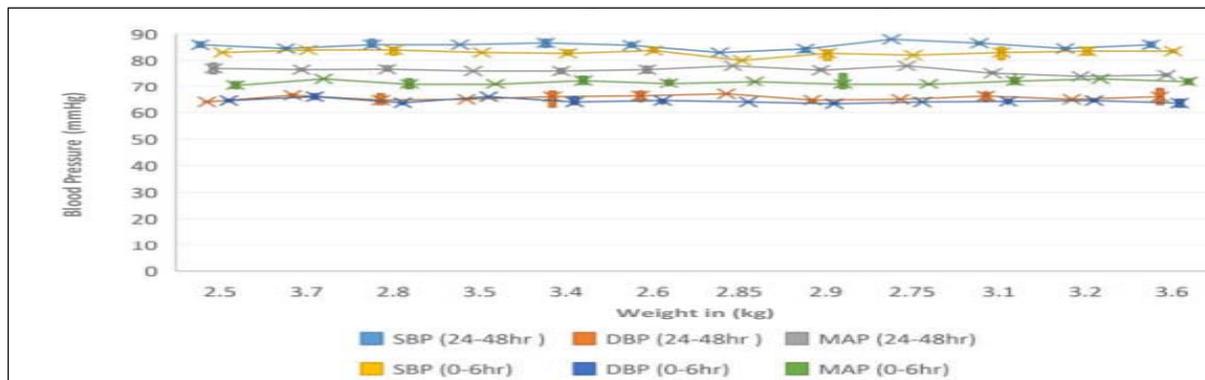


Figure 1: Blood pressure values in apparently healthy Hypertensive newborns (N=29) in relation to their weight in first 2 days.

N.B. The mean values of SBP , MAP and DBP of hypertensive newborns (N=29) were above 95th percentile as detected in our results and also (according to percentile curves generated by Pejovic et al. [1] and approved by Dionne et al. [7].

Table 2: Comparison of blood pressure between males and females of normotensive newborns (N=1971) and hypertensive newborns (N=29):

Normotensive Newborns				
	Total (N= 1971)	Female (N = 1031)	Male (N = 940)	P
At 0-6 hr				
SBP (mmHg)	65.1 ± 5.4	65.3 ± 5.7	65.2 ± 5.1	0.683
DBP(mmHg)	36.8 ± 4.3	36.6 ± 4.2	36.2 ± 4.9	0.051
MAP(mmHg)	46.4 ± 5.1	46.4 ± 5.0	46.2 ± 5.2	0.384
At 24-48 h				
SBP (mmHg)	65.2 ± 5.4	65.8 ± 5.7	65.3 ± 7.1	0.084
DBP(mmHg)	40.2 ± 4.3	40.6 ± 4.3	40.2 ± 4.8	0.054
MAP(mmHg)	49.4 ± 4.6	49.4 ± 4.1	49.1 ± 3.9	0.097
Hypertensive term newborns (N=29)				
	SBP (mmHg)	DBP (mmHg)	MAP(mmHg)	
At 0-6 hours				
Males (N = 13)	85.12 ±2.38	63.27± 2.55	74.1 ± 2.3	
Females (N=16)	85.22 ± 2	63.35±2.55	74.3± 2.3	
P	0.903	0.934	0.818	
At 24-48 hours				
Males (N = 13)	81.9 ± 3.1	63.25±2.35	71.3±2.3	
Females (N=16)	82.1 ± 2.35	63.34± 2.42	71.4 ±1.3	
P	0.845	0.920	0.883	

Table 3: Comparison between blood pressure values of normotensive (n=1971) and hypertensive (n=29) term healthy newborns according to mode of delivery.

	SBP (mmHg)	DBP(mmHg)	MAP(mmHg)
At 0-6 hours			
Vaginal (N = 722)	64.6 ± 0.57	38.90 ± 0.38	49.16 ± 1.3
C.S (N=1278)	64.55 ± 0.54	38.87 ± 0.33	49.23 ± 0.3
P	0.051	0.065	0.065
At 24-48 hours			
Vaginal (N= 722)	64.8 ± 0.58	38.22 ± 0.44	48.16 ± 0.46
C.S (N=1278)	64.75 ± 0.55	37.19 ± 0.43	48.12 ± 0.5
P	0.055	0.137	0.077
Hypertensive newborns			
At 0-6 hours			
Vaginal (N = 12)	85.12±2.38	63.27 ± 2.55	74.1 ± 2.3
C.S (N=17)	85.22 ± 2	63.35 ± 2.55	74.3 ± 2.3
P	0.903	0.934	0.819
At 24-48 hours			
Vaginal (N= 12)	82.2 ± 2.28	63.45 ± 2.55	71.5 ± 2.3
C.S (N=17)	82.1 ± 2.25	63.43 ± 2.52	71.6 ± 1.3
P	0.907	0.983	0.882

Table 4: Arterial blood pressure in the normotensive term newborns with distribution according to body weight.

Weight(kg)	SBP(mmHg)	DBP (mmHg)	MAP(mmHg)
Normotensive newborns			
At 0-6 hours			
2.5-3(kg)	64.2±0.57	39.1± 0.48	49.16± 0.51
3-3.5(kg)	63.9± 0.55	38.75±0.45	49.23 ±0.3
P	0.161	0.053	0.659
At 24-48 hours			
2.5-3(kg)	61.97± 0.45	38.20 ± 0.4	48.57±0.41
3-3.5(kg)	62.32±0.48	37.9±0.456	48.73 ± 0.4
P	0.053	0.068	0.297

Table 5: Laboratory findings in newborns diagnosed with hypertension (N=29).

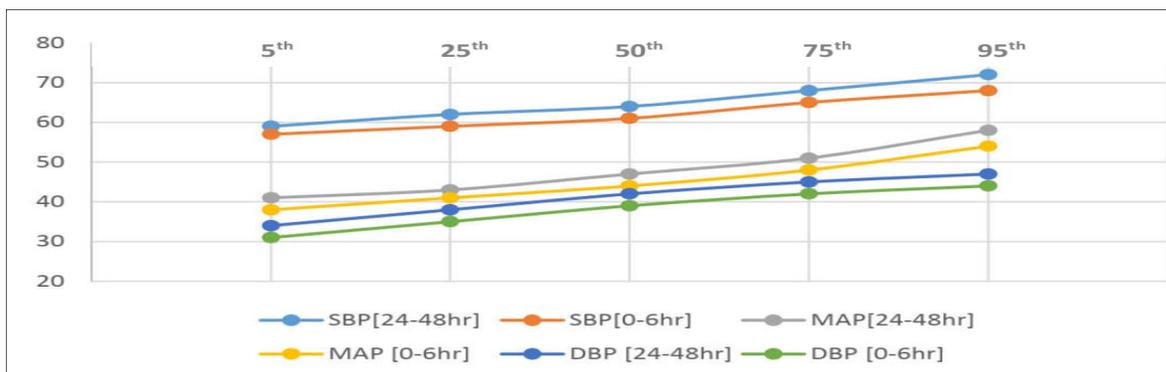
Lab	mean ±SD
WBCs	8000.16 ± 3.02 /dl
Hb	13.95 ± 1.45 g/dl
Hct	41.63 ± 5.01
Platelet count	300.000 ± 26 /dl
CRP (negative in all cases)	2.5 ± 0.7 mg/dl
BUN	15.83 ± 7.38 mg/dl
Creatinine* mean ±SD	0.83 ± 0.21 mg/dl
min - max	0.71 – 0.85 mg /dl

Table 6: Ultrasound findings in newborns diagnosed with hypertension (N=29).

Ultrasound & Doppler Findings	No.	%
Normal	2	6.9
Abnormal findings	27	93.1
Lt Renal hypoplasia	1	3.4
Unilateral Renal dysplasia	3	10.3
Unilateral hydronephrosis	9	31.0
Nephrocalcinosis	2	6.9
PUJ Obstruction	9	31.0
Polycystic kidney	2	6.9
Unilateral multi cystic kidney	1	3.4

Table (7) Blood pressure percentile values in apparently healthy term newborns .

	5 th	50 th	95 th
SBP[24-48hr] (mmHg)	59	64	72
SBP[0-6hr] (mmHg)	57	61	68
MAP[24-48hr] (mmHg)	41	47	58
MAP [0-6hr] (mmHg)	38	44	54
DBP [24-48hr] (mmHg)	34	42	47
DBP [0-6hr] (mmHg)	31	39	44

**Figure 2:** Percentiles of apparently healthy term newborns

Discussion

Hypertension in neonates was first described in the 1970s and has been a subject of great interest among neonatologists and other pediatric subspecialists ever since [9].

Different studies were carried out to measure blood pressure in newborns [1], [10], [11], [12]. From these studies the authors concluded that blood pressure in term newborns was not affected by the race or weight in those weighed >2500g however there were differences in their results regarding the value of blood pressure and this can be explained by the difference in the study characteristics of the newborns included in each study.

Our study population included only healthy aged from (36–40 weeks Gestation) neonates without any therapy or NICU admission. In our study, 2000 neonates were screened, of whom 29 (1.45 %) neonates showed systemic hypertension, 13 newborns of them were males and 16 were females. In a review of over 3000 infants admitted to a Chicago NICU, the overall incidence of hypertension was found to be 0.81% [13].

Our results are in agreement with Watkinson [14] who reported that incidence of hypertension in many reviewed studies ranges from 0.2-3 %. The mean values of SBP, MAP and DBP of hypertensive newborns (n=29) detected in our results were above 95th percentile (according to percentile curves generated by Pejovic et al. [1] and approved by Dionne et al. [7]. The mean SBP, DBP and MAP of apparently healthy normotensive newborns (Table 2) showed no statistically significant difference between males and females.

Our data agreed with Seliem et al. [15] who screened 2,572 newborn infants, 34

infants of them diagnosed with systemic hypertension (1.3%); 20 of these 34 newborn infants (59%) were males although the mean blood was higher in males than females but the difference was not significant. Also Sadoh and Ibhanebhor [16] documented that SBP, DBP, and MAP of female neonates were higher than those of male neonates in the first week of life but the difference was not statistically significant.

Our results of neonatal blood pressure are also supported by Nwokoye et al., [17] who documented that blood pressure values can be used interchangeably for both males and females at birth among term babies. However Gemelli et al. [18], documented that females have higher blood pressure values in the first days of life. This can be explained by the influence of sex on neonatal BP.

The mode of delivery was not significantly associated with change in BP in this study (Table 3). This is similar to the findings of Gemelli et al [18] who reported that the mode of delivery (either vaginally or CS) did not show any effect on neonatal blood pressure. Also our data agreed also with Sadoh and Ibhanebhor [16] who reported that neonatal hypertension is not affected by mode of delivery.

As regard blood pressure in the normotensive term newborns with distribution according to Body Weight. (Table 4) our results agreed with Pejovic et al. [1] who carried out a study on 400 newborns and has shown a similar correlation of gestational age and birth weight with blood pressure in neonates. The norms of blood pressure values are listed in (Table 7) which is similar to Nwokoye et al., [17] who reported that The 5th, 50th, and 95th percentile of BP

values at 0–24 hr of term newborns were lower than that measured at (25-48 hr.)

Also the blood pressure values in our study measured in the first 2 days showed slightly higher blood pressure values in the 2nd day more than the 1st day these data are supported by those reported by Kent et al. [19] who reported that the blood pressure values in healthy term infants in the postnatal ward were higher on day 2 compared to day 1 of life but not consistently thereafter.

The laboratory data which included CBC, CRP and the renal function of hypertensive apparently normal term newborns listed in (Table 5) were within normal neonatal ranges according to Mary et al., [8] although serum creatinine is quite high by neonatal standards this may reflect maternal values as all labs were done within 48 hr after birth.

Our study has demonstrated that 27 newborns (93.1 %) of hypertensive cases diagnosed with nephro-urological malformations and 2 newborns with coarctation of the aorta. Our data are in agreement with Janjua et al., [20] who reported that congenital urologic malformations as a cause of neonatal hypertension was carried out in Brazil, in which 13 of 15 hypertensive infants had urological causes.

The anatomical renal causes of neonatal hypertension which were found in our studied newborns (Table 6) included polycystic kidney (9 cases), PUV (9 cases), nephrocalcinosis (2 case) unilateral renal hypoplasia (1 case), unilateral renal dysplasia (3 cases), unilateral hydronephrosis (2 cases) and unilateral multicystic kidney (1 case).

Also our results are in agreement with Seliem et al., [15] who found that nephrourological malformations were the

most frequent etiology of neonatal hypertension. Our findings are supported by Vechkanova et al., [21] who found a causal relationship between hydronephrosis and elevated blood pressure. The underlying mechanisms contributing to the development of hypertension are complex and involve increased activity of the Renin-angiotensin-aldosterone system (RAAS), oxidative stress and Nitric oxide (NO) deficiency in the obstructed kidney. Our study results are supported by those of Martino *et al.*, [22] who demonstrated that approximately 5 – 10% of neonates with PUJO were hypertensive and in most cases relief of the obstruction normalized blood pressure.

Janjua et al., [20] documented that autosomal dominant and autosomal recessive polycystic kidney disease (PKD) may present in the neonatal with severe nephromegaly and hypertension. The the majority of infant with recessive PKD are usually discovered to be hypertensive during the first year of life. The most severely affected infants with PKD are at risk for development of congestive heart failure due to severe, malignant hypertension.

In our study we found that 2 infants (0.1%) were diagnosed as coarctation of the aorta diagnosed by echocardiography .This is in agreement with the study done by Lanzarini et al, [23] who stated that coarctation of the aorta has been reported as the second most frequent aetiology of neonatal hypertension so we should suspect the possibility of coarctation of the aorta in hypertensive neonates after exclusion of renal causes if there is difference in measuring blood pressure in four limbs .All pediatricians should be aware of this possibility .

Nwokoye et al., [17] reported that newborns who developed hypertension between 0 and 24 h require only further observation, but in the second 24 h of life, newborns who still have or develop hypertension may require further investigation.

Although the American Academy of Pediatrics does not recommend universal screening of blood pressure in term healthy newborns but states it is important to screen BP in infants in whom coarctation of the aorta or renal disease is suspected [24].

We noted that some cases with renal anomalies have no regular antenatal follow up or did not have detailed antenatal ultrasound (US) reports. This attracts our attention to the importance of high resolution ultrasound for early detection of renal anomalies that can help us in follow up of those newborns for detection of hypertension.

Our hypertensive newborns of renal aetiology are on regular follow up at pediatric nephrology clinic in the university hospital.

Conclusion

This study provides that renal anomalies were the most common causes for neonatal systemic hypertension in term apparently healthy discharged newborns. Beside that this study provided normative BP values for healthy full term AGA newborns in the first 48 hours of life.

These values can be used in the evaluation of BP in newborns and can help in the development of Egyptian percentiles for neonatal blood pressure.

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Statements

Ethics approval and consent to participate

This study protocol and the consents were approved and deemed sufficient by the Ethical Committee of Pediatric Department, Al-Azhar University and informed written consent was obtained in every case from their legal guardians.

Consent for publication

The contents and material of the manuscript have not been previously reported at any length or being considered for publishing elsewhere.

Availability of data and material

“Not applicable”

Conflict of interest

The authors declare no conflict of interest.

Funding

The authors declare that this research work didn't receive any fund.

Acknowledgements

We would like to thank all patients and their family members for their valuable contributions to the study.

Submitted	22/04/2021
Accepted	19/06//2021
Published online	28/07/2021