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***Research Article***

# NEONATAL OUTCOME IN MOTHER WITH PREGNANCY INDUCED HYPERTENSION – A PROSPECTIVE OBSERVATIONAL STUDY

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## ABSTRACT

*Background*: Hypertensive disorder of pregnancy is common medical problem in pregnancy. Hypertension in pregnancy is the second leading cause of maternal death and presents an increased risk of complications to the new born. Data regarding clinical outcome of babies born to mother with pregnancy induced hypertension is scant.

*Methods*: This study is a prospective observational study on mother's with Hypertensive disorder of pregnancy at rural tertiary care hospital. Primary objective is to measure short term outcome of neonates born to these mothers. Several other secondary outcomes were also measured. The study was undertaken over a period of two years from November 2017 to October 2019. All babies born to mothers having Hypertensive disorder of pregnancy and fulfilling the inclusion criteria were included in the study. A predesigned structured Performa was used to collect data in the post-natal wards. Data included neonatal outcomes such as Hypoglycemia, Hypocalcemia, Seizures, APGAR score, NICU admission, feed intolerance, IUGR, MAS, foetal IUD/still birth and other related factors.

*Results*: A total of 125 mothers were included in the study with mean age between 21 – 25 years. Of the included mothers 16% had Gestational hypertension (GH), 12.8 % had Severe Pre-Eclampsia (SPE), 60% had Preeclampsia (PE) and 8.8 % had Eclampsia (E). Majority of mothers had normal vaginal delivery except in Eclampsia. About 15%, 35.3%, 27.6% and 100% of the women in GH, SPE, Pre-Eclampsia and Eclampsia respectively had abnormal umblical doppler. Birth asphyxia was seen in about 20% of the neonates in GH group, 47.1% in SPE, 26.3% in Pre-Eclampsia group and all neonates in Eclampsia group. Thrombocytopenia was present in 25% of the new born to GH mothers, 58.8% of the SPE, 23.7% of Pre-Eclampsia and 50% of Eclampsia women. IUD/ Still birth was present in 11.8% of SPE group and 16.7% of the women with Eclampsia. These results had statistically significant difference between the different groups of pregnancy induced hypertension.

*Conclusion*: Neonatal complications and such outcomes are seen in children born to mothers with hypertensive disorders of pregnancy. Prospective, continuous surveillance and further studies are needed to improve neonatal outcome in this population.

***Keywords****: Gestational Hypertension, Severe Preeclampsia, Eclampsia, Preeclampsia*

## INTRODUCTION

Hypertensive disorder of pregnancy is a common medical problem during pregnancy. It is the commonest cause of perinatal morbidity and mortality. Hypertension in pregnancy is defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or by increase in SBP ≥ 30 mmHg, or in DBP ≥ 15 mmHg, from preconception or first trimester blood pressure confirmed by two measuring, 6 hours apart. Hypertension in pregnancy is the second leading cause of maternal death, accounting for 20% of maternal deaths (Gofton *et al.,* 2001) and presents an increased risk of complications for the foetus, including increased NICU involvement, preterm delivery and low birth weight (Berg *et al.,* 2003) and even foetal death (Villar *et al.,* 2006). The literature available shows that, around 8% of the pregnancies are complicated with hypertensive disorders (Roberts *et al.,* 2003). Hypertensive disorder of pregnancy is the general classification for hypertensive diseases during pregnancy which include Gestational Hypertension or GH (without protenuria), Severe Pre-Eclampsia (SPE), Pre-Eclampsia (PE) (with protenuria), and Eclampsia (E) (Pre-Eclampsia with convulsion).

Several classifications of hypertension in pregnancy have been used in the past, of which only two have received the widest acceptance, that of ACOG and that of ISSHP (Hoffman, 2011).

In Hypertensive disorder of pregnancy, the uteroplacental perfusion will be reduced as result of abnormal cytotrophoblast invasion of spiral arterioles. Placental ischemia leads to widespread activation or dysfunction of maternal vascular endothelium that results in enhanced formation of endothelin and thromboxane, increased vascular sensitivity to angiotensin-2 and decreased formation of vasodilator such as Nitric oxide and Prostacyclin (Upadhya *et al.,* 2018). Foetal complications are related to the severity and duration of Hypertensive disorder of pregnancy. Majority of foetal complications occur due to prematurity and hypoxia which includes: Intra Uterine Growth Restriction, Intra Uterine Death, Low Birth Weight, Small For Date babies, Low APGAR score, Perinatal asphyxia, Meconium aspiration syndrome, persistent pulmonary Hypertension, Hypothermia, Hypoglycemia, Hypocalcemia, Polycythemia, jaundice, feeding difficulties, feed intolerance, Necrotizing Enterocolitis, late-onset sepsis, pulmonary hemorrhage, and in long term poor growth and neurodevelopmental outcomes when they reach the school going age and adulthood (Hannaford *et al.,* 1997*;* Seely *et al.,* 1999*).* They are also more susceptible to develop adult-onset diseases in their infancy and adolescence (Wolde *et al.,* 2011).

The hypertensive diseases of pregnancy account for most of the perinatal losses especially in low resource settings (Adu-Bonsaffoh *et al.,* 2017). The adverse perinatal outcomes associated with hypertensive disorders are generally referable to placental insufficiency, placental abruption and prematurity related complications (Giffod *et al.,* 2000). The adverse perinatal outcomes are generally most serious in severe preeclampsia/eclampsia and are usually dependent on the gestational age at delivery as well as the severity of the disease process. Data regarding clinical outcome of babies born to Hypertensive Disorder of pregnancy in mother's is scant, Hence, this study was undertaken to study the clinical profile of Babies born to mothers with Hypertensive disorder of pregnancy so that one can identify key risk factors which will help in interventions during antenatal period so that there will be better neonatal outcome. Very few Indian studies on neonatal outcome in mother with Hypertensive disorder of pregnancy have been conducted. This study is a prospective observational study on new born of mothers with Hypertensive Disorder of pregnancy at rural tertiary care hospital.

## MATERIALS AND METHODS

The study protocol was approved by the university Ethics committee. A hospital based prospective observational study was undertaken over a period of two years from November 2017 to October 2019 on Neonates born to Hypertensive mother of pregnancy in MVJ Medical College and Research Hospital. About 125 neonates born to hypertensive mothers were included as the study sample. An informed consent was obtained from the father/ nearest relative of the neonate.

The prevalence of hypertensive disorders in pregnancy is 8% and sample size was calculated by using following formula, $N=4Z\alpha 2pq/\partial 2$, N=required sample size, P = estimated proportion in the population (8%), q = 100-p (92%), $Z\alpha = 1.96$, $\alpha = 0.05$, $\partial$ = the percentage of error (5%). The calculated sample size is 124 which is rounded to 125 patients.

The inclusion criteria are all Neonates born to mothers diagnosed with Hypertensive disorder of Pregnancy both inborn (including IUD, still birth) and out born. Exclusion criteria are babies born to mother when pregnancy is complicated by any other risk factors for increase in maternal or foetal morbidity and mortality such as Diabetes mellitus, Rh incompatibility, babies born with major congenital malformation, any other medical illness such as severe Anaemia, chronic hypertension, renal disease, heart disease and connective tissue disease and babies born to mother who did not undergo antenatal check-ups.

Weight of the new born was recorded immediately after birth. The infant's gestation age was calculated as the number of days passed between the first day of mothers last menstrual period (LMP) and her date of delivery. If mother was not sure about the LMP, New Ballad score was used and 1st trimester scan (if available) was used. Gestational age (GA) was categorized as pre-term (<37 completed weeks), term (37

to 40 weeks), post-dated (above 40 to 42 weeks), post term (>42 weeks). Birth weight was categorized as normal birth weight (2.5 to 4 kg), low birth weight (<2.5kg), Very low birth weight (<1.5kg), extremely low birth weight baby (<1kg).

The included mothers were interviewed in the post-natal wards using a predesigned structured Proforma, and other relevant data were taken from obstetric records of the mother. Babies were observed for immediate outcomes in the early neonatal period. Neonatal outcomes were compared among different groups (gestational hypertension, Preeclampsia, Severe preeclampsia and Eclampsia) of hypertensive disorder of pregnancy. All observations were recorded in Proforma.

**STATISTICAL ANALYSIS**

The data thus obtained was entered into an excel sheet and was transferred and analysed using Statistical Package for Social Services (version 20). The categorical variables were presented as frequencies and percentages and quantitative variables were analysed by using measures of central tendency and dispersion. Chi square test and Fischer exact test and independent sample T test or Mann Whitney U test was used for comparing the quantitative variables as tests of significance.

**RESULTS**

**Primary outcomes:**

About 70% of the women with Gestational hypertension had normal vaginal delivery. Also, 70.6% of the women with SPE, 68.4% with preeclampsia and 83.3% with Eclampsia had caesarean section. The mean birth weight in mothers with GH was 2.31 kgs, SPE was 1.59 kgs, Preeclampsia was 2.06 kgs and Eclampsia was 1.41 kgs. This difference in birth weight of neonates was statistically significant.

Majority of the women with GH had not received any anti-hypertensive medication. About 64.7% in SPE and 48.7% in preeclampsia group received Labetalol and 83.3% in Eclampsia group received $MgSO_4$ + Labetalol.

NICU admission was needed in 20% of the neonates born to Gestational hypertension. About 82.4% of the neonates in SPE group, 55.3% in preeclampsia and 83.3% in the Eclampsia group had NICU admission (Table 2). About 37.0% of the neonates in GH group, 64.7% in SPE, 35.5% in preeclampsia and all neonates in Eclampsia group had APGAR score of less than 7 at 1 minute. About 10.0% of the neonates in GH group, 47.1% in SPE, 17.1% in preeclampsia and 83.3% in Eclampsia group had APGAR score of less than 7 at 5 minutes.

**Table 1: Distribution of the study group according to Diagnosis and Maternal age**

| Maternal age | GH<br>N (%) | SPE<br>N (%) | Preeclampsia<br>N (%) | Eclampsia<br>N (%) | Total<br>N (%) |
|---|---|---|---|---|---|
| **< 20 years** | 9 (45.0) | 4 (23.5) | 23 (30.3) | 3 (25.0) | 39 (31.2) |
| **21 – 25 years** | 9 (45.0) | 10 (58.8) | 33 (43.4) | 5 (41.7) | 57 (45.6) |
| **26 – 30 years** | 2 (10.0) | 1 (5.9) | 17 (22.4) | 3 (25.0) | 23 (18.4) |
| **31 – 35 years** | 0 (0) | 2 (11.8) | 3 (3.9) | 1 (8.3) | 6 (4.8) |
| **Total** | 20 (100) | 17 (100) | 76 (100) | 12 (100) | 125 (100) |

***$\chi^2$ value=8.738 df=9 p value=0.462, NS***

**Secondary outcomes:**

Pulmonary Hemorrhage, Feed intolerance, NEC presence, Renal impairment Hyperbilirubinemia, Sepsis, Thrombocytopenia and Asymmetrical IUGR were seen in the different groups as shown in Table 2 and the difference between the different groups of pregnancy induced hypertension were statistically significant for these outcomes. Chi square statistics and p value is found in Table 2.

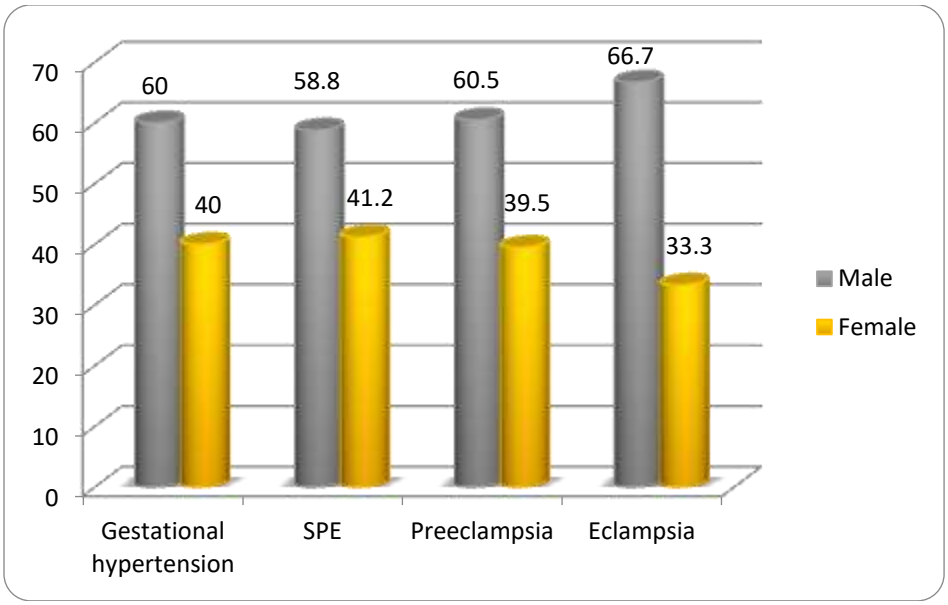


**Figure 1: Distribution of the study group according to Diagnosis and sex of the baby**

MAS was present in 11.8% of the neonates born to women with SPE and 16.7% with Eclampsia. IUD/ Still birth was present in 11.8% of SPE group and 16.7% of the women with Eclampsia. All the above results were found to have statistically significant difference between the different groups of pregnancy induced hypertension.

NST was reactive in 20% of GH, 41.2% of SPE, 18.4% of Preeclampsia and 50% of Eclampsia groups. About 57.4% of the neonates with reactive NST were born through caesarean section. Among those with reactive NST,18.1% had birth asphyxia, 98.9% had MAS, 29.8% had APGAR at 1 minutes of < 7 and 10.6% had APGAR at 5 minutes of < 7. Mode of delivery, birth asphyxia, APGAR at 1 minute and 5 minutes had statistically significant difference with reactive NST.

**Table 2: Neonatal outcomes in different groups of pregnancy induced hypertension.**

| Neonatal outcomes | GH N (%) | SPE N (%) | PE N (%) | Eclampsia N (%) | X2 value | P value |
|---|---|---|---|---|---|---|
| **NICU admission** | 4 (20) | 14 (82.4) | 42 (55.3) | 10 (83.3) | 18.966 | 0.00 |
| **Abnormal umblical doppler** | 3 (15) | 6 (35.3) | 21 (27.6) | 12 (100) | 28.051 | 0.00 |
| **Birth asphyxia** | 4 (20) | 8 (47.1) | 20 (26.3) | 12 (100) | 27.795 | 0.00 |
| **Pulmonary haemorrhage** | 1 (5) | 0 (0) | 1 (1.3) | 3 (25) | 15.968 | 0.001 |
| **Feed intolerance** | 2 (10) | 8 (47.1) | 26 (34.2) | 8 (66.7) | 11.858 | 0.008 |
| **Renal impairment** | 0 (0) | 3 (17.6) | 8 (10.5) | 5 (41.7) | 12.604 | 0.006 |
| **Hyperbilirubinemia** | 6 (30) | 14 (82.4) | 51 (67.1) | 10 (83.3) | 14.899 | 0.002 |
| **Sepsis** | 1 (5) | 5 (29.4) | 9 (11.8) | 6 (50) | 14.726 | 0.002 |
| **NEC present** | 0 (0) | 1 (5.9) | 3 (3.9) | 5 (41.7) | 24.135 | 0.000 |
| **Thrombocytopenia** | 5 (25) | 10 (58.8) | 18 (23.7) | 6 (50) | 10.377 | 0.016 |
| **Asymmetrical IUGR** | 5 (25) | 11 (64.7) | 41 (53.9) | 8 (66.7) | 14.592 | 0.027 |

***P<0.05 is significant***

**Table 3: Distribution of the study group according to antihypertensive medications taken by mother and related neonatal outcome**

| | **Labetalol N (%)** | **Methyl Dopa N (%)** | **$MgSO_4$+Labetalol N (%)** | **Nifedipine N (%)** | **Nil N (%)** |
|---|---|---|---|---|---|
| **NICU admission** | 26 (48.1) | 4 (80.0) | 0 | 15 (48.4) | 10 (43.5) |
| **Preterm delivery** | 13 (24.1) | 0 | 5 (41.7) | 6 (19.4) | 7 (30.4) |
| **Hypoglycemia** | 13 (24.1) | 0 | 5 (41.7) | 6 (19.4) | 7 (30.4) |
| **Birth asphyxia** | 15 (27.8) | 2 (40.0) | 10 (83.3) | 7 (22.6) | 10 (43.5) |
| **IUGR** | 33 (61.2) | 1 (20.0) | 12 (100) | 20 (64.6) | 3 (13.0) |

Hypoglycaemia was present in 15% of the neonates born to mother with GH, 35.3% born to SPE, 25% born to preeclampsia mother and 25% born to Eclampsia mother. Hypocalcemia was present in 15% of neonates born to GH mother, 41.2% of SPE, 21.1% of Preeclampsia and 33.3% of Eclampsia women. Seizures were present in 5% of GH group, none in SPE, 6% in Preeclampsia and 25% in Eclampsia group. TTNB was present in 20% of the neonates born to GH, 41.2% of SPE, 28.9% of preeclampsia and 8.3% of Eclampsia group. The PPHN was present in 3.9% of the neonates born to Preeclamptic women. None of the neonates born to GH, SPE and Eclampsia mother had PPHN. Polycythemia was present in about 20% of the neonates in GH group, 35.3% in SPE, 23.7% in Preeclampsia and 58.3% in Eclampsia group. Leucopenia was present in 10% of the women with GH, 5.9% with SPE, 5.3% with preeclampsia and 25% with Eclampsia. These finding were statistically insignificant.

## DISCUSSION

Hypertension in pregnancy is the second leading cause of maternal death, accounting for 20% of maternal deaths (Gofton *et al.,* 2001) and presents an increased risk of complications for the foetus, including increased NICU admission, preterm delivery and low birth weight *(Berg et al., 2003)* and even foetal death (Villar *et al.,* 2006). In Hypertensive disorder of pregnancy, the uteroplacental perfusion will be reduced as a result of abnormal cytotrophoblast invasion of spiral arterioles. Placental ischemia leads to widespread activation or dysfunction of maternal vascular endothelium that results in enhanced formation of endothelin and thromboxane, increased vascular sensitivity to angiotensin-2 and decreased formation of vasodilator such as Nitric oxide and Prostacyclin (Upadya, 2018).

Foetal complications are related to the severity and duration of Hypertensive disorder of pregnancy. Majority of foetal complications occur due to prematurity and hypoxia which includes: Intra Uterine Growth Restriction (IUGR), Intra Uterine Death (IUD), Low Birth Weight (LBW), Small for date babies, Low APGAR score, Perinatal asphyxia, Meconium aspiration syndrome (MAS), persistent pulmonary hypertension, hypothermia, hypoglycemia, hypocalcemia, polycythemia, jaundice, feeding difficulties, feed intolerance, necrotizing enterocolitis, late-onset sepsis, pulmonary haemorrhage, and in long term, poor growth and Neurodevelopmental outcomes when they reach the school going age and adulthood (Wolde *et al.,* 2010). The adverse perinatal outcomes associated with hypertensive disorders are generally referable to placental insufficiency, placental abruption and prematurity related complications (Gifford *et al.,* 2000). The adverse perinatal outcomes are generally most serious in severe preeclampsia/ Eclampsia and are usually dependent on the gestational age at delivery as well as the severity of the disease process.

In this study majority of the pregnant women with GH, SPE, Preeclampsia and Eclampsia were aged between 21 – 25 years. Adu—Bonsaffoh et al observed that majority of the women with preeclampsia, GH, chronic hypertension and preeclampsia superimposed on chronic hypertension were aged between 20 – 34 years (Adu-Bonsaffoh, 2017). In a study by Kheir *et al.,* most of the women affected by hypertensive

disorders were aged between 26 – 30 years (36.2%) *(Kheir et al.,* 2014*)*. A study by Bridwell *et al.,* had shown that the mean age of women with HDP was 28.4 years (Bridwell *et al.,* 2019).

Majority of the women with GH, SPE, preeclampsia and Eclampsia were primigravidae. A study by Bonsaffoh et al revealed most of the women with preeclampsia, gestational hypertension, chronic hypertension and preeclampsia superimposed on chronic hypertension had gravidity of 2 – 4 *(Adu-Bonsaffoh.,* 2017*)*. In a study by Kheir *et al.,* about 58% of the hypertensive women were multiparous *(Kheir et al.,* 2014*)*. A study by Asseffa *et al.,* also showed similar results (Asseffa *et al.,* 2019). A study by Bridwell *et al.,* had noted that about 61.1% of the women with HDP were Parous women (Bridwell *et al.,* 2019*)*.

The mean birth weight of the women with GH was 2.31 kgs, SPE was 1.59 kgs, preeclampsia was 2.06 kgs and Eclampsia was 1.41 kgs. Adu -Bonsaffoh *et al.,* had shown that, 40.7% with preeclampsia, 14.7% with gestational hypertension, 33.3% with preeclampsia superimposed on chronic hypertension had low birth weight (Adu-Bonsaffoh, 2017*)*. Kheir *et al.,* had shown that, LBW and VLBW were different among different hypertensive groups. Most of them were found in the pregnancy induced hypertension group (Kheir *et al.,* 2014).

Majority of our study population had vaginal deliveries. A study by Asseffa *et al.,* had showed that, about 72.5% of the women with pregnancy induced hypertension had normal vaginal deliveries (Asseffa *et al.,* 2019*)*. Only 20% of the neonates born to women with Gestational hypertension had NICU admission. A study by Adu–Bonsaffoh *et al.,* had noted that 36.4% of the neonates born to preeclampsia, 18.5% with gestational hypertension, 8.7% with chronic hypertension and 19% with preeclampsia superimposed on chronic hypertension were admitted to NICU (Adu-Bonsaffoh., 2017*)*.

Significant number of neonates in the study had seizures, feed intolerance, hyperbilirubinemia, sepsis, thrombocytopenia, leucopenia. Hassan *et al.,* had observed that, 13.33% had PNA with seizure, about 40% of the neonates had feed intolerance, 38.33% had suspected sepsis, 20% had thrombocytopenia, 20% had Meconium aspiration syndrome (MAS), 18.33% had reduced total count and all the neonates had hyperbilirubinemia (Hassan *et al.,* 2015*)*. Kheir *et al.,* had shown that, 38% of the babies had sepsis during their stay in the neonatal unit and 21% had thrombocytopenia (Kheir *et al.,* 2014). This study showed 4 mothers with IUD. A study by Adu–Bonsaffoh *et al.,* had shown that, 9.3% with preeclampsia, 5.4% with GH, 4.3% with chronic hypertension and 4.8% with preeclampsia superimposed on chronic hypertension had still birth (Adu-Bonsaffoh, 2017*)*. Bridwell had observed that 18.6% of the women with HDP had stillbirth (Bridwell *et al.,* 2019). No studies were available to compare the results regarding abnormal doppler, TTNB, PPHN, Pulmonary haemorrhage, Birth asphyxia, NST reactivity, renal impairment, Hypocalcemia and Hypoglycemia.

## CONCLUSION

This study has shown that, majority of the newborns born to women with pregnancy induced hypertension were aged between 21 – 25 years, primigravid and had gestational age of 37 weeks. The mean birth weight of the new born were low and majority were delivered by normal vaginal delivery. The babies born to women with Eclampsia had adverse neonatal outcomes including NICU admission, hypoglycaemia, hypocalcemia, birth asphyxia, APGAR score of less than 7, seizures, feed intolerance, NEC, renal impairment, Hyperbilirubinemia, Sepsis, Polycythemia, Thrombocytopenia, Leucopenia, MAS, IUD/ Still birth and IUGR. Being an observational study has its own weaknesses due to the methodology of such studies. But this study was able to bring out many important aspects of neonatal outcomes that needs to be kept in mind while treating new born of mothers with Hypertensive disorders of pregnancy. Further randomised control trials and cohort studies in this subject are needed to improve neonatal outcome in this population.

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