VOLUME - 10, ISSUE - 12, DECEMBER - 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Paediatrics

AN OBSERVATIONAL STUDY ON RISK OF HYPOGLYCEMIA, HYPOTENSION AND BRADYCARDIA IN NEONATES OF MOTHERS TAKING ANTENATAL LABETALOL

Dr R Harish — Post Graduate, Department of Pediatrics, Rajah Muthiah Medical College and Hospital, Annamalainagar, Chidambaram - 608002, Tamilnadu.

Prof Dr R Ramanathan* — Head of the Department, Department of Pediatrics, Rajah Muthiah Medical College and Hospital, Annamalainagar, Chidambaram - 608002, Tamilnadu. *Corresponding Author

Dr V Jayashree — Professor, Department of Obstetrics and Gynecology, Rajah Muthiah Medical College and Hospital, Annamalainagar, Chidambaram - 608002, Tamilnadu.

ABSTRACT

Background: Labetalol, beta blocker is the most common drug used in management of gestational hypertension. In multiple case studies, -blockers have been linked to severe symptoms of -adrenergic blockade in neonates, such as hypotension, bradycardia, and hypoglycemia. In this context, this study objective was to assess the incidence of neonatal hypoglycemia, hypotension and bradycardia among neonates with exposure during fetal period.

Methods: By convenience sampling, around 245 antenatal mothers with any forms of hypertension were enrolled and their baseline data were collected. Then the blood pressure, heart rate and blood glucose level of neonates were recorded. The incidence of hypoglycemia, hypotension and bradycardia of neonates were assessed.

Results: 245 Antenatal mothers were enrolled for baseline study. With attrition of 9.7% and exclusion of low birth weight babies, around 199 neonates were enrolled in final follow up. The incidence of hypoglycemia among neonates was 60.3 per 1000 new borns of antenatal hypertension mothers. The bradycardia and hypotension incidence were found to be 4% and 3%

Conclusion: Our findings recommend that labetolol is safe to use in pregnancy as it has very low incidence of hypoglycemia and haemodynamic variations in neonates. But still, need for routine blood glucose monitoring as per protocol in neonates born to Antenatal mothers who used labetolol can be recommended so that we can detect and treat these disorders as early as possible to prevent complications.

KEYWORDS : neonatal hypoglycemia, gestational hypertension, labetalol

INTRODUCTION:

Hypertension is one of the prevalent conditions that affects 3-10% of all pregnancies.[1] Gestational hypertension is defined as blood pressure more than or equal to 140/90 mmHg after 20 weeks of gestation. When accompanied by proteinuria above 300 mg/hr, then it fulfills the criteria for preeclampsia diagnosis and might progress to eclampsia which is characterized by seizures with hypertension. Preeclampsia is a life-threatening event for the mother and fetus. Also hypertension in pregnancy has increased the risk of neonatal mortality and morbidity.[2]

To combat the complications of hypertension, antihypertensives are prescribed during the Gestational period for antenatal mothers with hypertension. Labetalol, a non-selective β and α1 antagonist, is a widely prescribed medication globally for both long-term and acute management of maternal hypertension.[3] Labetalol is regarded as a safe medicine in term pregnancies. But it has lipophilic properties, so it can cross the placental barrier easily.[4]

However, in multiple case studies, β -blockers have been linked to severe symptoms of -adrenergic blockade in neonates, particularly in preterm newborns, such as hypotension, bradycardia, and hypoglycemia.[5,6] Also studies have shown sympathetic blockade in exposed neonates has led to increased risk of neonatal hypoglycemia when labetalol is used in late pregnancy.[4]

So, the main objective of our study is to assess the incidence of neonatal hypoglycemia, hypotension and bradycardia among babies with fetal exposure to labetalol indicated for hypertension

METHODOLOGY:

Study design: Prospective study

Study population: Antenatal mother with any form of hypertension on labetolol at baseline and neonates of these antenatal mothers at follow up

Inclusion Criteria:

All antenatal mothers with a diagnosis of Hypertension during check-up at any gestational age

Exclusion Criteria:

1. Mother with diabetes; 2.Mothers taking terbutaline and oral hypoglycaemic agents; 3. Mother with diagnosed fetal anomaly during anomaly scan 4. At follow up, neonates born to mother with other risk factors of neonatal hypoglycemia like low birth weight, sepsis, etc

Sampling size:

Incidence of neonatal hypoglycemia among labetalol exposure during the fetal period as per a study done by Heida et al[6] is 47.3% with alpha error at 5% and absolute precision (d) as 7% and attrition rate of 20%, the sample size was calculated to be 244 rounded to 245.

Study period: March 2020 – December 2021

Sampling method:

By convenient sampling, the antenatal mothers with hypertension attending OPD were selected every day until the desired sample size is achieved.

Data collection method:

After obtaining the necessary permission, the study was conducted. A pretested semi-structured questionnaire was administered in the local language after getting informed written consent from the participants. Antenatal mothers with hypertension were enrolled and socio-demographic data like age, residence, contact details, socioeconomic status, and blood pressure were obtained. Then the participants were followed up after delivery to assess blood glucose of their neonates at 2 hours of birth. This follow-up was done by direct

visit or through phone (with concerned pediatrician) if delivered in other than our Govt. medical college.

Study variables and Operational definition:
Socio-demographic data:

- Age: completed age in years as per participants own words
- Residence: as per the participants own words
- Socio-economic status:[7]

As per the Marketing Research Society of India(MRSI)scale, the S.E.S is classified into upper (I), upper-middle(II), lower-middle(III), Upper lower(IV) and lower lower(V) based on the education of chief earner and number of durable items in their family

Hypertension:
In our study, the participants with high blood pressure during pregnancy with either systolic >140mmhg or diastolic >90mmhg or any one of the below.

Gestational hypertension. Mother has high blood pressure that develops after 20 weeks of pregnancy. There is no excess protein in the urine or other signs of organ damage; Chronic hypertension. Chronic hypertension is high blood pressure that was present before pregnancy or that occurs before 20 weeks of pregnancy; Chronic hypertension with superimposed preeclampsia. This condition occurs in women with chronic hypertension before pregnancy who develop worsening high blood pressure and protein in the urine or other blood pressure-related complications during pregnancy; Preeclampsia. Preeclampsia occurs when hypertension develops after 20 weeks of pregnancy and is associated with signs of damage to other organ systems, including the kidneys, liver, blood or brain.[8]

All the Antenatal mothers in our study were having an intake of labetalol oral or iv as per physician instructions for hypertension.

Neonatal hypoglycaemia:
The blood test for glucose level was measured by glucose oxidase test (reagent strips). The neonates were screened as per protocol. The blood glucose level less than 40 mg/dl was considered to have hypoglycemia.[9]

Neonatal bradycardia:
If a neonate heart rate is less than 100 beats per minute, then the baby is considered to have bradycardia.[11]

Neonatal hypotension:
If blood pressure falls less than the 10th percentile for the given gestational age, then neonate is considered to have hypotension[10]

Birth weight: as measured using the weighing scale in kgs.

Analysis:
The data were entered in Microsoft Excel and analyzed using SPSS 23.0 software. The descriptive results were given in proportion with 95% C.I.

RESULTS:
In our study, around 245 antenatal mothers were enrolled and their babies were followed up at birth to 72 hours. Around 64% of the mothers were of age 20-30 years. Only 7.3% of the mothers were above 35 years. The majority of the mothers belonged to socio-economic class III and above (Tab.1).

The mothers with gestational hypertension were around 50.6% and 47.3% were having preeclampsia. Only around 2% of mothers had either chronic hypertension or preeclampsia superimposed on chronic hypertension. No mothers had eclampsia (Tab.1).

The data of babies of 24 mothers were not obtained due to reasons like unable to contact mother, had neonatal death, IUD or baby was very sick & unstable. So, in total 221 babies of hypertensive mothers were included and the data were obtained. The attrition rate of our study is 9.7%. And also 22 babies had low birth weight (Fig.1). These low birth weight babies were also excluded from the studies.

6.03% of neonates (n=12) with labetalol exposure during the fetal period had hypoglycemia (Fig.2). Among the neonates with labetalol exposure, around 4% (n=8) and 3% (n=6) had bradycardia and hypotension (Fig.3).

Tab.1: Details of Antenatal Mothers with Labetolol Intake for Hypertension (N=245)

S. No	Demographic variable	n	%
1	**Age in years**		
	<20	31	12.65
	20-25	96	39.18
	25-30	61	24.89
	30-35	39	15.91
	>35	18	7.34
2	**Socio-economic status**		
	I	11	4.48
	II	21	8.57
	III	84	34.28
	IV	86	35.1
	V	43	17.55
3	**Gravid**		
	Primi	126	51.4
	Multi	119	48.6
4	**Type of hypertension**		
	Gestational hypertension		
	Preeclampsia	124	50.6
	Chronic hypertension	116	47.3
	Chronic hypertension superimposed	3	1.2
	on preeclampsia	1	0.41

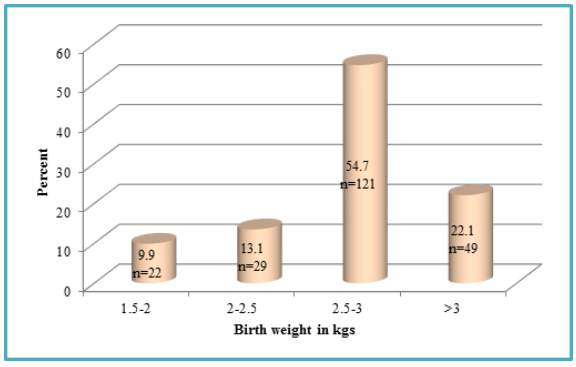

Fig.1: Details of Neonates Birth Weight (N=221)

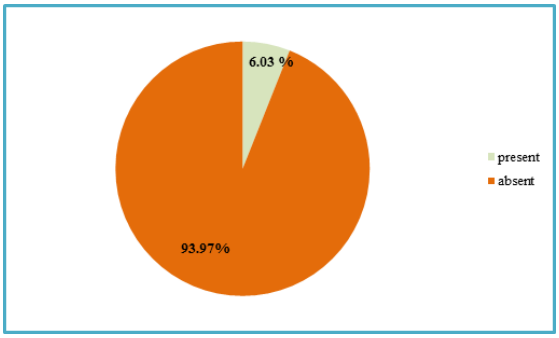

Fig.2: Distribution of Neonatal Hypoglycaemia (N=199)

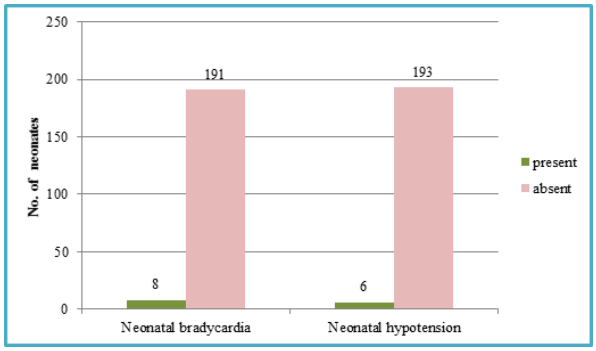

Fig.3: Distribution of Neonatal Bradycardia and Neonatal Hypotension (N=199)

DISCUSSION:

In our study, the majority of the Antenatal mothers were having gestational hypertension and preeclampsia. Similar to our study, a prospective population study have shown an incidence of pre-eclampsia and gestational hypertension were much higher than other types of hypertension.[12]

The number of mothers whose babies were followed up at birth was 221 and 22 babies had low birth weight. Among the low birth weight babies, around 6 (27%) babies had hypoglycemia among 22 babies. A Indian study has shown that more than 30% had hypoglycemia among low birth weight.[13] As the low birth weight per se is a risk factor of neonatal hypoglycemia, to obtain the exact incidence of neonatal hypoglycemia due to labetalol exposure, these LBW babies were excluded from our study.

Around 6.03% had neonatal hypoglycemia in our study among 199 babies with weight above 2 kg. i.e The incidence of neonatal hypoglycemia is 60.3 per 1000 among neonates who were exposed to labetolol during fetal. A case-control study conducted among severe preeclampsia, has shown around 47% of labetalol-exposed mothers had hypoglycaemia but there was no significant association with labetolol exposure and neonatal hypoglycaemia.[6] The over-representation from our study results may be due to differences in study design and sample size. The difference in hypertension type mothers included might also have influenced our study results as we have included all types of hypertension mothers whereas the above study only severe preeclampsia mothers were included.

Another cohort study have reported that the incidence of hypoglycemia among neonates exposed to labetalol during the fetal period as 5.1% which is similar to our study results.[14]

In our study, 3% and 4% had hypotension and bradycardia. Similar to our study, the above cohort study also have shown the incidence of neonatal bradycardia among labetalol exposure during the fetal period as 7%.[6] Through α1-adrenoreceptor blockade, Labetalol causes peripheral vasodilatation which in turn decreases the total peripheral vascular resistance while β-blockade prevents reflex tachycardia. Also though the β-blocking effect causing hypotension would be unlikely without a bradycardia, it remains to be determined whether α1-adrenoreceptor blockade or β-blockade contribute to hypotension in newborn infants exposed to labetalol. Despite concerns about its safety in fetuses, labetalol appears to have a reasonably large hemodynamic safety margin.[6]

The main strength of our study is an observational study that has nil recall bias. Also, the allowable attrition rate for a prospective study is 20% but in our study, our attrition rate is 9.7% which is very less. So this might have prevented the over or under-representation of the incidence report. And also as this is a follow up study, the other causes of neonatal hypoglycemia has been excluded which has improved the validity of our results.

The limitation of our study is there was no control group to find the risk ratio of labetalol with non-labetolol exposed patients. This suggests a need for further comparative research studies in the same setting.

CONCLUSION:

Neonates delivered to women who were on labetalol for hypertension during pregnancy have only 4% and 6% of neonatal bradycardia and hypoglycemia. Though labetolol is considered safe to use, we recommend a need for including routine blood glucose monitoring as per protocol for neonates of labetolol mother as it is feasible investigation and also early identification of neonatal hypoglycemia will reduce the complications.

Conflict of Interest: Nil
Funding: Nil
Ethical Committee Approval: The study is approved by institutional ethical committee board.

Acknowledgement: The authors would like to thank the antenatal mothers for their active participation in our study.

REFERENCES

1. Chesley's Hypertensive Disorders in Pregnancy - 4th Edition [Internet]. [cited 2021 Dec 2]. Available from: https://www.elsevier.com/books/chesleys-hypertensive-disorders-in-pregnancy/taylor/978-0-12-407866-6
2. Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P, Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. Pregnancy Hypertens. 2014 Apr; 4(2): 105–45.
3. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD001449.
4. Saotome T, Minoura S, Terashi K, Sato T, Echizen H, Ishizaki T. Labetalol in hypertension during the third trimester of pregnancy: its antihypertensive effect and pharmacokinetic-dynamic analysis. J Clin Pharmacol. 1993 Oct;33(10):979–88.
5. Brosset P, Ronayette D, Delhoume B, Lacapeyre F, Alain J, Collet D, et al. [Metabolic and cardiovascular effects of beta-blockers taken by the mother in newborn infants]. Presse Med. 1988 Mar 19;17(10):467–70.
6. Heida KY, Zeeman GG, Van Veen TR, Hulzebos CV. Neonatal side effects of maternal labetalol treatment in severe preeclampsia. Early Hum Dev. 2012 Jul;88(7):503–7.
7. New socio economic classification 2011 mrsi [Internet]. [cited 2021 Dec 2]. Available from: https://www.slideshare.net/reachformore/new-socio-economic-classification-2011-mrsi
8. High blood pressure and pregnancy: Know the facts - Mayo Clinic [Internet]. [cited 2021 Dec 2]. Available from: https://www.mayoclinic.org/healthy-lifestyle/pregnancy-week-by-week/in-depth/pregnancy/art-20046098
9. Hypoglycemia_new070208.pdf [Internet]. [cited 2021 Dec 2]. Available from: https://www.newbornwhocc.org/pdf/Hypoglycemia_new070208.pdf
10. Sahni M, Jain S. Hypotension in Neonates. NeoReviews [Internet]. 2016 Oct 1 [cited 2021 Dec 2];17(10):e579–89. Available from: https://doi.org/10.1542/neo.17-10-e579
11. Neonatal bradycardia: treatment [Internet]. [cited 2021 Dec 2]. Available from: https://www.openanesthesia.org/neonatal_bradycardia_treatment/
12. The incidence of pregnancy hypertension in India, Pakistan, Mozambique, and Nigeria: A prospective population-level analysis - PubMed [Internet]. [cited 2021 Dec 2]. Available from: https://pubmed.ncbi. nlm.nih.gov/ 30978179/
13. Study of hypoglycemia in neonates with low birth weight | Pediatric Review: International Journal of Pediatric Research [Internet]. [cited 2021 Dec 2]. Available from: https://pediatrics.medresearch.in/ index.php/ijpr/article/view/576
14. Bateman BT, Patorno E, Desai RJ, Seely EW, Mogun H, Maeda A, et al. Late Pregnancy Blocker Exposure and Risks of Neonatal Hypoglycemia and Bradycardia. Pediatrics [Internet]. 2016 Sep [cited 2021 Dec 2]; 138(3): e 20160731. Available from: https://www.ncbi.nlm.nih. gov/pmc/articles/P MC 5005024/