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## Clinical and haematological features of newborns of mothers with hypertensive disorders in pregnancy in Lagos, Nigeria

DOI:<http://dx.doi.org/10.4314/njp.v47i3.10>

Accepted: 2nd October 2019

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**Abstract:** *Background:* Newborns of mothers with hypertensive disorders in pregnancy have an increased risk of preterm delivery, low birth weight, perinatal asphyxia and haematological derangements such as polycythaemia, thrombocytopenia and neutropenia. These morbidities are associated with uteroplacental insufficiency. The haematological derangements however have not been studied in detail in African neonates.

*Objective:* To determine the clinical and haematological features of newborns of hypertensive mothers  
*Methods:* Cross-sectional study involving 250 newborns; 125 newborns each of hypertensive mothers (cases), and normotensive mothers (controls). The babies were examined following delivery, their clinical data were recorded, and umbilical cord blood samples were analysed for haematological indices.

*Results:* Preterm deliveries were significantly higher amongst infants of hypertensive mothers (31.2%) compared with controls (12.0%);  $p = 0.000$ . Similarly, the birth weight, length and head

circumference of the cases were significantly lower than the controls;  $p = 0.008$ ,  $0.003$  and  $0.004$  respectively. Low fifth minute APGAR scores occurred more frequently in cases (8.0%) than controls (0.8%),  $p=0.010$ ; whilst the mean haematocrit was also significantly higher in cases than the controls,  $p = 0.013$ . The median absolute neutrophil count and platelet count were significantly lower in cases than controls;  $p=0.023$  and  $0.047$  respectively. Thrombocytopenia was identified in 40.0% of the cases compared to 27.2% of the controls,  $p = 0.041$

*Conclusion:* The present study has shown that newborns of hypertensive mothers have an increased risk of neonatal morbidities such as preterm birth, LBW and thrombocytopenia compared to the newborns of mothers with normal blood pressure in pregnancy, hence close attention needs to be paid to them with emphasis on their haematological system.

**Key words:** newborn, pregnancy, hypertension, hypertensive disorders, haematological, clinical

### Introduction

Hypertensive disorders in pregnancy constitute a leading cause of perinatal morbidity and mortality, complicating about five to ten percent of all pregnancies.<sup>1</sup> Hypertensive disorders in pregnancy are reportedly more common amongst Africans than other populations,<sup>2</sup> with incidence as high as 17% in northern Nigeria.<sup>3</sup> Newborns of hypertensive mothers developed complications such as preterm delivery, low birth weight and perinatal asphyxia.<sup>4</sup> Earlier studies also reported thrombocytopenia in 9.2% to 36.1%, and neutropenia in as high as 58.1% of babies of them, with increased risk of nosocomial infections.<sup>5-8</sup> Thrombocytopenia when severe can cause intracranial bleeds which may lead to

severe debility in the future. A Nigerian study demonstrated polycythaemia in 8.6% of them, but other haematological parameters were not studied.<sup>9</sup> The neonatal morbidities associated with maternal hypertension occur as a result of uteroplacental insufficiency which leads to ischaemia, foetal hypoxia and reduced nutrient supply to the foetus.<sup>4</sup>

Since previous research showed that haematological parameters of Africans differ from those of Caucasians and other races,<sup>10</sup> it was thought that the haematological system of African neonates may respond differently to maternal hypertension compared with previous reports in other populations. Hence the need for the study. The study aimed to document the clinical and haematological features of newborns of hypertensive mothers in

order to achieve better outcomes in them.

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## Materials and methods

The study was carried out at the labour ward and in-born neonatal ward of the Lagos University Teaching Hospital (LUTH), Lagos, Nigeria over an eight month period September 2014 to April 2015. Ethical approval for the study was obtained from the Health Research Ethics Committee of the hospital. Informed consent was also obtained from the mothers or the fathers when mothers were too ill to give consent.

Neonates born to mothers diagnosed with hypertensive disorders in pregnancy (Gestational hypertension, pre-eclampsia-eclampsia, chronic hypertension and pre-eclampsia superimposed on chronic hypertension) by an obstetrician in the study centre were enrolled. Hypertension in the mother was defined as systolic blood pressure of 140mmHg or greater or diastolic blood pressure of 90mmHg or greater or both on more than one occasion at least 4-6 hours apart.<sup>[11]</sup> Neonates of mothers with normal blood pressure in pregnancy delivered in the study centre were also enrolled as controls. Normal blood pressure in the mother was defined as blood pressure 120/80mmHg.<sup>12</sup> Subjects were recruited consecutively until the calculated sample size of 125 subjects each, was achieved for both cases and controls.

Neonates of mothers with conditions like severe anaemia, connective tissue diseases, diabetes mellitus, chorioamnionitis and other febrile illnesses that may alter the haematologic profile of their newborn; neonates of mothers on drugs like aspirin and warfarin with potential haematologic consequences in pregnancy; neonates of mothers with prehypertension; defined as systolic blood pressure 120–139 mmHg and/or diastolic 80–89 mmHg<sup>12</sup> and neonates who were products of multiple gestation which is known to be associated with anaemia and polycythaemia were all excluded.

Information on the gestational age, maternal illness in pregnancy, type of hypertensive disorder in pregnancy, blood pressure measurements, presence of proteinuria and convulsions and perinatal drugs was obtained from the mothers' case notes.

Immediately following delivery of the newborn, birth weight, length, head circumference, gestational age and APGAR scores were documented. The appropriateness of the baby's weight for gestational age was determined using the Olowe's standards of intrauterine growth for an African population at sea level.<sup>13</sup>

Also, at the point of delivery of the baby and placenta, 5 mls of venous cord blood was obtained into an ethylene diamine tetra acetate bottle and transported to the laboratory immediately for a complete blood count analysis. Blood samples that could not be analyzed immediately were stored in a refrigerator (temperature 2-4°C) at the central research laboratory for analysis within six hours of collection. The blood samples were analysed for packed cell volume (PCV); white blood cell (WBC)

count and differentials; platelet count and red cell indices.

The haematological tests were carried out in the Haematology laboratory of the hospital using Sysmex Haematology auto analyzer model KX-21N made by Sysmex Corporation, Kobe, Japan.

## Data analysis

Data analysis was done using the Statistical Package for the Social Sciences (SPSS) for Windows version 17. Continuous variables were tested for distribution of data set, and expressed as means and standard deviations or median and range, as appropriate. Percentages were calculated for categorical data. Pearson Chi-square test was used to assess associations between categorical variables. For continuous variables with normal distribution, student t test or Analysis of variance (ANOVA) was used to assess differences in means between two or more groups respectively. For skewed data, Mann-Whitney U-test or Kruskal-Wallis test was used to assess difference in median between two or more groups respectively. Probability (*p*) values less than 0.05 were accepted as statistically significant (two-tailed analysis).

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## Results

Two hundred and fifty mother-newborn pairs were enrolled in the study. This comprised of 125 pairs with hypertensive disorders in pregnancy as cases, and another 125 pairs with normal maternal blood pressure in pregnancy as controls. Majority of the mothers with hypertensive disorders in pregnancy had gestational hypertension (47.2%) and pre-eclampsia-eclampsia (46.4%), while chronic hypertension and pre-eclampsia superimposed on chronic hypertension accounted for only 1.6% and 4.8% respectively.

The general characteristics of the newborns are depicted in Table 1. Newborns of hypertensive mothers that were delivered via caesarean section (70.4%) were significantly more than that of controls (48.8%)  $p=0.000$ . Also, a significantly higher proportion of newborns of mothers with hypertensive disorders in pregnancy were delivered preterm compared to the controls 31.2% versus 12.0% ( $p=0.000$ ). There was no significant difference in gender distribution between the cases and controls.

The clinical features of the newborns of hypertensive mothers and controls are illustrated in Table 2. Majority of both subsets of study subjects had 5th minute APGAR scores greater than six. However, low 5th minute APGAR scores (APGAR score less than seven) occurred ten times more frequently amongst the newborns of hypertensive mothers than those of normotensive mothers; 8.0% and 0.8% respectively ( $p = 0.010$ ). The data distribution of the birth weight in the cases and controls was skewed; hence the difference in median between cases and controls was used. The birth weight, length and head circumference of the newborns of hypertensive mothers was significantly lower than the con-

trols. In contrast to controls, a higher proportion of newborns of hypertensive mothers were small for gestational age but the difference was not statistically significant (5.6% vs. 1.6%:  $p = 0.133$ ).

**Table 1:** Characteristics of the newborns of hypertensive mothers and controls

	Cases N=125(100%)	Controls N=125(100%)	<i>p-value</i>
<i>Gestational maturity</i>			
Preterm	39 (31.2)	15 (12.0)	0.000*
Term	86 (68.8)	110 (88.0)	
Mean gestational age $\pm$ SD	36.6 $\pm$ 3.8	37.9 $\pm$ 2.4	0.001*
<i>Gender</i>			
Male	69 (55.2)	57 (45.6)	
Female	56 (44.8)	68 (54.4)	0.129

\**p*-value is significant

**Table 2:** Clinical features of the newborns of hypertensive mothers and controls

	Cases N = 125 (100%)	Controls N = 125 (100%)	Statistics	<i>p-value</i>
<i>1<sup>st</sup> minute APGAR score</i>				
<5	14 (11.2)	8 (6.4)		
5-6	39 (31.2)	17 (13.6)	$\chi^2 = 14.8$	0.001*
7-10	72 (57.6)	100 (80.0)		
Mean $\pm$ SD	6.6 $\pm$ 1.8	7.1 $\pm$ 1.4	$t = 2.9$	0.005*
<i>5<sup>th</sup> minute APGAR score</i>				
<5	2 (1.6)	0 (0.0)		
5-6	8 (6.4)	1 (0.8)	$\chi^2 = 7.8$	0.010*#
7-10	115 (92.0)	124 (99.2)		
Mean $\pm$ SD	8.7 $\pm$ 1.3	9.2 $\pm$ 0.9	$t = 3.4$	0.001*
BW (g) Median (Range)	2900.0 (500-4800)	3200.0 (1010-5250)	$U = 7.0$	0.008*
Length (cm) Mean $\pm$ SD	46.6 $\pm$ 5.1	48.2 $\pm$ 2.7	$t = 3.0$	0.003*
HC(cm) Mean $\pm$ SD	33.2 $\pm$ 3.2	34.2 $\pm$ 1.8	$t = 2.9$	0.004*
<i>Appropriateness for GA</i>				
SGA	7 (5.6)	2 (1.6)		
AGA	108 (86.4)	117 (93.6)	$\chi^2 = 4.1$	0.133#
LGA	10 (8.0)	6 (4.8)		

\**p*-value is significant, #Fisher exact derived *p*-value

**Table 3:** Haematological parameters of the newborns of hypertensive mothers and controls

	Cases N = 125 (100%)	Controls N=125 (100%)	<i>p-value</i>
Mean Haematocrit $\pm$ SD	48.4 $\pm$ 9.1	45.8 $\pm$ 7.0	0.013*
Median WBC (Range)	10900 (1500 – 34000)	11400 (1300 – 37600)	0.198
Median ANC (Range)	4763 (294 – 22780)	5451 (424 – 32336)	0.023*
Median Platelet count (Range)	173x10 <sup>3</sup> (41-683x10 <sup>3</sup> )	208 x10 <sup>3</sup> (48-460 x10 <sup>3</sup> )	0.047*
Mean MCV $\pm$ SD	110.5 $\pm$ 10.6	108.2 $\pm$ 9.4	0.080
Mean MCH $\pm$ SD	35.5 $\pm$ 4.7	35.1 $\pm$ 3.4	0.527
Mean MCHC $\pm$ SD	32.1 $\pm$ 3.6	32.7 $\pm$ 2.5	0.118

\**p*-value is significant

WBC- white blood cell, ANC- absolute neutrophil count, MCV- mean corpuscular volume, MCH- mean corpuscular haemoglobin, MCHC- mean corpuscular haemoglobin concentration

The haematological parameters of newborns of hypertensive mothers and controls are illustrated in Table 3. The white blood cell count, absolute neutrophil count and platelet count of the cases and controls had skewed data distributions, hence the difference in median in those categories were used. The median values of the absolute neutrophil and platelet counts were significantly lower in the cases compared with those of controls,  $p = 0.023$  and  $0.047$  respectively. On the other hand, the mean haematocrit was significantly higher amongst the newborns of hypertensive mothers than the controls,  $p = 0.013$ . However, the other haematological parameters including the total white blood cell count and red cell indices did not show any significant difference between the cases and controls ( $p > 0.05$  in each case). Table 4 shows the distribution of the haematological derangements detected in both cases and controls. The level of thrombocytopenia detected in the newborns of hypertensive mothers (40.0%) was significantly higher than in the controls (27.2%),  $p = 0.041$ . Seven of the thrombocytopenic babies comprising six cases and one control had severe thrombocytopenia. There was no significant difference between the levels of neutropenia detected in the newborns of hypertensive mothers compared to the controls ( $p = 0.307$ ). Majority of the cases (75.2%) and controls (71.2%) had normal haematocrit levels.

Associations between the clinical variables such as gender, gestational maturity and birth weight on the one hand, and haematological derangements in the newborns (of hypertensive mothers) on the other, are illustrated in Tables 5 and 6. Table 5 shows that neutropenia was significantly more common in the preterm babies (20.5%) of hypertensive mothers compared to their term counterparts (5.8%),  $p = 0.017$ . It also illustrates an increase in the incidence of neutropenia and leukopenia with decreasing birth weight in the newborns of mothers with hypertensive disorders in pregnancy,  $p = 0.045$  and  $0.029$  respectively.

There was no significant difference across the subcategories of gender, gestational maturity and birth weight of the newborns of hypertensive mothers with regard to anaemia and thrombocytopenia as illustrated by Table 6.

**Table 4:** Haematological derangements in the newborns of hypertensive and normotensive mothers

	Cases N=125 (100%)	Controls N=125 (100%)	<i>p-value</i>
<i>Haematocrit</i>			
Anaemia	28 (22.4)	36 (28.8)	0.121*
Normal	94 (75.2)	89 (71.2)	
Polycythaemia	3 (2.4)	0 (0.0)	
<i>WBC count</i>			
Leukopenia	19 (15.2)	11 (8.8)	0.279
Normal	92 (73.6)	97 (77.6)	
Leukocytosis	14 (11.2)	17 (13.6)	
<i>ANC</i>			
Neutropenia	13 (10.4)	10 (8.0)	0.307
Normal	60 (48.0)	51 (40.8)	
Neutrophilia	52 (41.6)	64 (51.2)	
<i>Platelet count</i>			
Thrombocytopenia	50 (40.0)	34 (27.2)	0.041*+
Normal	72 (57.6)	90 (72.0)	
Thrombocytosis	3 (2.4)	1 (0.8)	

<sup>+</sup> *p* is significant, \*Fisher exact derived *p*-value  
 WBC- white blood cell, ANC- absolute neutrophil count  
 Anaemia- Haematocrit < 42%, Polycythaemia – Haematocrit > 65%, leukopenia – WBC <5000cells/mm<sup>3</sup>, Leucocytosis – WBC >20000cells/mm<sup>3</sup>, Neutropenia – ANC <1750cells/mm<sup>3</sup>, Neutrophilia – ANC >5400cells/mm<sup>3</sup>, Thrombocytopenia - platelet count < 150000cells/mm<sup>3</sup>, Thrombocytosis - platelet count >450000

**Table 5:** Association between leucopenia and neutropenia and clinical parameters of newborns of hypertensive mothers

	Leucopenia N = 19 (%)	p-value	Neutro- penia N=13 (%)	p-value
<i>Gender</i>				
Female (56)	7 (12.5)	0.272	4 (7.1)	0.381*
Male (69)	12(17.4)		9 (13.0)	
<i>Gestational maturity</i>				
Preterm (86)	10 (25.6)	0.079	8 (20.5)	0.017 <sup>+</sup>
Term (39)	9 (10.5)		5 (5.8)	
<i>Birth weight</i>				
Normal (86)	8 (9.3)	0.029* <sup>+</sup>	6 (7.0)	0.045* <sup>+</sup>
LBW (25)	7 (28.0)		3 (12.0)	
VLBW (9)	3 (33.3)		2 (22.2)	
ELBW (5)	1 (20.0)		2 (40.0)	

<sup>+</sup> *p* is significant, \*Fisher exact derived *p*-value  
 Leukopenia – white blood cell count < 5,000cells/mm<sup>3</sup>  
 Neutropenia – absolute neutrophil count < 1750cells/mm<sup>3</sup>,  
 LBW – low birth weight (1500 - 2499g), VLBW – very low birth weight (1000 – 1499g), ELBW – extremely low birth weight (<1000g)

**Table 6:** Association between thrombocytopenia and anaemia and clinical parameters of newborns of hypertensive mothers

	Thrombo- cytopenia N = 50 (%)	p- value	Anaemia N=28 (%)	p-value
<i>Gender</i>				
Female (56)	21 (37.5)	0.60	13 (23.2)	0.844
Male (69)	29 (42.0)		15 (21.7)	
<i>Gestational maturity</i>				
Preterm (86)	16 (41.0)	0.87	11 (28.2)	0.294
Term (39)	34 (39.5)		17 (19.8)	
<i>Birth weight</i>				
Normal (86)	32 (37.2)	0.57	15 (17.4)	0.108
LBW (25)	13 (52.0)		7 (28.0)	
VLBW (9)	3 (33.3)		4 (44.4)	+
ELBW (5)	2 (40.0)		2 (40.0)	

Thrombocytopenia – Platelet count < 150000cells/mm<sup>3</sup> Anaemia- Haematocrit < 42%,  
 LBW – low birth weight (1500 - 2499g), VLBW – very low birth weight (1000 – 1499g), ELBW – extremely low birth weight (<1000g)

## Discussion

The present study demonstrates an increased risk of preterm delivery, low birth weight, low APGAR scores and neonatal haematological derangement such as thrombocytopenia in newborns of mothers with hypertensive disorders in pregnancy compared with newborns of mothers with normal blood pressure in pregnancy. These

findings are similar to those reported in previous studies in Asia, Europe<sup>5-7, 14, 15</sup> and Nigeria.<sup>9, 16</sup>

Preterm delivery occurred nearly three times more frequently in hypertensive mothers than in the mothers with normal blood pressure in the present study. This is similar to the findings by Onyiriuka and Okolo in Benin, Nigeria, who identified preterm births in 29.3% of the newborns of hypertensive mothers, compared to 12.1% of the controls.<sup>9</sup> Also, Nadkarni, Bahl and Parekh in India reported comparable findings of preterm births in 23% of newborns of hypertensive mothers compared to 2.0% in the controls.<sup>15</sup> The high incidence of preterm delivery in hypertensive mothers in the present study may be attributed mostly to the need to terminate their pregnancies via medical or surgical interventions to preserve the mother and foetus' health especially in those with severe hypertension. Indeed, the present study had a high caesarian section rate of 70.4% in hypertensive mothers which may have led to the high preterm delivery rate.

Low first and fifth minute APGAR scores occurred more frequently in the newborns of hypertensive mothers compared with the controls in the present study. This may be explained by maternal hypertension which would decrease uteroplacental blood flow, thereby resulting in foetal hypoxia and subsequently perinatal asphyxia.<sup>17</sup> This finding is comparable to that of the study by Onyiriuka and Okolo<sup>[9]</sup> which reported perinatal asphyxia in 8.2% of the newborns of hypertensive mothers and 1.6% of the controls. Also, Nadkarni, Bahl and Parekh<sup>15</sup> in India had earlier reported similarly high figures for perinatal asphyxia in the newborns of hypertensive mothers with a prevalence of 14% in subjects and 7% amongst controls. A low fifth minute APGAR score is one of the features considered in the diagnosis of perinatal asphyxia, and for the purpose of this study, the diagnostic pre-requisite of perinatal asphyxia was restricted to this.

The birth weight, length and head circumference of the newborns of hypertensive mothers were significantly lower than those of controls. Olusanya and Solanke<sup>16</sup> in Lagos, Nigeria had reported comparable findings of 18.1% of newborns of hypertensive mothers with LBW. Onyiriuka and Okolo<sup>9</sup> in Benin, Nigeria had also reported a high rate of LBW babies in 39.5% of the newborns of hypertensive mothers. The high rate of delivery of low birth weight babies to hypertensive mothers in these Nigerian studies, including that of the present study, may be related to the high preterm delivery rate in these studies. Also, small for gestational age babies might have contributed to this high prevalence of LBW in infants of hypertensive mothers in Nigeria. This implies that the problems of prematurity as earlier elucidated, or features of intrauterine growth restriction may be seen in the low birth weight newborns of hypertensive mothers. The health care implication of this finding is the importance of close monitoring of these low birth weight babies in order to identify and manage problems of prematurity or intrauterine growth restriction.

The present study demonstrated a mean haematocrit that

was significantly higher amongst the newborns of hypertensive mothers compared to the controls. Three newborn babies of hypertensive mothers had polycythaemia while none of the controls had the same. Also, anaemia occurred more frequently in the controls than in the cases, but the difference was not significant. The haematocrit level demonstrated in the newborns of hypertensive mothers in the present study was different from that of previous studies<sup>9,18</sup> that showed a higher frequency of polycythaemia in the newborns of hypertensive mothers compared with that of the present study. Onyiriuka and Okolo<sup>9</sup> demonstrated a significantly higher frequency of polycythaemia in the newborns of hypertensive mothers with 8.6% and 2.2% of subjects and controls respectively identified as polycythaemic.

Polycythaemia was however the expected finding because hypertension in pregnancy may cause uteroplacental insufficiency leading to foetal hypoxia which then stimulates erythropoiesis with the resultant polycythaemia. The low incidence of polycythemia in the present study is however comparable to the study by Bolatet *al*<sup>7</sup> in Turkey, which did not detect polycythaemia in any of the newborns of hypertensive mothers studied, but rather, detected neonatal anaemia in one of them. The higher incidence of neonatal anaemia detected in the present study amongst both cases and controls may be attributed to the practice of early umbilical cord clamping which still subsists at the study centre. An earlier report<sup>18</sup> had associated this practice with neonatal anaemia. Neonatal anaemia may manifest as poor weight gain, tachypnoea, congestive cardiac failure and apnoea in the newborn and if it is not treated on time can lead to the demise of the baby. Hence, it is important to identify and treat this haematological derangement early. The frequency of thrombocytopenia detected in the present study was significantly higher among the newborns of hypertensive mothers (40.0%) compared to the controls (27.2%). Six of the thrombocytopenic babies of hypertensive mothers had severe thrombocytopenia which necessitated platelet transfusion. A similar finding was reported by Bhat and Cherian<sup>6</sup> in India where 36.1% of the newborns of hypertensive mothers had thrombocytopenia, with nearly 50% of these recorded as severe thrombocytopenia. On the contrary, Burrows and Andrew,<sup>5</sup> recorded lower levels (9.2 %) of thrombocytopenia among the newborns of hypertensive mothers studied. The possible mechanisms of thrombocytopenia include reduced platelet production secondary to depression of the megakaryocytic lineage associated with foetal

hypoxia, microangiopathic sequestration of platelets, and destruction of platelets in the placental thrombi. Severe thrombocytopenia may cause intracranial bleeding with the resultant neurologic sequelae, therefore these babies need close monitoring for early detection and intervention.

The absolute neutrophil count of the cases in the present study was significantly lower than those recorded in the controls. This may be explained by uteroplacental insufficiency resulting in inhibition of foetal bone marrow production of the myeloid lineage, thereby causing a decrease in neutrophil production.<sup>19</sup> However, the level of neutropenia and leukopenia found in the cases and controls were not significantly different and this is similar to findings by Gray and Rodwell.<sup>8</sup> The report of Sivakumar *et al*<sup>14</sup> was one extreme that did not record neutropenia in any of the newborns of hypertensive mothers studied, while Bolatet *al*<sup>7</sup> was the other extreme in which as many as 58.1% of the newborns of hypertensive mothers had neutropenia. However, neutropenia occurred more frequently in the preterm babies compared to term babies of hypertensive mothers. Also, amongst the newborns of hypertensive mothers, as birth weight reduced, the incidence of neutropenia increased. Prematurity is a known risk factor of neonatal sepsis, and neutropenia further increases this risk,<sup>8</sup> therefore, intensive measures to prevent and also early detection and treatment of infection should be put in place for these babies.<sup>8</sup>

In the present study, there was no significant difference in the values of the red cell indices comprising MCV, MCH and MCHC between the cases and controls; this is similar to the finding by Bolatet *al*.<sup>7</sup> They attributed this to the micronutrient levels that were not significantly different between the newborns of hypertensive and normotensive mothers in their study, micronutrient levels were however not assessed in this present study.

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## Conclusion

In conclusion, the present study has shown that newborns of hypertensive mothers have an increased risk of neonatal morbidities compared to the newborns of mothers with normal blood pressure in pregnancy, hence close attention needs to be paid to them with emphasis on their haematological system.

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