Patterns of Blood Pressure in Infants who Survived from a Neonatal Intensive Care Unit

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Abstract: Background: Neonates admitted and treated at neonatal intensive care units (NICU) are at increased risk of developing hypertension. We measured blood pressure of infants who survived from the neonatal Intensive Care Unit (NICU) during follow up. We are reporting the patterns of blood pressure of these infants. Short of appropriate BP apparatus, BP is not routinely measured in resource limited settings. Timely identification of high BP could help to avert the occurrence of target organ damage. Objectives: To assess the pattern of blood pressure and associated factors for hypertension in infants who survived from the NICU. Materials and methods: This is a cross sectional study conducted from January 2015 to September 2016 at Tikur Anbessa Hospital High Risk Infant Clinic (HRIC). Three measurements were taken at each visit and mean blood pressure was taken for analysis. Infants with high BP in the first visit were followed for two more visits 4 weeks apart. Systolic or diastolic blood pressure > 95th percentile for gender and age is considered hypertension. Results: Blood pressure was measured for 394 infants from 1 month to 24 months of age. More than half (56.1%) were male. Eleven infants (2.8%) were hypertensive in three subsequent visits; 3 were females and 8 males. Four were admitted at birth because of prematurity, low birth weight; small for gestational age, hypothermia and sepsis but 7 were term infants with perinatal asphyxia and sepsis. Binary logistic regression didn’t show statistically significant association between high BP and patient characteristics at admission. Conclusion and recommendation: Routine blood pressure monitoring should be the standard practice in the care of high risk infants. Longitudinal studies are recommended to see the pattern and associated risk factors for HBP in survivors of the NICU.

Keywords: high risk infant clinic; neonate, Ethiopia; neonatal intensive care unit; high blood pressure

1. Introduction
The problem of hypertension in the neonatal intensive care units (NICU) is well known from the early seventies (1). The recent advances in neonatal intensive care have made it possible for the evaluation, diagnosis and care of newborns with hypertension (2). Many investigators have shown that renovascular or renal parenchymal diseases are the most common causes of hypertension in the early years of infancy (3, 4). It is estimated that hypertension occurs in 0.2-3% of newborns admitted to the NICU though standardization of blood pressure measurement in this age group is not completely settled (2,4). The incidence of hypertension increases in infants with broncho-pulmonary dysplasia, patent ductus arteriosus, intraventricular hemorrhage, and indwelling umbilical arterial catheters. In such cases the incidence increases to approximately 9% (4).

Direct measurement of neonatal blood pressure from an artery is the most accurate method in the neonatal intensive care units but with its own limitations; it requires expensive equipment, entering an artery is a risk factor for introducing infection and predisposes to thrombotic complications (5). Nowadays, oscillometric technique is the most widely used non-invasive method for measuring BP in several NICUs.

In older children, BP is affected by age and body size and many studies have shown that in full term and preterm newborns BP is dependent on gestational age, post natal age as well as birth weight (6-8). Though the definition of normal blood pressure and hypertension in newborn infants is not completely settled, the Zubrow et al study (9) has managed to show that hypertension is considered when the BP fell above the upper limit of the 95% confidence interval for infants of similar gestational or post conceptual age.

For standardization of blood pressure in infants following discharge from our NICU we used the percentile curves generated by the second task force (10). Newborns who survived the NICU are at increased risk of developing hypertension in late childhood but
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We hypothesize that gestational age at birth, procedures done at the NICU and complications of prematurity affect the BP of infants who were admitted and treated at the NICUs.

1.1 Materials and methods

1.1.1 Setting: This study was conducted at the Department of Pediatrics and Child Health HRIC of Tikur Anbessa Specialized Teaching Hospital. The clinic is run by three nurses who are stationed there and a second year pediatric resident on rotation bases supervised by a neonatologist. In the clinic growth is monitored and medical checkups are done but BP measurement is not routine.

1.1.2 Study subjects: This is a cross sectional study conducted from January 2015 to September 2016. Blood pressure was measured for all infants beyond one month of age attending HRIC in their regular follow up visits. Three BP measurements were taken at each visit by a second year pediatric resident using a manual aneroid sphygmomanometer. Infants were sitting on the lap of their care takers, cuff bladder length covering at least 80% of the arm circumference and width covering 2/3rd of the arm length was used. Mean blood pressure was taken for analysis and systolic or diastolic blood pressure that lies above the 95th percentile for gender and age is considered hypertension according to the report of the Second Task Force on Blood Pressure Control in children (10). If the mean of the three blood pressure measurements in a single visit is normal no further measurement was taken on subsequent visits but for those whose mean systolic, diastolic or both blood pressure was >95th percentile a repeat measurement was taken four weeks apart for two more consecutive visits. An infant is declared hypertensive when BP is above 95th percentile for age and gender is three consecutive visits when age is corrected for prematurity.

1.1.3 Data collection process

Maternal and infant demographic data was collected from mothers and the record using a structured questionnaire. Three blood pressure measurements were taken at each visit by a pediatric resident who is attending the high risk infant clinic at 2-5 minute intervals in a quiet state using an appropriate manual sphygmomanometer whose bladder length covers at least 80% of the arm circumference and width covers 2/3 of the arm length. The age of study subjects ranges from one month to 24 months. The principal investigator calculated the mean of the three blood pressure measurements and computed with the standard for age and gender. Blood pressure measurement was not taken for infants who were below one month of age because of technical difficulty.

1.1.4 Statistical analysis

The data was entered, cleaned and analyzed using SPSS for windows version 20 soft ware. Binary logistic regression model was used to identify the factors associated with the development of hypertension in infants who were discharged from the neonatal intensive care unit and P-values <0.05 (95% confidence interval) was considered to have significant association.

1.1.5 Ethical clearance

Verbal consent was obtained from care takers attending the infant and the study was approved by the Institutional Review Board of College of Health Sciences of Addis Ababa University.

1.2 Results

Blood pressure was measured for all 394 infants from the age of 1 month to 24 months from January 2015 to September 2016 at the high risk infant clinic during their regular follow up visits. There were 173 females (43.9%) and 221 males (56.1%). There were 44 infants (11.2%) with hypertension whose systolic, diastolic or both blood pressure measurement was >95th percentile for age and gender during the first measurement. When blood pressure was measured for these infants on two consecutive visits over 4 weeks apart, 11 infants (2.8%) were found to be hypertensive. Among these 8 were males. The pattern of BP is as shown in fig 1 and 2.

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Figure 2: Patterns of diastolic BP in infants who survived the NICU of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

Among these 11 infants with hypertension, 4 (36.4%) were admitted at birth because of prematurity, low birth weight, small for gestational age, hypothermia and sepsis but the remaining 7 (63.6%) were term infants who had perinatal asphyxia and sepsis. Table 1 shows admission diagnosis of infants to the NICU.

Table 1: Admission diagnosis of children who survived from the NICU, Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia (n=394)

| Diagnosis                           | Number | Percent (%) |
|-------------------------------------|--------|-------------|
| Term, AGA, sepsis                   | 49     | 12.4        |
| Preterm, LBW, SGA, hypothermia, sepsis | 44     | 11.2        |
| Term, AGA, hypothermia, sepsis      | 38     | 9.6         |
| Term, AGA, PNA, sepsis              | 34     | 8.6         |
| Preterm, LBW, SGA, RDS, sepsis      | 25     | 6.3         |
| Term, LBW, SGA, sepsis              | 19     | 4.9         |
| Preterm, LBW, SGA, sepsis           | 18     | 4.6         |
| Preterm, LBW, SGA, RDS              | 13     | 3.3         |
| Term, LBW, SGA, hypothermia, sepsis | 12     | 3.0         |
| Term, AGA, PNA                      | 11     | 2.8         |
| Preterm, LBW, AGA, RDS, sepsis      | 10     | 2.6         |
| Preterm, LBW, AGA, hypothermia, sepsis | 9      | 2.3         |
| Preterm, LBW, SGA, RDS, neonatal hyperbilirubinemia, sepsis | 8 | 2.0 |
| Term, LBW, SGA, RDS, sepsis         | 7      | 1.8         |
| Preterm, LBW, AGA, sepsis           | 7      | 1.8         |
| Term, AGA, PNA, neonatal hyperbilirubinemia | 7 | 1.8 |
| Term, AGA, neonatal hyperbilirubinemia, sepsis | 6 | 1.5 |
| Preterm, LBW, SGA, RDS, neonatal hyperbilirubinemia | 5 | 1.3 |
| Others                              | 72     | 18.3        |
| TOTAL                               | 394    | 100%        |

AGA=appropriate for gestational age, LBW=low birth weight, SGA=small for gestational age, PNA=perinatal asphyxia, RDS=respiratory distress syndrome
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From 394 infants 18 (4.6%) had umbilical venous catheterization out of these 2 infants developed hypertension. Hundred and thirty one infants (33.2%) were hospitalized at birth for over 10 days and among these 4 (1%) developed hypertension on follow up. First and 5th minute Apgar score was known for 253 infants (64.2 %) but all infants with hypertension at the third visit had a reported Apgar score at birth of ≥ 7 at the 5th minute. Eighteen mothers (4.6%) were hypertensive during pregnancy and were on anti-hypertensive medications from these mothers one infant developed hypertension. Three mothers were on steroids during pregnancy but no infant from these mothers developed hypertension. Two hundred thirty nine mothers (60.7%) took iron and folic acid and 154 (39.1%) took iron only during pregnancy. There was no maternal history of alcohol or heroin intake during pregnancy. Binary logistic regression was done to see associated factors for the development of hypertension and gender, 5th minute Apgar score, mode of delivery, birth order of the infant, admission diagnosis and drugs taken during pregnancy seems to have no association with high BP in the studied infants (P>0.05 at 95% confidence interval). Table 2 shows demographic characteristics of infants in relation to their BP.

Table 2: Demographic characteristics of infants who survived from NICU and with hypertension at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia

| Variable               | Number | %  | Hypertension first record | Hypertension second record | Hypertension third record | p-value |
|------------------------|--------|----|---------------------------|---------------------------|---------------------------|---------|
| Gender                 |        |    |                           |                           |                           |         |
| Female                 | 173    | 43.9 | 12                        | 3.0                       | 5                         | 1.3     | 3   | 0.8 | .755 |
| Male                   | 221    | 56.1 | 32                        | 9.1                       | 12                        | 3.0     | 8   | 2.0 |
| Apgar score            |        |    |                           |                           |                           |         |
| 3-6                    | 50     | 12.7 | 8                         | 2.0                       | 1                         | 0.3     | 1   | 0.3 | .829 |
| 7-10                   | 203    | 51.5 | 24                        | 6.1                       | 5                         | 1.3     | 5   | 1.3 |
| Mode of delivery       |        |    |                           |                           |                           |         |
| SVD                    | 238    | 60.4 | 33                        | 8.4                       | 12                        | 3.0     | 7   | 1.8 | .119 |
| C/S                    | 155    | 39.3 | 11                        | 2.8                       | 5                         | 1.3     | 4   | 1.0 |
| Birth order            |        |    |                           |                           |                           |         |
| First born             | 232    | 58.9 | 27                        | 6.9                       | 10                        | 2.5     | 8   | 2.0 | .227 |
| Second and above       | 162    | 41.1 | 17                        | 4.3                       | 7                         | 1.8     | 3   | 0.8 |
| Maternal drugs         |        |    |                           |                           |                           |         |
| Anti-HTN steroid       | 18     | 4.6  | 3                         | 16.7                      | 1                         | 5.6     | 1   | 5.6 | .126 |
|                        | 3      | 0.8  | 0                         | 0                         | 0                         | 0       | 0   | 0   |

1.3 Discussion
This is the first study in Ethiopia and there are no many literatures studying the prevalence of hypertension in infants who survived from the neonatal intensive care units globally. A 2.8% prevalence of hypertension in our subjects in three consecutive visits is similar to a study done by Friedman and Hustead which is 2.6% but twice as high as the Australian study which is 1.3% (11, 12). In most reports the prevalence of hypertension in survivors of the neonatal intensive care units ranges from 0.2-3% (13-18). This is in agreement with our finding. Our study didn’t show statistically significant gender differences in the occurrence of hypertension in infants who are survivors of NICU. A 6 month follow up of infants by mercury sphygmomanometer showed no gender differences in blood pressure (18, 19) which is similar to our finding. In a follow up of 65 infants after discharge from the neonatal intensive care unit the incidence of hypertension was 43% in infants who had bronchopulmonary dysplasia and 4.5% without bronchopulmonary dysplasia (20). We didn’t have any infant with the diagnosis of bronchopulmonary dysplasia. In a study done by Friedman and Hustead and Singh et al (11, 15); infants who developed...
hypertension had lower Apgar score, did have slightly longer NICU stays than infants with normal blood pressure though the differences were not statistically significant. Alagappan and Malloy (25) found out that preterm and very low birth weight infants are at increased risk of hypertension but twice as common in these infants with bronchopulmonary dysplasia. Our study didn’t show preterm birth to be a risk factor for hypertension but they might develop hypertension at later years. We found out that admission diagnosis to the NICU, duration of hospital stay, mode of delivery, birth order of the infant and gestational age at birth didn’t have statistically significant association with the development of hypertension (P<0.05). The association of umbilical arterial catheterization and the development of neonatal hypertension were described by many investigators (21-24). In these studies hypertension was recorded in infants with umbilical arterial catheterization even in the absence of thrombi in the renal arteries. In our NICU; umbilical venous catheterization is the practice whenever there is a need and the rate of umbilical venous catheterization was only 4.8% among NICU admissions; among these only 2 infants developed hypertension. This lower rate of hypertension in our infants could be because of lower number of infants with umbilical catheterization and shorter duration of catheterization.

Prolonged total parenteral nutrition (TPN), substances taken during pregnancy like cocaine or heroin, and neonates with extracorporeal membrane oxygenation (ECMO) lead to hypertension (26) but in our NICU there are very few cases with TPN which are given for a short duration, ECMO is not practiced and no mother had cocaine or heroin intake during pregnancy.

1.4 Limitations of the study
We didn’t follow the study subjects with routine BP monitoring in the course of their follow up years.

1.5 Conclusion and recommendation
A prevalence rate of hypertension of 2.8% warrants more infants could develop hypertension at later years and routine blood pressure monitoring should be the standard practice in the care of high risk infants.

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