#### STUDY OF RISK FACTORS CONTRIBUTING TO ADVERSE NEONATAL OUTCOME IN HYPERTENSIVE MOTHERS COMPARED TO NON HYPERTENSIVE MOTHERS

Swapna K. Pillai<sup>1</sup>, Razin Nazarullah<sup>2</sup>

#### HOW TO CITE THIS ARTICLE:

Swapna K. Pillai, Razin Nazarullah. "Study of Risk Factors Contributing to Adverse Neonatal Outcome in Hypertensive Mothers Compared to Non Hypertensive Mothers". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 48, June 15; Page: 8304-8312, DOI: 10.14260/jemds/2015/1206

**ABSTRACT:** AIM: To study the various risk factors in hypertensive mothers that contribute to adverse neonatal outcome in the form of low birth weight when compared to non-hypertensive mothers. SETTING: The study was conducted in the Inborn NICU and New born Follow up clinic of Department of Paediatrics in a rural Government medical college Hospital. STUDY DESIGN: Prospective cohort study. MATERIALS AND METHODS: INCLUSION CRITERIA: CASES: Consecutive sample of mothers with pregnancy induced hypertension during the study period who have given consent for the study were interviewed and their live born babies were included as cases. **CONTROLS:** Consecutive sample of live born babies born to non-hypertensive mothers in the same study period were included as controls. Exclusion Criteria: Babies with major congenital anomalies chromosomal anomalies, intrauterine death were excluded. METHODOLOGY: Details of maternal risk factors were collected. Anthropometric parameters, systemic examination, development and maturity of the babies were assessed. **STATISTICAL TESTING:** Significance testing was done using chi square test, odds ratio, analysis of risk ratios and correlation testing. P values greater than .05 were considered non-significant. Spss 16 Software package was used for statistical analysis. **RESULTS:** The incidence of low birth weight in this study was 45.6% which is considerably higher than in controls (16.6%) and in the general population (19.1%). 33.8% of babies were preterm among the cases compared to 6.1% among controls. Among mothers with hypertension detected before 30 weeks, 90.3% had low birth weight babies. Among mothers with severe hypertension, 86.4% had low birth weight babies compared to 29.8% among those with mild hypertension.92.3% pregnancies with Doppler abnormalities had LBW. 70.8% of LBW babies had antenatal intra uterine growth restriction.90.1% of hypertensive mothers with albuminuria had associated LBW. 100% babies had low birth weight when mother had eclampsia and renal function abnormality. CONCLUSION: Risk factors associated with hypertension have a link with low birth weight and adverse outcome in babies.

**KEYWORDS:** Low birth weight, Pregnancy induced hypertension, Risk factors, Neonatal outcome.

**INTRODUCTION:** Pregnancy associated hypertensive disorders are emerging as the most common medical disorder in the antenatal period.<sup>1</sup> Apart from the problems in the expectant mother, it leads to a state of chronic placental insufficiency with reduced blood flow to the various organs in the foetus. This, in turn, adversely affects the growth and development of the foetus. The most widely accepted theory for the pathophysiology of preeclampsia is based on a model of impaired implantation that results in placental hypoperfusion and hypoxia.<sup>2</sup> The placenta then releases substances into the maternal circulation that adversely affect endothelial function. Endothelial dysfunction manifests as greater vascular reactivity to circulating vasoconstrictors like angiotensin,

reduced production of endogenous vasodilators like prostacyclin and nitric oxide.<sup>3</sup>There is increase in vascular permeability and tendency towards platelet consumption and coagulopathy. The end result is hypertension, proteinuria secondary to glomerular injury, edema, tendency for extravascular fluid overload and intravascular hemoconcentration. The reduced capillary recruitment and reduced capability of further dilation of capillaries after venous congestion observed in women with PIH may suggest a significantly reduced functional capacity of the microcirculation and increased load on capillary endothelium in pregnancy complicated by gestational hypertension.<sup>3</sup>

The present study aims at studying the different associated risk factors in a mother with hypertension when compared to non-hypertensive mothers and their effects on the outcome of the babies especially on the birth weight. This will throw light on the different risk factors<sup>4</sup> and by modifying them, we can improve the outcome of babies.

**AIMS:** To study the various risk factors in hypertensive mothers that contribute to adverse neonatal outcome when compared to non-hypertensive mothers.

#### MATERIALS AND METHODS

**STUDY DESIGN:** Prospective cohort study.

**SETTING:** The study was conducted in the Maternity ward, Inborn NICU and Newborn Follow up clinic of Department of Pediatrics in a rural Government medical college Hospital.

**STUDY POPULATION:** Consecutive sample of mothers with pregnancy induced hypertension during the study period in Government Medical College who have given consent for the study during the period were interviewed and their live born babies were included as cases. Babies with major congenital anomalies, chromosomal anomalies and intrauterine death were excluded. Consecutive sample of live born babies born to non-hypertensive mothers in the same study period were included as controls.

The maternal data including age,sex, parity, gravidity, gestational age of detection of hypertension, trend of BP, past obstetric history, family history, development of complications in the mother, details of antenatal foetal surveillance, medications given to the mother, natal history, details regarding postnatal period are collected. Babies are examined immediately after birth. Anthropometric parameters, systemic examination, development and maturity are assessed. Gestational age is assessed using modified New Ballard score. History and clinical examination was done for the control group also. Statistical testing- Continuous variables were expressed as mean and standard deviation. Other tests used were risk ratio, fisher's t test and pearson's probability test.

**OBSERVATIONS AND RESULTS:** Out of these 420 babies, 206 were females (48.9%) and 214 were males (50.8%). Among cases there were 46.6% females and 53.4% male cases. Among controls, there were 51.4% females and 48.6% males.

Weight	Number of cases	Number of controls		
1-1.5	9	0		
1.5-2	32	3		
2-2.5	55	31		
>2.5	114	176		
Total	210	210		
Table 1: Showing the distribution of cases and controls according to birth weight				

J of Evolution of Med and Dent Sci/ eISSN- 2278-4802, pISSN- 2278-4748/ Vol. 4/ Issue 48/ June 15, 2015

Lowest weight of survived baby was 1.01kg. Median birth weight was 2.42kg. There were 45.5% low birth weight with 4.28% very low birth weight babies among cases. There were 16.22% low birth weight babies among controls with 1.46% very low birth weight babies. There is 2.5 times increase in low birth weight among cases when compared to controls.

Gestational age of baby	Number of cases	Number of controls			
<28 weeks	0	0			
28-30 weeks	3	0			
30-33 weeks	10	0			
34-36 weeks	58	13			
Term	139	197			
Total	210	210			
Table 2: Distribution of survived babies according to gestational age					

33.8% babies were below 37 weeks of gestation among cases. Of the 210 babies born to hypertensive mothers, 71 were preterm (33.8%). Most premature baby was 28 weeks 6 days. Mean gestational age of preterm babies of hypertensive mothers was 35 weeks. 6.1% controls were preterm among controls.

Dick Factor	Number of	Number of	Number of normal		
Risk Factor	mothers	LBW babies	birth weight babies		
HT detected before 30 weeks	31	28(90.3%)	3(9.6%)		
HT detected after 30 weeks	179	68(37.9%)	111(62.01%)		
Mild HT	151	45(29.8%)	106(70.1%)		
Severe HT	59	51(86.4%)	8(13.55%)		
Doppler abnormality present	26	24(92.3%)	2(7.6%)		
Doppler abnormality absent	184	72(39.1%)	112(60.8%)		
IUGR present in antenatal USG	72	68(94.44%)	4(5.5%)		
IUGR absent in antenatal USG	138	28(20.2%)	110(79.7%)		
Oligohydramnios present in antenatal USG	67	62(92.5%)	5(7.4%)		
Oligohydramnios absent in antenatal USG	143	34(23.7%)	109(76.22%)		
Antenatal maternal renal function abnormality present	4	4(100%)	0		
Antenatal maternal renal function abnormality absent	206	92(44.6%)	114(55.3%)		
Maternal albuminuria present	51	46(90.1%)	5(9.8%)		
Maternal albuminuria absent	159	50(31.44%)	109(68.5%)		
Maternal eclampsia present	4	4(100%)	0		
Maternal eclampsia absent	206	92(44.6%)	114(55.3%)		
Table 3: Showing relation between maternal risk factors and birth weight of babies					

J of Evolution of Med and Dent Sci/ eISSN- 2278-4802, pISSN- 2278-4748/ Vol. 4/ Issue 48/ June 15, 2015

Among mothers with hypertension detected before 30 weeks, 90.3% had low birth weight babies whereas 37.8% had low birth weight among mothers with hypertension detected after 30 weeks. [Ref: table 3] There is a statistically significant positive co relation between high blood pressure detection before 30 weeks and occurrence of low birth weight with odds ratio=15.0167, Risk ratio=7.5703, log odds=2.7092, Pearson probability=.567, Fischer exact test one tailed=3.5556e-1.

Among mothers with severe hypertension, 86.4% had low birth weight babies compared to 29.8% among those with mild hypertension. [Ref: table 3]. There is a statistically significant association between severity of hypertension and occurrence of low birth weight with odds ratio=15.235, risk ratio=11.0833, p value=.001. [Ref: Fig. 1 and table 3]

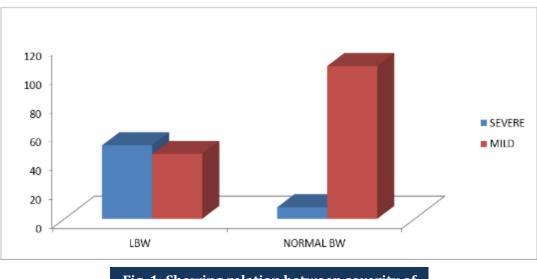
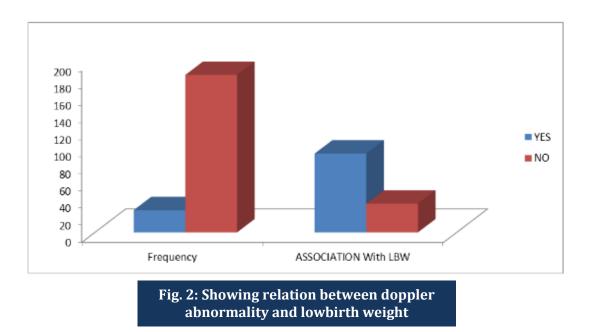
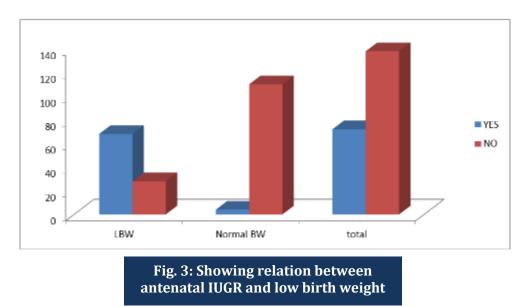


Fig. 1: Showing relation between severity of hypertension and birthweight of babies



J of Evolution of Med and Dent Sci/eISSN-2278-4802, pISSN-2278-4748/Vol. 4/Issue 48/June 15, 2015 Pag

- 12.4% of pregnancies of hypertensive mothers had associated Doppler abnormalities.
- 92.3% pregnancies with Doppler abnormalities had LBW. There is a statistically significant association between antenatal Doppler abnormality and occurrence of low birth weight babies with an odds ratio=18.667, risk ratio=11.0833, Fischer test=2.914567e-14.
- 34.3% of pregnancies had antenatal USG abnormality among hypertensive mothers.
- 70.8% of LBW babies had antenatal USG abnormality.[ table 3 and figure 2]



There is a significant association between antenatal ultrasound abnormality and occurrence of low birth weight with odds ratio=2.4286, risk ratio=20.1875, fisher t test=3.554989e-1. [Ref: Figure 3].

64.5% of LBW babies had antenatal oligohydramnios. There is a statistically significant association between oligohydramnios and occurrence of low birth weight with odds ratio=27.03, risk ratio=12.6214. 31.9% pregnancies of hypertensive mothers were associated with reduced liquor:

- 90.1% of hypertensive mothers with albuminuria had associated LBW.
- There is a positive association between albuminuria and low birth weight with odds ratio=20.056 and risk ratio=10.925 and Fisher t test value=3.9457e-14.
- There is statistically significant positive correlation between eclampsia and low birth weight. (Correlation co efficient=.78). All patients with renal function abnormalities had associated LBW. [Ref: table 3].

**DISCUSSION:** Babies born to hypertensive mothers are of major concern because of associated antenatal, natal and post natal complications and their effect on growth and development. The endothelial dysfunction is responsible for the symptoms and complications of preeclampsia like proteinuria, renal impairment, thrombocytopenia and seizures.<sup>5</sup>A prospective analysis of the maternal antenatal profile and its effect on the baby's birth weight was done in this study. 464 mothers were included in the cohort initially. Parents of 22 babies did not give consent for the study. 5 babies had major congenital anomalies and hence were excluded. 6 babies were of twin gestation and hence were excluded. 11 were lost on follow up. Only singleton gestation was included since

multiple pregnancies have a different set of problems associated with them. 210 cases (Babies of hypertensive mothers) and 210 controls (Babies of non-hypertensive mothers) were finally included of which 206 were females (48.9%) and 214(50.4%) were males. The important problems identified among babies born to hypertensive mothers in this study were low birth weight and prematurity. which is comparable to study done by Yang Y et al<sup>6</sup> and Ashworth et al.<sup>7</sup>

The incidence of low birth weight in this study was 45.6% which is considerably higher than in controls (16.6%) and in the general population (19.1%). Lowest weight of survived baby was 1.01 kg. The lowest gestational age of survived baby was 28 weeks 5 days. This is similar to the studies done by Manganaro<sup>8</sup> et al who found 48% incidence of low birth weight among babies of hypertensive mothers. Odegard<sup>9</sup> et al found that there is 50% SGA with PIH early in pregnancy.

Incidence of SGA is 35.24% in hypertensive group vs. 14.2% in control group. This is comparable to the studies done by Sandhya et al, Buga et al and Xionget al<sup>10</sup> and Allanson et al.<sup>11</sup> Roberts S, Algert. C.S.<sup>12</sup> also found that there is increased risk of SGA in hypertension. Differences in mean birth weight between women with preeclampsia and normotensive women ranged from -547.5g to 239.5g for gestational age categories ranging from  $\leq 32$  weeks to  $\geq 42$  weeks and the birth weights were statistically significantly lower among mothers with preeclampsia who delivered at  $\leq 37$  weeks, with an average difference of -352g according to study by Allanson et al.

There was 33.3% of preterm babies in the hypertensive group vs 6.1% in the control group. This is comparable to the study done by Yadav et al where the incidence of preterm delivery is 28.3% in the cases group vs. 3.3% in the control group. Study by Buga<sup>13</sup> et el found 34% incidence of preterm delivery.

**MATERNAL PREDICTORS OF ADVERSE OUTCOME IN BABIES:** Mothers with high blood pressure detected between 20-30 weeks had 90.3% risk of low birth weight babies in contrast to 56.1% when blood pressure was detected after 34 weeks. There is a statistically significant association between detection of hypertension before 30 weeks and the occurrence of low birth weight babies. This is comparable to the study done by Swenningsen<sup>14</sup> et al which showed increased rate of small for date babies and other complications associated with earlier gestational age of detection of hypertension. Martinez A,<sup>15</sup> Orgado J found that severe hypertension and early onset of hypertension is associated with increased incidence of low birth weight.

Hence close follow up should be done in those with early onset of hypertension and early delivery of these babies should be planned at a gestational age at which they can be salvaged to reduce the long term morbidity. In our study, 86.44% mothers with severe hypertension had low birth weight babies in contrast to 29.8% in those with mild hypertension. There is a statistically significant association between severity of hypertension and occurrence of low birth weight babies. This is comparable to the study done by Sibai<sup>16,17</sup> et al which showed increased low birth weight babies and other perinatal complications associated with severe hypertension with onset before 35 weeks whereas mild hypertension detected near term was associated with minimum complications. Bushbinder found that severe hypertension is associated with increased preterm delivery and lower gestational age at birth.

Of the 210 hypertensive mothers, 98 were primipara and 112 were multipara. Of the controls, 104 were primipara and 96 were multipara. However the relation between maternal parity and severity of complications was not found to be significant. 34.3% of pregnancies had antenatal USG abnormality among hypertensive mothers. 12.4% of pregnancies of hypertensive mothers had

associated Doppler abnormalities. 92.3% pregnancies with Doppler abnormalities had LBW. There is a statistically significant association between antenatal Doppler abnormalities and occurrence of low birth babies. This is comparable to the study done by Soutif et al which showed increased incidence of IUGR in those with Doppler abnormalities. In our set up, Doppler is done only after admission. If facilities are available, early Doppler scan at 20 weeks will identify those mothers who may have future problems and will help us to prognosticate and find out those requiring early intervention. In this study, 31.9% pregnancies of hypertensive mothers were associated with reduced liquor. 64.5% of LBW babies had antenatal oligohydramnios.

There is a statistically significant correlation between antenatal oligohydramnios and occurrence of low birth weight babies in hypertensive mothers. 90.1% of hypertensive mothers with albuminuria had associated LBW which is statistically significant with an odds ratio of 20.5. This is comparable to the study done by Lin C.M.<sup>18</sup> et al which showed increased rate of IUGR in patients with proteinuria. (Odds ratio=2.3). All patients with renal function abnormalities had associated LBW. 100% pregnancies associated with eclampsia had LBW. Swenningsen<sup>9</sup> et al found that there is increased rate of caesarean section in babies of hypertensive mothers. NICU admission is 37.1% among cases vs 10% among controls. This is comparable to the study done by Yadav et al which showed 40% newborn admissions among babies of hypertensive mothers vs 6.25% among non-hypertensive mothers. There is a statistically significant increase in complications in the babies of mothers with severe hypertension compared to controls and those with mild hypertension. There is no statistically significant difference between babies of mothers with mild hypertension and controls regarding newborn complications. Median birth weight of babies of mothers with hypertension is 2.44kg. Median birth length of hypertensive babies is 46.57cm. Median birth head circumference of hypertensive babies is 31.98 cm.

Median birth weight of control babies is 3.3kg. Median birth length of control babies is 49.5cm.Median birth head circumference of control babies is 34.3cm. There was twice the incidence of term SGA and preterm SGA among cases compared to controls.

**CONCLUSIONS:** Early onset of hypertension before 30 weeks, severe hypertension, Doppler abnormalities, oligohydramnios and proteinuria in mothers with PIH were predictive of adverse outcome in the form of low birth weight in the babies. Eclampsia and renal function abnormalities of the mothers led to low birth weight babies.

**RECOMMENDATIONS:** Early gestational age of onset of hypertension, severe hypertension and albuminuria are associated with more adverse outcomes. Doppler scan if done early can detect abnormalities which will help to prognosticate and intervene early enough for a better outcome Low birth weight babies of PIH mothers especially those with albuminuria, eclampsia, RFT abnormalities should be closely followed up as more problems can be expected in them.

**LIMITATIONS:** Exact matching of cases and controls based on gestational age and birth weight could not be done as controls were taken from consecutive sample of babies who were willing to come for follow up.

#### **REFERENCES:**

- 1. American College of Obstetricians and Gynaecologists. Practice bulletin 33: Diagnosis and Management of Pre eclampsia and Eclampsia. January 2002.
- 2. Levine R. J, Maynard SE, et al. Circulating angiogenic factors and risk of pre eclampsia. N Engl J Med 2004; 350:672-683.
- 3. Rusavy Z, Petrova B, et al: Changes in capillary diameters in pregnancy-induced hypertension. Hypertens Pregnancy. 2015; 8:1-7.
- 4. Mudjari NS, Samsu N, et al: Management of hypertension in pregnancy. Acta Med Indones. 2015 Jan; 47(1):78-86.
- 5. Lambert G, Brichant JF, et al: Pre eclampsia: an update. Acta Anaesthesiol Belg. 2014; 65(4):137-49.
- 6. Yang Y, He Y, Li Q, Wang Y: preconception blood pressure and risk of preterm delivery. FertilSteril.2015; 4: 23-24.
- 7. Ashworth J.R, et al: Loss of endothelium dependent relaxation in myometrial resistance arteries in pre eclampsia. Br J. Obstet Gynaecol 1997; 104:1152-1158.
- 8. Manganaro R, Mami C, Marando N, Paolata A, Palmara A, Gemelli M. Infants born to hypertensive mothers: a clinical epidemiological study. Minerva Ginecol 1996; 48 (3):73-76.
- 9. Odegard et al: Preeclampsia and fetal growth. Obstet Gynaecol 1990; 96:950-952.
- 10. Xiong X, Sandhya et al: Impact of pregnancy induced hypertension on fetal growth. Am J Obstet Gynaecol 1999; 180:207-213.
- 11. Allanson ER, Muller M et al: Causes of perinatal mortality and associated maternal complications in a South African province: challenges in predicting poor outcomes.BMC Pregnancy Childbirth. 2015 Feb; 15: 10-15.
- 12. Robert, Algert C.S: Population based trends in pregnancy induced hypertension and pre eclampsia Med J Aust.2005; 182(7): 332-335.
- 13. XuXiong, Nester N et al: Am. J. Epidemiol. 2002; 155 (3): 203-209.
- 14. N. W. Svenningsen M.D, H. Liedholm, A. Åberg: Hypertension in pregnancy and infant, a controlled followup study: Acta Obstet Gynaecol Scand Suppl 1994; 118: 103-106.
- 15. Martinez Orgado, Saez Perez et al: Prediction of complications in babies of hypertensive mothers: An Esp Pediatr 1991; 35(4):233-237.
- 16. Sibai BM, Mercer BM, Schiff E, et al. Aggressive versus expectant management of severe pre eclampsia between 28-32 weeks gestation: A randomised control trial. Am. J. Obstet Gynaecol 1994; 171: 818-822.
- 17. Sibai BM. Diagnosis, prevention and management of pre- eclampsia. Obstet Gynecol 2005; 105(2]: 402-410.
- 18. Lin C, et al: Comparison of associated high risk factors and perinatal outcomebetween symmetric and asymmetric intra uterine growth retardation. Am J Obstet Gynaecol 1991; 164:1535-1541.

#### **AUTHORS:**

- 1. Swapna K. Pillai
- 2. Razin Nazarullah

#### **PARTICULARS OF CONTRIBUTORS:**

- 1. Assistant Professor, Department of Paediatrics, Sree Gokulam Medical College, Thiruvananthapuram.
- 2. Assistant Professor, Department of Paediatrics, Sree Gokulam Medical College, Thiruvananthapuram.

#### FINANCIAL OR OTHER COMPETING INTERESTS: None

# NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Swapna K. Pillai, Villa No. 2, Sudarsana Villas, Near Kavinkulangara Devi Temple, Karikkakam-695021, Thiruvananthapuram. E-mail: swapna.pillai@gmail.com

> Date of Submission: 04/05/2015. Date of Peer Review: 05/05/2015. Date of Acceptance: 09/06/2015. Date of Publishing: 13/06/2015.