DOI: 10.7860/JCDR/2022/55451.16787

Original Article

Obstetrics and Gynaecology Section

Adverse Outcomes in Pregnancy with Chronic Hypertension with and without Superimposed Preeclampsia in Urban South Indian Population: A Prospective Observational Study

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ABSTRACT

Introduction: Pregnant women with chronic hypertension and who developed superimposed Preeclampsia (PE) had a higher rate of adverse maternal and perinatal outcomes. Prospective data on the outcome of pregnancies with chronic hypertension are sparse.

Aim: To evaluate the maternal and perinatal outcomes in pregnancies complicated by chronic hypertension with and without superimposed PE in South Indian population.

Materials and Methods: A two group, parallel, prospective observational study was carried out in 270 women with singleton pregnancy and chronic hypertension, with and without superimposed PE, also who received antenatal care and delivered in the Department of Obstetrics and Gynaecology at Fernandez Hospital, Hyderabad, Telangana, India from March 2019 to February 2020. A total of 180 women had chronic hypertension without superimposed PE and 90 had superimposed PE (group A, 180 cases; group B, 90 cases). The medical records were reviewed with specific reference to the treatment, development of Foetal Growth Restriction (FGR), maternal and perinatal outcomes. FGR was considered as the primary outcome variable. Secondary variables were stillbirth rate, low birth weight, Neonatal Intensive Care Unit (NICU) admissions, Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) at 5 minutes, gestational age at delivery, caesarean section rate and maternal complications. Categorical variables were assessed by Pearson's Chi-square test. Continuous variables were assessed by unpaired Student t-test.

Results: The mean maternal age in group A was 32±5 years and in group B was 30±4 years. Adverse maternal outcomes like abruption, Haemolysis, Elevated Liver enzymes, and Low Platelets (HELLP) syndrome, and pulmonary oedema were all low in women without superimposed PE than those with superimposed PE (1.6% vs 12.2%, p-value <0.001). There were no maternal deaths in either group. Compared to group A, group B showed higher FGR rate (15.5% vs 51.1%, p-value <0.001), preterm deliveries (<37 weeks) (50.5% vs 80% p-value <0.001), stillbirths (0 vs 13.3%), low APGAR at 5 minutes (1.1% vs 16.6%, p-value <0.001), low birth weight (21.2% vs 71.1%, p-value <0.001), NICU admissions (14.4% vs 43.3%, p-value <0.001). There was no significant difference in the caeserean section rate between the groups (69.4% vs 74.4%, p-value=0.39).

Conclusion: Maternal and perinatal morbidity was higher in women having chronic hypertension with superimposed PE. They need vigilant maternal and foetal surveillance and should be counseled about all the possible adverse outcomes.

Keywords: Abruption, Foetal growth restriction, Preterm delivery, Stillbirth

INTRODUCTION

Chronic hypertension in pregnancy is defined as blood pressure ≥140 mmHg systolic and/or 90 mmHg diastolic before pregnancy or, in recognition that many women seek medical care only once pregnant, before 20 weeks of gestation, use of antihypertensive medications before pregnancy, or persistence of hypertension for >12 weeks after delivery [1]. Chronic hypertension presents special challenges to healthcare providers. It is estimated to complicate 3% to 5% of pregnancies [1]. Increasing rates of prevalence of chronic hypertension in pregnancy is being observed now-a-days, which may be attributable to increase in maternal age, obesity and the changing lifestyle of women in their reproductive years. Chronic hypertension in pregnancy is associated with many adverse maternal and perinatal outcomes, the most common being the development of superimposed PE [2]. About 17% to 25% of pregnant women with chronic hypertension develop superimposed PE [3].

Superimposed Preeclampsia (PE) is defined by the criteria as women with hypertension alone in early gestation, who then develop proteinuria after 20 weeks of gestation or experience a sudden exacerbation of hypertension, or need to escalate the antihypertensive drug dose especially when previously well controlled with these medications, or women with hypertension and proteinuria before 20 weeks of gestation and have sudden manifestation of [1]:

- Thrombocytopenia- Platelet count <1 lakh/cc
- Impaired liver function tests- Elevated Liver transaminases to twice the normal concentration.
- New development of renal insufficiency- Serum creatinine >1.1 mg/dL or doubling of serum creatinine in the absence of other renal diseases
- Pulmonary oedema
- Cerebral or visual disturbances
- Symptoms like severe headache, nausea, vomiting, blurring of vision, epigastric pain and oliguria.
- Have sudden, substantial increase in protein excretion.

Maternal adverse outcomes include eclampsia, HELLP syndrome, abruption, pulmonary oedema, disseminated intravascular coagulation, increased rate of induction of labour and caeserean section [4]. Perinatal adverse outcomes include increased risk of foetal growth restriction, intrauterine foetal demise, preterm delivery both spontaneous and iatrogenic increased NICU admissions, increased perinatal mortality [5-7].

These complications are more in chronic hypertensives with superimposed PE than those without. Though there are few studies on adverse outcomes of chronic hypertension in pregnancy, but studies comparing chronic hypertension with and without superimposed PE are less [7,8]. More so, such evidence in the context of Indian population is sparse. Hence, this study was conducted to establish the contemporaneous data, in-depth analysis and evidence-based management of chronic hypertension. It helps in counseling the woman regarding possible adverse events and need for monitoring the mother and foetus.

MATERIALS AND METHODS

A two group, parallel, prospective, observational study was conducted in the Department of Obstetrics and Gynaecology at Fernandez Hospital, Hyderabad, Telangana, India, a tertiary care centre in urban South India from March 2019 to February 2020.Institutional Ethics Committee (Reg.No: ECR/933/inst/TG /2O17) approval was obtained prior to the start of study vide (with reference number 11-2019). Written informed consent was obtained from the subjects.

Sample size calculation: Sample size was calculated by using the sample size calculator for comparative study of percentages allowing an α error of 5% at a power of 80%, with reference values obtained from a similar study Chappell LC et al., [7]. A total sample size of 180 was obtained based on proportions of FGR in the study groups with 120 in hypertensive pregnancy without superimposed PE group and 60 in the group with superimposed PE. It was decided to increase the study sample size by 66% to study the outcomes in a larger population.

Inclusion and Exclusion criteria: Pregnant women with singleton pregnancy and chronic hypertension, who attended and received antenatal care at Fernandez Hospital, Hyderabad were included into the study. They were followed-up till their delivery whereas, women with multiple gestation, chromosomally or structurally anomalous babies were excluded from the study.

Study Procedure

Pregnant women, were sequentially recruited and grouped into either of group A or group B based on the absence (group A) or presence (group B) of superimposed PE. The primary outcome variable measured was foetal growth restriction. Secondary variables were stillbirth rate, low birth weight, NICU admissions, APGAR at 5 minutes, gestational age at delivery, caeserean section rate and maternal complications. Preterm delivery and low birth weight were defined as per World Health Organisation (WHO) [9,10].

Strict definitions of chronic hypertension and superimposed PE as per American College of Obstetrics and Gynaecology (ACOG 2013) was used [1,11-13]. Lifestyle modification like regular walking, exercises and regular Blood Pressure (BP) monitoring at home was advised [14]. Antihypertensives were started in women with blood pressure ≥150/100 mmHg. Women who were already on antihypertensives like beta blockers, Angiotensin-Converting Enzyme (ACE) inhibitors, Angiotensin Receptor Blockers (ARBs) were changed to those safe in pregnancy (labetalol, nifedepin, methyldopa, hydralazine, metaprolol) [15,16]. Investigations like haemogram, urine examination, liver and renal function tests, serum electrolytes, ultrasound abdomen and renal artery doppler, fundoscopy for hypertensive retinopathy screening were done to assess the severity of the disease and evaluation of secondary causes of hypertension (secondary hypertension is the hypertension due to any underlying cause like connective tissue disorders, renal disorder etc.) [1]. Findings suggestive of secondary hypertension are: resistant hypertension, hypokalemia (serum potassium level <3 mEq/L), elevated serum creatinine level (>1.1 mg/dL), strong family history of renal disease.

An addition of other antihypertensives were done based on the control of hypertension and with development of PE [17,18]. Women with uncontrolled hypertension even with a multidrug regimen received magnesium sulphate and termination of pregnancy was done if indicated. Their medical records were reviewed and maternal characteristics like age, Body Mass Index (BMI), parity, maternal adverse outcomes i.e., abruption, HELLP syndrome, acute kidney injury, gestational age at delivery and mode of delivery were studied.

Foetal monitoring was done by serial growth scans from 26 weeks, performed by senior foetal medicine consultants in a standardised manner as per International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) guidelines [19]. Diagnosis of FGR, staging, surveillance and timing of delivery were done as per guidelines from the Integrated management of foetal growth restriction by the center for maternal and foetal medicine Barcelona [20]. This study is one among those reporting foetal outcomes using the Barcelona protocol.

Perinatal outcomes studied were the development of FGR, stage of FGR, birth weight, stillbirth rate, APGAR at five minutes, NICU admissions.

STATISTICAL ANALYSIS

The FGR was considered as the primary outcome variable. Superimposed PE or without superimposed PE was considered as the primary explanatory variable. Age, BMI and parity were considered as potential confounding variables to all. Continuous variables were summarised as mean and standard deviations, and significance of difference between means of both groups were assessed by unpaired Student t-test. Categorical variables were summarised by frequency and proportions and significance of difference between proportions of both groups were assessed by Chi-square test. A p-value <0.05 was considered statistically significant. IBM Statistical Package for the Social Sciences (SPSS) version 22.0 was used for statistical analysis [21].

RESULTS

The mean maternal age in group A was 32±5 years and in group B was 30±4 years. Maternal age, parity and BMI were comparable between the two groups. Incidence of foetal growth restriction is significantly higher in group B compared to group A (15.5% vs 51.1%, p-value <0.001). The frequency of preterm delivery was higher in group B (50.5% vs 80%, p-value <0.001). NICU admissions (14.4% vs 43.3%, p-value <0.001) and incidence of low birth weight (21.2% vs 71.1%, p-value <0.001) were also higher in group B. There was no significant difference in caesarean section rates (69.4% vs 74.4%, p-value=0.39) between the two groups and there were no maternal deaths observed in both the groups [Table/Fig-1].

Outcome	Group A (without superimposed PE) N=180	Group B (with superimposed PE) N=90	p-value
Maternal age (Mean±SD)	32±5 years	30±4 years	0.004[a]
BMI (median)	31	28	0.004
Multiparity	48 (26.6%)	21 (23.3%)	0.05[b]
Complications	3 (1.6%)	11 (12.2%)	<0.001[b] No statistical test was applied due to 0 subjects in group A with individual complications
Abruption	3 (1.6%)	3 (3.3%)	
HELLP syndrome	0	2 (2.2%)	
Acute kidney injury	0	4 (4.3%)	
Pulmonary oedema	0	2 (2.2%)	
Secondary hypertension	12 (6.6%)	11 (12.2%)	0.123[b]
Already on antihypertensives	77 (42.7%)	39 (43.3%)	

Change in medication	58 (32.2%)	29 (32.2%)	
FGR	28 (15.5%)	46 (51.1%)	<0.001[b]
Stage of FGR			
1	20 (71.4%)	22 (47.82%)	No statistical test was applied for significance between different stages of FGR
2	6 (21.4%)	15 (32.6%)	
3	2 (7.1%)	8 (17.39%)	
4	0	1 (2.1%)	
Mode of delivery			
Vaginal delivery	55 (30.5%)	23 (25.5%)	0.39[b]
Caeserean section	125 (69.4%)	67 (74.4%)	
Gestational age at delivery <37 weeks	91 (50.5%)	72 (80%)	<0.001[b]
Mean gestational age at delivery	37±3 weeks	34±3.71 weeks	<0.001[a]
Neonatal outcomes: Stillbirths	0	12 (13.3%)	No statistical test was applied due to 0 value in group A
APGAR at 5min (<7)	2 (1.1%)	15 (16.6%)	<0.001[b]
Low birth weight (<2.5kg)	38 (21.2%)	64 (71.1%)	<0.001[b]
NICU admissions	26 (14.4%)	39 (43.3%)	<0.001[b]
Onset of illness (weeks)			
≤ 34 weeks gestation	180	64	No statistical test was applied due to 0 value in group A
>35 weeks gestation	0	26	

[Table/Fig-1]: Demographic characteristics, maternal and neonatal outcomes in pregnancies with chronic hypertension with versus without superimposed preeclampsia. [a]-unpaired student t-test. [b]-Chi-square test; AKI: Acute kidney imjury

Stillbirths were seen only in group B (13.3% i.e. 12/90). Of this six were intrauterine foetal demise due to severe FGR and uncontrolled hypertension. The other six were termination of pregnancy due to abruption, AKI, imminent eclampsia. [Table/Fig-2]. These women needed termination of pregnancy within a week of onset of superimposed preeclampsia due to severity of the disease. There were no maternal deaths in either group.

S. No.	Cause	Gestational age at delivery	Stage of FGR	Number of stillbirth
1	Intrauterine foetal demise	32	2	1
2		26	2	1
3		26	2	1
4		25	2	1
5		24	2	1
6		30	2	1
Termination of pregnancy				
7	Abruption	24	2	1
8	AKI	20	1	1
9	Imminent Eclampsia	26	3	1
10		25	3	1
11		26	1	1
12		21	1	1

[Table/Fig-2]: Causes of stillbirths.

DISCUSSION

Incidence of adverse maternal outcomes like abruption, HELLP syndrome, pulmonary oedema, and AKI were high among those with superimposed PE than those without, supporting the results of other longitudinal studies by Chappell LC et al., (3% vs 0% for HELLP) and Sibai BM et al., (3% vs 1.5% for abruption) [7,8]. Seely EW, 15 subjects have observed that incidence of foetal growth restriction in chronic hypertensive pregnant women with superimposed PE was double the rates observed in those without superimposed PE, which is like what was observed in the present study wherein, threefold increased incidence was observed in the present study study (15.5% vs 51.1%). Chappell LC et al., reported incidence of low birth weight among the two groups as 21% vs 48%, while our observation in the study population was 21.2% vs 71.1% between group A vs group B [7]. The reasons behind such higher incidences of foetal growth restrictions and low birth weight in our study population are not very clear and probably may be attributable to ethnicity, poor hypertension control and maternal nutritional status.Recent studies in Indian population by Verma I et al., in 2021 concluded that FGR in PE group is about 62% vs 17% in chronic hypertension group which is very similar to our study, while another study published in 2020 by Kumar N and Yadav A also reported higher FGR in PE group compared to chronic hypertension [22,23]. However, due to differences in the study design of both these studies compared with the present study and the analysis done to specifically identify the outcomes of different hypertensive disorders of pregnancy rather than comparing outcomes in chronic hypertension in pregnancy with vs without superimposed PE, as in the present study study, makes it inappropriate to draw any comparative conclusions from both these studies.

Preterm births (<37 weeks) were seen in 50.5% of group A and 80% of group B. These figures are markedly higher than those reported in the other studies by Chappell LC et al., (15% and 51% respectively) and Lecarpentier E et al., (20% vs 57%) [7,24]. This difference was possibly due to increased iatrogenic preterm deliveries in view of uncontrolled hypertension. Stillbirths were seen only in group B (13.3%), there were no stillbirths in group A. The stillbirth rate was higher in comparison with other studies like Chappell LC et al., (3%, 4% respectively), Sibai BM et al., (4% and 8%) and Lecarpentier E et al., (4%,4% respectively) [7,8,24]. One possible explanation for this unexpected result would be difference in the ethnicity. A significantly higher incidence of low APGAR scores at 5 minutes (1.1% vs 16.6%) was observed in the present study while other similar studies have reported no significance (1% vs 2% by Becker DA et al., and 3% vs 10% by Lecarpentier E et al., [24,25]. NICU admissions (14% vs 43%) observed in the present study are similar to those observed in other similar studies like Casagrande L et al., (18% vs 45% for NICU admissions) [26].

Regular maternal supervision and intensive foetal surveillance for superimposed PE is justified for early identification of evolving complications, optimising the treatment, timing of delivery and reducing adverse outcomes. This study provides contemporaneous data, indepth analysis which helps in counseling the woman regarding possible adverse events, need for monitoring the mother and foetus. Multicentric studies including a larger population, not just from a tertiary care centers but including the rural health setups, can provide much more comprehensive information.

Limitation(s)

The present study had a small sample size and hence the validation and extrapolation for larger population becomes a limitation. Hence needs further studies with large data. There might be chances of selection bias as the sample was not randomised, although authors recruited the patients sequentially and allocated to either of the groups based on presence or absence of superimposed PE. As the study was conducted in a tertiary perinatal center, generalisability in a low resource setting would be a challenge in terms of a thorough evaluation, monitoring and management. There can be other confounding factors like low BMI, low socio-economic status that may have their own effects on foetal growth restriction.

CONCLUSION(S)

The incidence of adverse maternal and perinatal outcomes were more amongst those with superimposed PE than those without. Using Barcelona protocol, the high prevalence of foetal growth restriction, suggesting that heightened surveillance strategies are needed in clinical practice has been highlighted.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 08, 2022
- Manual Googling: Jun 18, 2022
- iThenticate Software: Jul 25, 2022 (15%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 04, 2022**
Date of Peer Review: **Feb 25, 2022**
Date of Acceptance: **Jun 20, 2022**
Date of Publishing: **Aug 01, 2022**