ORIGINAL RESEARCH

Cardiac morbidities in term neonates with hypoxic ischemic encephalopathy: A prospective study

[1]Dr. Himanshu Gaur, [2]Dr. Ghanshyam Das, [3]Dr. Ajay Gaur, [4]Dr. Puneet Rastogi

[1]Junior Resident, [2]Professor, [3]Professor and Head, Department of Paediatrics, Gajra Raja Medical College, M.P., India
[4]Professor and Head, Department of Cardiology, Gajra Raja Medical College, Gwalior, M.P., India

Corresponding Author
Dr. Ghanshyam Das
Professor, Department of Paediatrics, Gajra Raja Medical College, M.P., India
Email: drghanshyamh@rediffmail.com

Received: 22 April, 2023 Accepted: 26 May, 2023

ABSTRACT

Introduction- Hypoxic ischemic encephalopathy is a significant cause of morbidity and mortality and a common indications for admission of sicknew-born care unit (SNCU). Perinatal asphyxia leads to multiorgan involvement among that cardiac involvement is quite common. Further cardiac investigation on follow-uparerequired for better understanding and early diagnosis of associated heart disease. **Objectives-** 1. To compare the cardiac changes before 7 days of postnatal life in term neonates of hypoxic ischemic encephalopathy with healthy terms neonates. 2 To compare the cardiac changes at 3 months of follow-up in term neonates with hypoxic ischemic encephalopathy and healthy term neonates. **Methods-** This was a hospital based prospective study . Data regarding socio-demographic details, details of clinical presentation of asphyxiated newborn, antenatal, natal and post natal history was collected. Two dimensional echo cardiography , Chest X-ray findings were also recorded. **Results:-**Among 80 neonates, 3 certified ,6 not given consent and 7 were loss of follow up seen. Hence 64 neonates assessed in which 34 were case and 30 were control. Among 34 cases with in 7 postnatal day having 17(50%) atrial septal defect, 3(8.8%) ventricular septal defect, 5 (14.7%) atrial septal defect and ventricular septal defect and 9(26.5%) were having no cardiac abnormality. In 30 controls 8(26.7%) atrial septal defect and 22(73.3%) having no cardiac abnormality. **Conclusion:-** Majority of cardiac morbidity among hypoxic ischemic encephalopathy and cases resolves by 3 months of age. Two dimension echocardiography and follow up helps in early detection and intervention may reduce infant mortality and morbidity.

Keywords:-Hypoxic ischemic encephalopathy, Two dimension echocardiography, Neonates.

INTRODUCTION

Perinatal asphyxia is a common problem with the incidence varies from 0.5 – 2% of live births.[02] It is an important cause of morbidity and mortality and a frequent cause of admission to neonatal intensive care units (NICU). In India, in rural regions of the Uttar Pradesh[03] and Maharashtra[04] 23% and 25% of neonatal mortality were attributed to birth asphyxia, respectively. Hospital-based studies in Nepal[05]and South Africa[06] estimated that birth asphyxia accounted for 24% and 14% of perinatal mortality, respectively. Hypoxic ischemic organ damage can occur at antepartum prenatal asphyxia (50%), at intrapartum perinatal (birth) asphyxia (40%) or after delivery as postpartum asphyxia (10%).[07]Acute maternal infections, pre-maturity of a newborn and multiple births are the most frequent natural risk factors leading to hypoxic conditions in a newborn. Severe birth asphyxia results in myocardial ischemic injury. The incidence of clinical cardiac dysfunction in perinatal asphyxia varies from 24-31%.[08]Myocardial involvement leading to cardiogenic shock remains one of the commonest challenges in management and significant cause of mortality in neonates suffering from perinatal asphyxia. Clinically cardiac dysfunction in perinatal asphyxia manifest asrespiratory distress, congestive heart failure, triscupid insufficiency and myocardial ischemia leading to cardiogenic shock. Electrocardiographic and echocardiographic studies have been done previously to study cardiac dysfunction in perinatal asphyxia. ECG changes were T wave inversion, T wave flattening, ST segment depression and significant Q wave indicating

infarction.[09]Echocardiographic findings include tricuspid regurgitation, mitral regurgitation, right and left ventricular hypokinesia and ventricular dilatation. Hence this study intend for 2D echocardiographic finding in neonates at time of hospitalization and at 3 months of follow up.

Previous studies did not comment on long term follow up of HIE new-born's. This study aimed to assess cardiac changes in term neonate with hypoxic ischemic encephalopathy with the objectives to assess the cardiac changes before 7 days of posnatal life in term hypoxic ischemic encephalopathy neonates and healthy terms neonates and to assess the cardiac changes on 3 months of follow-up in term neonates with hypoxic ischemic encephalopathy and healthy term neonates.

MATERIALS AND METHODS

This prospective cohort study was carried out at Kamla Raja Children Hospital, G.R. Medical College, Gwalior (M.P.). Written informed consent was obtained from the parents.

Two dimension echocardiography was done by "GE HEALTH CARE VIVID 55" machine with multi frequency linear probe. Two dimension echocardiography done by expert Cardiologist from the Department of Cardiology, G.R. Medical College Gwalior. High frequency probe (5.0-7.5 MHz) used to perform two dimension echocardiography in apical, short axis, long axis and subcostal views. Echocardiography was done after stabilization of the baby suffering asphyxia related severe morbidities in the SNCU of Kamla Raja children Hospital, Gwalior.

SAMPLE SIZE

40-40 Cases and controls were enrolled, finally 34 cases and 30 controls included as per inclusion criteria for the analysis.

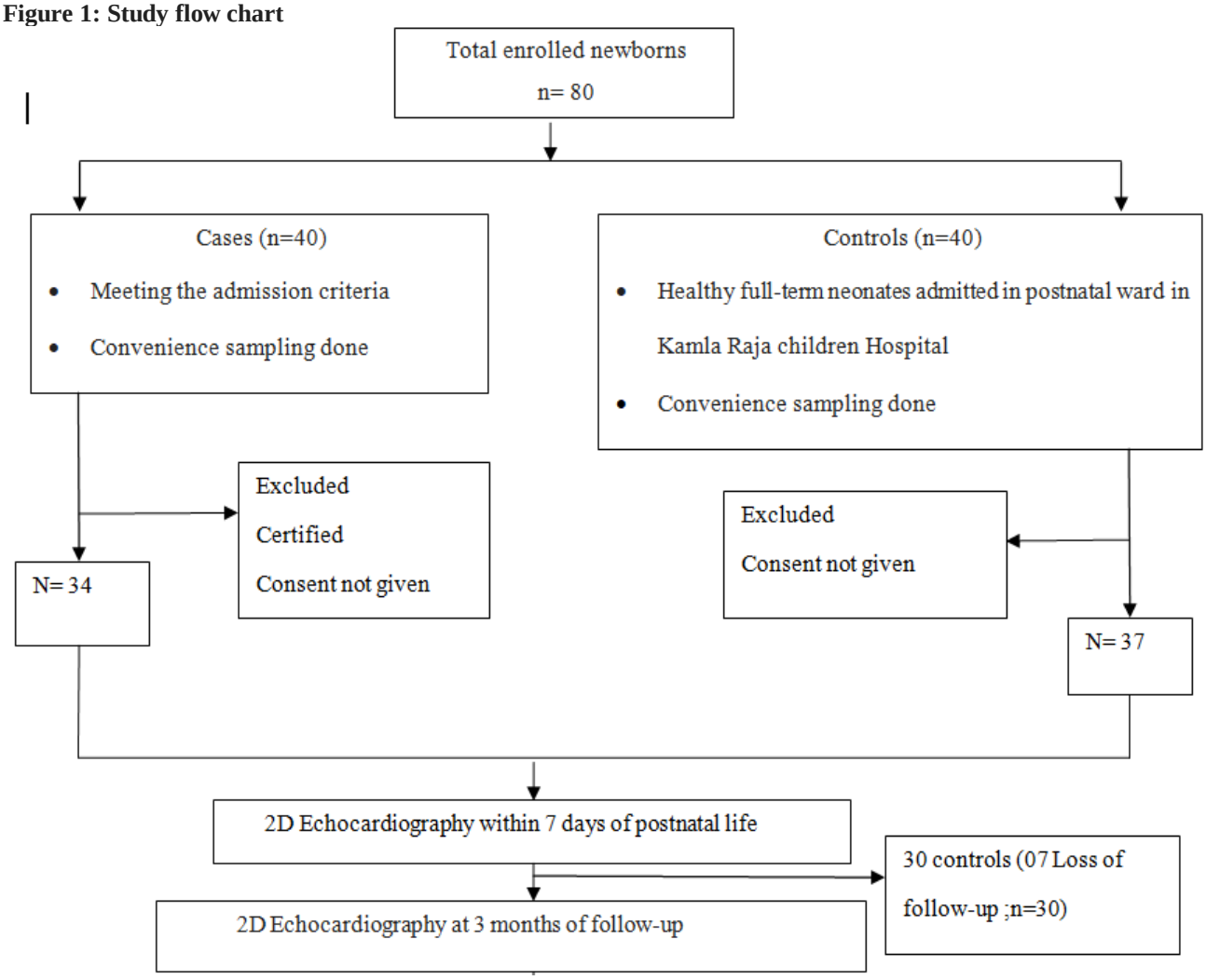
INCLUSION CRITERIA

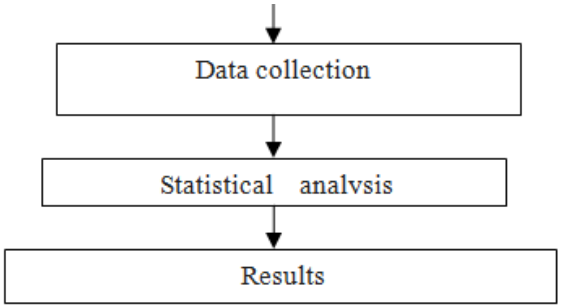
- Evidence of hypoxic ischemic encephalopathy as per Sarnatet al.[10] clinical staging of hypoxic ischemic brain Injury .
- Term neonates

EXCLUSION CRITERIA

- Prematurity
- Large for gestational age
- Major or lethal congenital malformation

Figure 1: Study flow chart





RESULTS

In the present study 34 cases and 30 controls were included in the analysis. Gender, booked/unbooked history, Residence, weight were not differ for the cases and controls. ANC complications was found significantly higher among the cases as compared with the control (82.4 % vs 10%). (Table 1)

Table 1: Distribution of case and control according baseline demography.

Demography	Categories	Case	Control	p Value
Sex	Male	17 (50%)	16 (53.3%)	0.808
	Female	17 (50%)	14 (46.7%)	
Registration	Booked	22(64.7%)	21(70%)	1.000
	Unbooked	12(35.3%)	09(30%)	
Gestational age	Term	34(100%)	30(100%)	1.000
	Preterm	0	0	
ANC complications	No	06 (17.6%)	27 (90%)	<0.001
	Yes	28(82.4%)	03(10%)	
Residence	Rural	19 (55.9%)	17 (56.7%)	0.950
	Urban	15 (44.1%)	13 (43.3%)	
Weight (g) Mean ±2 SD		2.77±0.54	2.79±0.46	0.813

Table 2 showing out of 10 MR with in 7 days 08 were turned to be NAD and out of 03 TR with in 7 days 02 were turned to be NAD.(Table 2)

Table 2: Comparison of valvular lesions with in 7 days and 3rd month of postnatal life

MR/TR WITH IN 7 PND	AT 3 MONTHS			Total	P value	
	MR	NAD	TR			
MR	2		8	0	10	<0.001
NAD	0		51	0	51	
TR	0		2	1	3	
Total	2	61	1	64		

MR was significantly higher among the cases as compared with the controls (09 cases vs 01 control). RV dilatation and LV dilation was absent among the cases and controls.(Table 3)

Table 3: Distribution of cases according to Echocardiography within 7 postnatal days

Echocardiography Findings		Control	Cases	p value
LVEF		>60%	>60%	NA
TR	Present	0	03	0.241
	Absent	30	31	
MR	Present	01	09	0.015
	Absent	29	25	
RV dilatation	Present	00	00	NA
	Absent	30	34	
LV dilatation	Present	00	00	NA
	Absent	30	34	
PPHN	Yes	3	0	0.241
	No	31	30	

DISCUSSION

Perinatal asphyxia is the most common cause of morbidity and mortality in India. There is currently no clear physiologic or radiological characteristic that enables an early identification of neonates who are at elevated risk to develop cardiac dysfunction in prenatal asphyxia. Perinatal asphyxia damages the central nervous system and is associated with

multiorgan involvement.

Study done by **Barbara michnicwicz et al**[16] observed persistent pulmonary hypertension of newborn in 8.8% of asphyxiated newborns. Similarly **Lakshminrusimha et al**[17] found out association between severity of HIE and persistent pulmonary hypertension of newborn. Incidence of PPHN was 22% among asphyxiated neonates. These studies favored observation in this study in which 8.8% of asphyxiated neonates were having PPHN and none of controls were developed such conditions.

Instudyby **Jain D et al**[13] they found no significant correlation among incidence of perinatal asphyxia and birth weight of newborns. Birth weight was also one of the criteria on which we compared the incidence of perinatal asphyxia but it came out to be insignificant with P value of 0.813 among which birth weight Mean ±SD was 2.77±0.27 of cases and 2.79±0.28 of controls.

Nikyar et al[18]studied correlation between gestational age of newborn and perinatal asphyxia like another study **Licht et al**[19]in which they also figured out no significant correlation. This study included only term newborn so we did not compare this parameter.During this study many newborns were provided with different types of ventilations. Among cases 47%(n=16) got bag and mask ventilation, 10% (n=3) were provided with bag and tube ventilation and 43% (n=15) did not need resuscitation, in control(n=30) no newborn needed any mode of resuscitation. This correlation found out to be statistically significant with p value <0.001

The prevalence of persistent pulmonary hypertension of newborn was 8.8% in newborns with HIE in this study sample.This study also observed course of valvular lesions among all newborns. We assessed mitral regurgitation (MR) and tricuspid regurgitation (TR) from 7 postnatal life to 3 months of followup and observed that 15.6%(n=10) newborns were having MR which reduced to 3.1%(n=2), 4.6% (n=3) having TR which reduced to 1.5%(n=1) and 79.7%(n=51) were not having cardiac valvular lesion which increased to 95.3%(n=61) at 3months of followup. Jain D. et al [11] observed that tricuspid regurgitation (TR) was the most common finding, present in eleven (35.48%) neonates with perinatal asphyxia. No significant difference was found among neonates in three HIE groups with respect to tricuspid regurgitation (p = 0.71) or mitral regurgitation (p = 1). They observed TR was the most common valvular lesion but in our study we observed MR is most common among all cardiac lesions.

LIMITATION OF STUDY

Long term follow up was not a part of this study.

CONCLUSION

Early detection of cardiac lesion has the potential to optimize neonatal care during hospital stay. Cardiology follow up along with neuro developmental follow up should be done to evaluation for cardiac complication in this high risk population.

REFERENCES

1. World Health Organization. Basic Newborn Resuscitation: A Practical Guide. Geneva,Switzerland:WorldHealthOrganization;1997.Availableat:www.who.int/reproductivehealth/publications/newborn_resus_citation/index.html
2. Rowe, R. D., & Hoffman, T. (1972). Transient myocardial ischemia of the newborn infant: a form of severe cardiorespiratory distress in full-term infants. The Journal of pediatrics, 81(2).
3. Baqui, A. H., Darmstadt, G. L., Williams, E. K., Kumar, V., Kiran, T. U., Panwar, D., &Santosham, M. (2006). Rates, timing and causes of neonatal deaths in rural India: implications for neonatal health programmes. Bulletin of the World Health Organization, 84.
4. Bang, A. T., Bang, R. A., Baitule, S., Deshmukh, M., & Reddy, M. H. (2001). Burden of morbidities and the unmet need for health care in rural neonates-a prospective observational study in Gadchiroli, India. Indian pediatrics, 38(9).
5. Stanton, C., Lawn, J. E., Rahman, H., Wilczynska-Ketende, K., & Hill, K. (2006). Stillbirth rates: delivering estimates in 190 countries. The Lancet, 367(9521).
6. Buchmann, E. J., Pattinson, R. C., &Nyathikazi, N. (2002). Intrapartum-related birth asphyxia in South Africa lessons from the first national perinatal care survey. South African Medical Journal, 92(11).
7. Dilenge, M. E., Majnemer, A., &Shevell, M. I. (2001). Topical review: Long-term developmental outcome of asphyxiated term neonates. Journal of child neurology, 16(11).
8. Rajakumar, P. S., Vishnu Bhat, B., Sridhar, M. G., Balachander, J., Konar, B. C., Narayanan, P., & Chetan, G. (2009). Electrocardiographic and echocardiographic changes in perinatal asphyxia. The Indian Journal of Pediatrics.
9. Wu, M. H., Chen, H. C., Lu, C. W., Wang, J. K., Huang, S. C., & Huang, S. K. (2010). Prevalence of congenital heart disease at live birth in Taiwan. The Journal of pediatrics, 156(5).
10. Sarnat, H. B., &Sarnat, M. S. (1976). Neonatal encephalopathy following fetal distress: a clinical and electroencephalographic study. Archives of neurology, 33(10).
11. Bibi, S., Gilani, S. Y. H., & Bibi, S. (2018). Spectrum of congenital heart disease in full term neonates. Journal of Ayub Medical College Abbottabad.
12. Mirza, M. A., Ritzel, R., Xu, Y., McCullough, L. D., & Liu, F. (2015). Sexually dimorphic outcomes and inflammatory responses in hypoxic-ischemic encephalopathy. Journal of neuroinflammation.
13. Jain D, Pandey AK, Das BK, Prasad DR.(2016). Cardiac function in perinatal asphyxia. J Appl Med Sci.
14. Øyen, N., Poulsen, G., Boyd, H. A., Wohlfahrt, J., Jensen, P. K., &Melbye, M. (2009). National time trends in congenital heart defects, Denmark, 1977-2005. American heart journal.
15. Bosi, G., Garani, G., Scorrano, M., Calzolari, E., & Party, T. I. W. (2003). Temporal variability in birth prevalence of congenital heart defects as recorded by a

general birth defects registry. The Journal of pediatrics.
16. Michniewicz, B., Al Saad, S. R., Karbowski, L. M., Gadzinowski, J., Szymankiewicz, M., &Szpecht, D. (2021). Organ complications of infants with hypoxic ischemic encephalopathy before therapeutic hypothermia. Therapeutic Hypothermia and Temperature Management.
17. Lakshminrusimha, S., Shankaran, S., Laptook, A., McDonald, S., Keszler, M., Van Meurs, K., ... & Higgins, R. D. (2018). Pulmonary hypertension associated with hypoxic-ischemic encephalopathy—antecedent characteristics and comorbidities. The Journal of pediatrics.
18. Nikyar, B., Sedehi, M., Mirfazeli, A., Qorbani, M., &Golalipour, M. J. (2011). Prevalence and pattern of congenital heart disease among neonates in Gorgan, Northern Iran (2007-2008). Iranian journal of pediatrics.
19. Licht, D. J., Shera, D. M., Clancy, R. R., Wernovsky, G., Montenegro, L. M., Nicolson, S. C., &Vossough, A. (2009). Brain maturation is delayed in infants with complex congenital heart defects. The Journal of thoracic and cardiovascular surgery.
20. Dalal, E. A., &Bodar, N. L. (2013). A study on birth asphyxia at tertiary health centre. National Journal of Medical Research.
21. Liljestrom, L., Wikstrom, A. K., Agren, J., & Jonsson, M. (2018). Antepartum risk factors for moderate to severe neonatal hypoxic ischemic encephalopathy: a Swedish national cohort study. Acta obstetricia et gynecologica Scandinavica.
22. Wasden, S. W., Chasen, S. T., Perlman, J. M., Illuzzi, J. L., Chervenak, F. A., Grunebaum, A., &Lipkind, H. S. (2017). Planned home birth and the association with neonatal hypoxic ischemic encephalopathy. Journal of Perinatal Medicine.
23. Boos, V., Tietze, A., Berger, F., &Bührer, C. (2019). Therapeutic hypothermia after perinatal asphyxia in infants with severe, ductal-dependent congenital heart disease. Pediatric Critical Care Medicine.