A Descriptive Study of Impaired Circadian Rhythm of Blood Pressure in Women with Hypertensive Disorders of Pregnancy and its Foetomaternal Outcome

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Abstract: *Introduction: According to the World Health Organization (WHO) hypertensive disorders are the cause of most of the maternal deaths (25.7%) and therefore considered the main complication for pregnant women. Physiologically blood pressure is higher during the day time (between 09AM to6 PM) and lower at night (10 pm to 3:00 am). During night both systolic and diastolic blood pressure readings drop by about 10-20%. Material and Methods: This was a Descriptive type of observational study. Morning mean diastolic pressure (M) (between 6 am to 10 am) and nocturnal mean diastolic pressure (N) (between 10 pm to 3 am) of minimum 2 days of admission was noted and ratio of M/N was calculated. Result: In this study we included 100 patients. Out of 100 patients 54 patients were of gestational hypertension, 30 patients were of mild preeclampsia and 16 patients were of severe preeclampsia. Mean age for group A was 24.29 years, for group B it was 24.5 years and for group C it was 23.81 years. Morning DBP for group A was 103.8 followed by 97 of group B and 94.3 for group C. The mean nocturnal DBP for group A was 98.2 followed by 105.9 for group B and 115 for group C. Conclusion: We concluded that blunting/ reversal of circadian rhythm of blood pressure indicates progress of disease to its more severe form.*

Keywords: Impaired Circadian Rhythm, Hypertensive Disorders, Pregnancy, Blood pressure, Foetomaternal

1. Introduction

Pregnancy is a complex and well-regulated temporal event in which several steps are finely or chest rated including implantation, decidualization, placentation, and parturition.[1] Pregnancy induced hypertension (PIH) complicates about 6-10% of pregnancies and pre-existing hypertension complicates 1–5% of pregnancies.[2] According to the World Health Organization (WHO) hypertensive disorders are the cause of most of the maternal deaths (25.7%) and therefore considered the main complication for pregnant women.

The definition of hypertension in pregnancy is based on absolute blood pressure (BP) values (Systolic BP≥140mmHg or Diastolic BP≥90mmHg), and distinguishes as mild blood pressure (140–159/90–109mmHg) and severe blood pressure (≥160/ 110 mmHg).[2] It is recommended that a diagnosis require at least two determinations at least 4 hours apart, although on occasion, especially when faced with severe hypertension, the diagnosis can be confirmed within a shorter interval (even minutes).[3]

Despite all the recent progress in medicine, especially related to HDP, in developing countries there are still high rates of maternal death and complications associated to HDP.

The rise in blood pressure (BP) associated with clinical visit (white coat effect) may have a different mechanism and explanation and could represent a "healthy sympatethic system" different from the basic mechanism of white coat hypertension (persistently raised clinic BP together with a normal BP outside the clinic).[4]

Physiologically blood pressure is higher during the day time (between 09AM to6 PM) and lower at night (10 pm to 3:00 am). During night both systolic and diastolic blood pressure readings drop by about 10-20%.[5] When compared to normotensive pregnancies, pregnant women with essential hypertension preserve a normal circadian variation of BP but with a greater fall in BP at night. In preeclampsia, the nocturnal decrease of BP is blunted and there is less variation among BP circadian values. Even reversal of circadian pattern of blood pressure has been reported. These changes may also develop much before the actual onset of hypertension in preeclampsia.

We conducted this study to found any association between impaired circadian rhythm of blood pressure and adverse maternal and perinatal outcome in women of hypertensive disorders of pregnancy.

2. Material and Method

This was a Descriptive type of observational study. The study included a Sample size of 100 pregnant women admitted at the Department of obstetrics and gynecology in SMS Medical College and attached hospitals, Jaipur, Rajasthan, India.

Inclusion criteria
1) All pregnant women between 20-35 years of age and singleton live pregnancy > 28 weeks of gestation
2) Diagnosed with hypertensive disorders of pregnancy
3) Not requiring termination of pregnancy within 2 days of admission.

Exclusion criteria
1) Pregnant women with polyhydramnios, placenta previa and any other obstetric complication affecting the fetomaternal outcome
2) Pregnant women with chronic medical illness such as diabetes mellitus, cardiac disease, thyroid disorder and autoimmune diseases
3) Pregnant women with BMI > 25.

The blood pressure of all antenatal women admitted will be measured and study population will be selected according to the protocol. Blood pressure will be measured using BP instrument and BP monitoring will be done for 48 hours or during her hospital stay whichever is more. Morning mean diastolic pressure (M) (between 6 am to 10 am) and nocturnal mean diastolic pressure(N) (between 10 pm to 3 am) of minimum 2 days of admission will be noted and ratio of M/N will be calculated. Maternal Prognosis will be assessed by occurrence of HELLP, eclampsia, end organ dysfunction, uncontrolled hypertension, oligohydramnios or doppler abnormalities. Foetal prognosis will be assessed by occurrence of low birth weight, IUGR (Its grade of severity), poor APGAR score, NICU admission and foetal demise.

3. Result

In this study we included 100 patients. Out of 100 patients 54 patients were of gestational hypertension, 30 patients were of mild preeclampsia and 16 patients were of severe preeclampsia. We classified and grouped gestational hypertension patients in group A, mild preeclampsia patients with group B and severe preeclampsia patients with group C. mean age for group A was 24.29 years, for group B it was 24.5 years and for group C it was 23.81 years.

Table 1: Distribution of patients according to Mean diastolic BP

Mean diastolic BP	Gestational Hypertension		Mild Preeclampsia		Severe Preeclampsia		P-value
	Mean	SD	Mean	SD	Mean	SD	
Morning DBP	103.8	37.6	97	43.7	94.3	38.2	0.0001
Nocturnal DBP	98.2	19.6	105.92	27.4	115	58.99	0.0001

In the above table morning DBP for group A was 103.8 followed by 97 of group B and 94.3 for group C. The mean nocturnal DBP for group A was 98.2 followed by 105.9 for group B and 115forgroupC.Majority 62.9% women in group A, 66.6% women in group B and 81.25% women in group C were unbooked. We calculated mean urine albumin, 24-hour urinary protein, serum total protein and A/G Ratio.

Table 2: Distribution of patients according to MDBP ratio

Parameter	Gestational Hypertension		Mild Preeclampsia		Severe Preeclampsia		P-value
	Mean	SD	Mean	SD	Mean	SD	
MDBP Ratio	1.04	0.1	0.9	0.04	0.8	0.02	0.0001

In the above table MDBP ratio for group A was 1.04 followed by 0.9for group Band 0.8for group C. Majority 64.81% women in group A, 53.3% women in group B and 68.7% women in group C were Hindu. Majority 79.6% women in group A followed by 80% women in group B and 87.5% women in group C were from rural area. majority 87.04% women in group A followed by 80% women in group B and 81.25% women in group C were from medium socio-economic status. mean haemotcrit, platelets, S. LDH, PT and INR for all the groups.

Table 3: Distribution of patients according to Umblical artery Doppler abnormality

Umblical Artery	Gestational Hypertension		Mild Preeclampsia		Severe Preeclampsia		P-value
	No. of Patient	Percentage	No. of Patient	Percentage	No. of Patient	Percentage	
Absent end diastolic flow, increased RI, PI, S/D ratio	3	5.56	2	6.67	2	12.50	0.007
Decreased end diastolic flow, increased RI, PI, S/D ratio	21	38.89	10	33.33	6	37.50	
Reversal end diastolic flow, increased RI, PI, S/D ratio	2	3.70	2	6.67	7	43.75	
Normal	24	44.44	13	43.33	0	0.00	

In the above table we found that 5.56% women in group A followed by 6.67% women in group B and 12.50%women in group C had absent end diastolic flow increased RI, PI, S/D ratio.Majority38.89% women in group A followed by 33.3% women in group B and 37.5% women in group Chad decreased end diastolic flow, increased RI, PI, S/D ratio. In 3.7% women in group A followed by 6.67% women in group B and 43.7% women in group C had Reversal end diastolic flow, increased RI, PI, S/D ratio. Majority 75.9% women in group A followed by 76.6% women in group B and 56.25% women in group C were of gravida one

Table 4: Distribution of patients according to Doppler abnormality

Doppler Founding		Gestational Hypertension		Mild Preeclampsia		Severe Preeclampsia		P-value
		No. of Patient	Percentage	No. of Patient	Percentage	No. of Patient	Percentage	
Middle Cerebral Artery	Brain sparing effect	29	53.7	14	46.67	15	93.75	0.08
CRP Ratio	<1(Abnormal)	29	53.7	14	46.6	14	87.5	0.01
	≥1 (Normal)	22	40.7	13	43.3	1	6.25	
Ductus Venosus	Absence of atrial systolic waveform	0	0	2	6.67	11	68.75	0.0001

In the above table we found that majority 53.7% women in group A followed by 46.67% women in group B and 93.75% women in group C had brain sparing effects. The majority 53.7% women in group A followed by 46.6% women in group B and 87.5% women in group C had abnormal CRP Ratio. In this study 6.67% women in group B followed by 68.7% women in group C had Absence of a trial systolic wave form.
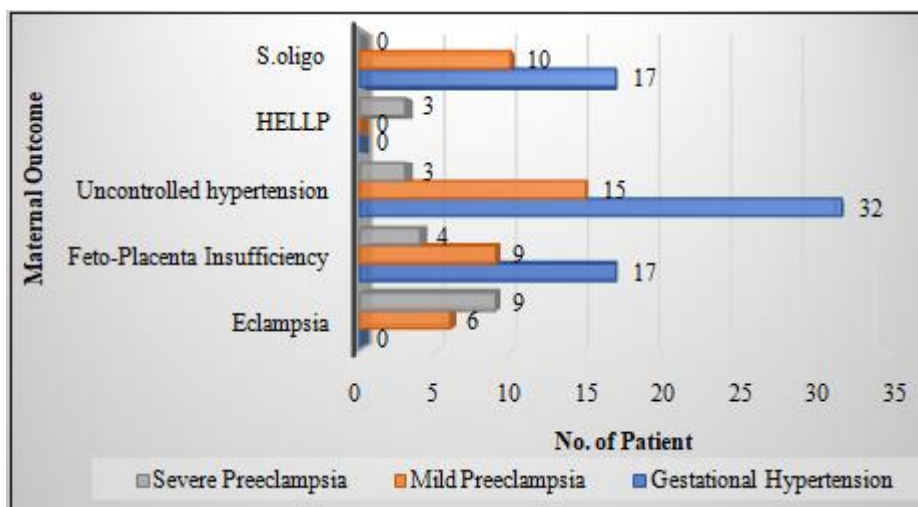

Figure 1: Distribution of patients according to Maternal Prognosis

In the above table we found that majority 59.26% women in group A followed by 50% women in group B and 18.7% women in group C had uncontrolled hypertension. Eclampsia was seen in 20% women in group B and 56.25% women in group C. We found that foeto-placental insufficiency was seen in 31.48%, 33.3% an 25% women in group A, B and C. Here we found that majority 38.89% neonate in group A followed by 53.3% neonate in group B and 87.5% neonate in group C had NICU admission. We found that low APGAR was seen in 3.7% neonates in group A followed by 13.3% in group B and 50% neonate in group C.

4. Discussion

Hypertensive disorders of pregnancy are one of the major causes of mater nalmorbidity and mortality leading to 10-15% of maternal deaths, especially in developing world. It may complicate about 3-10% of all pregnancies with variable incidence among different hospitals and countries.

We calculated mean nocturnal Diastolic BP and morning Diastolic BP on day 1and day 2 for all the groups. In this study the mean Mean diastolic BP ratio (MDBP) for group A was 1.04followed by 0.9 for group B and 0.8for group C.

Vijayvargia N et al[6] found that there is significant association between M/Nratio and categories of severity of hypertensive disorder of pregnancy. They also found that non dipping or increased nocturnal diastolic blood pressures causing reverse dipping pattern are associated with increased severity of disease. The ratio value of <1 indicates the patients with reverse dipper profile. As depicted above as the mean ratio falls the incidence of maternal complications (HELLP, eclampsia, endorgan dysfunction, uncontrolled hypertension) increase with maximum being 66.66 % at mean ratio value 0.76 to 0.88 followed by 47.6 % inrangeof0.89 to1.01;and above1.01 no adverse maternal event was noted. Similarly, Correiaetal

using diastolic blood pressure analysis Non dipper profile was associated with worse profile compared to those with dipper profile.

We found that 5.56% women in group A followed by 6.67% women in group Band 12.50% women in group C had absent end diastolic flow and increased RI, PI, S/D ratio and majority 38.89% women in group A followed by 33.3% women in group B and 37.5% women in group C had decreased end diastolic flow, increased RI, PI, S/D ratio. In 3.7% women in group A followed by 6.67% women in group B and 43.7% women in group C had Reversal end diastolic flow, increased RI, PI, S/D ratio. In middle cerebral artery we found that majority 53.7% women in group A followed by 46.67% women in group B and 93.7% women in group C had brain sparing effects. Similarly 53.7% women in group A followed by 46.6% women in group B and 87.5% women in group Chad abnormal CRP ratio and 6.67% women in group B followed by 68.7% women in group C has absence of a trial systolic waveform in ductus venous

Several investigators like Gramellini et al[7], Berkowitz et al and Fairlie et al[8] have demonstrated the correlation between abnormal Doppler indices of fetal vessels and adverse perinatal outcome and fetal distress. Yoon BH et al demonstrated that an abnormal umbilical artery Doppler waveform is a strong and independent predictor of adverse perinatal outcome in patients with preeclampsia.[9] A similar study by Smitha K et al[10] studied umbilicalartery PI, middle cerebral artery PI and MCA/UA PI ratio, a Doppler index that reflects both umbilical-placental and cerebral vascular beds for identifying compromised fetus. In the evaluation of fetal cerebral circulation we used middle cerebral artery, as it is most accessible vessel and it can be easily located on color Doppler.

Vijayvargia E et al[6] found that complications observed in this range were pulmonary edema (n=1), eclamptic fits (n=2), uncontrolled hypertension (n=1). They found that 3

patients reported to have pulmonary edema or fits belonged to category of preeclampsia without severe features. Thus, in these reverse dipper profiles was the only indicator of severity of disease process. They emphasis that 2 patients who did not report to have any adverse maternal event belong to category of preeclampsia with severe features. So, they were given magnesium sulfate prophylaxis and anti hypertensives as well. This has affected the outcome in this range of patients. Overall, 9 of 14 patients with maternal complications i.e., 64.3 percent could have been better managed with taking care of non-dipper or reverse dipper profile of diastolic BP also. The other 5 patients as already diagnosed as preeclampsia with severe features were given antihypertensives and magnesium sulfate prophyl axis with required monitoring.

5. Conclusion

We concluded that blunting/ reversal of circadian rhythm of blood pressure indicates progress of disease to its more severe form. 6 There, is increase in maternal complications like, uncontrolled hypertension, eclampsia abruptioplacentae with decreasing mean ratio of morning and nocturnal diastolic blood pressures (M/N). There also is an increase in fetal complications like IUGR, oligohydramnios with decreasing mean ratio (M/N). Monitoring the circadian pattern of blood pressures 6 hourly for patients of preeclampsia thus could be of great help in deciding for monitoring, timing of anti hypertensives and prophylactic medications and deciding for termination of gestation.

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