ORIGINAL RESEARCH

A study on clinico-biochemical profile and cardiac abnormalities in perinatal asphyxia in tertiary special newborn care unit

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ABSTRACT

Background: Perinatal asphyxia is one of the common neonatal problems leading to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) or the fetus (fresh stillbirth) is estimated to be around 23% of 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year(1). In India, approximately 2,50,000 to 3,50,000 infants death occur every year due to birth asphyxia, mostly within the first three days of life. In this study by estimating Renal functions, Serum Electrolytes, Serum Total calcium and Echocardiographic measurement of Ejection fraction and Degree of Pulmonary Hypertension in asphyxiated term newborns, we may able to initiate appropriate treatment at the earliest and helps in improving their neurodevelopmental outcome and preventing mortality

Aims and Objectives

- To Study the Clinical and Biochemical abnormalities in perinatal asphyxia in term newborns
- To Evaluate the Cardiac abnormalities in perinatal asphyxia in term newborns
- To Correlate the Clinical, Biochemical and Cardiac abnormalities with severity of HIE

Methodology: The study was approved by Ethical committee of Chengalpattu Medical college and Hospital. 129 neonates who are admitted in view of perinatal asphyxia in SNCU of Villupuram Medical college and Hospital as per predefined criteria are recruited into the Study after getting informed written consent from the parents.

Conclusion: It can be concluded from the study that babies born with moderate asphyxia had clinical features like seizures and respiratory distress in most of the cases where as babies with severe asphyxia had severe presentation in the form of Refractory seizures, shock, oliguria and feed intolerance.

Asphyxiated babies had developed elevated blood urea, serum creatinine levels along with lower serum sodium and total calcium levels in proportion to the severity of asphyxia. Babies with severe birth asphyxia had decreased ejection fraction indicating significant myocardial dysfunction and increased risk of developing pulmonary hypertension within 24 hours of birth.

Key words: Perinatal Asphyxiacongenital heart disease,holoprosencephaly

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Introduction

Perinatal asphyxia is one of the common neonatal problems leading to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) or the fetus (fresh stillbirth) is estimated to be around 23% of 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year[1]. In India, approximately 2,50,000 to 3,50,000 infants death occur every year due to birth asphyxia, mostly within the first three days of life. Around 20% of neonatal deaths in India as by NNPD occurs as result of perinatal asphyxia. In addition, 3,00,000 to 4,00,000 stillbirths occurs due to antepartum and intrapartum asphyxia[2].

In India, out of total deliveries one-third occurs in institution[3]. Hence most of the cases of perinatal asphyxia are referred late to hospitals. Although birth asphyxia is most commonly associated with multiple organ injuries, especially with poor

neurodevelopmental outcome, management mainly focuses on supportive care. To prevent the adverse events following asphyxia, neonates with high risk factors for developing asphyxia are identified and managed effectively.

Perinatal asphyxia may result in adverse effects on all major body systems. Many of these complications are potentially fatal. The proportion of involvement of various organ systems in asphyxia include cardiac 25%, pulmonary 23%, renal 50% and nervous system 28%[4]. The extent of multi-organ dysfunction (MOD) determines the early outcome of an asphyxiated neonate with result in neonate death as a consequence of organ damage or recovering completely.

Neonatal asphyxia is one of the major causes for neonatal mortality in the developing countries.Birth asphyxia is one of the important cause for development of neurological handicap both in term and Pre-term infants. Around 3to13% of infants with cerebral palsy have evidence of intrapartum asphyxia[5].

This study was to evaluate the clinical, biochemical and cardiac abnormalities of newborns with asphyxia which helps in early management and also to find out the correlation between these abnormalities with severity of HIE

Study justification

Perinatal asphyxia is a major contributor for neonatal death in developing countries. It is one among the preventable causes for cerebral injury in newborns. Despite the increasing understanding of the mechanisms leading to and resulting from neonatal asphyxia, early determination of brain damage following hypoxic-ischemic events still remains the hardest problems in neonatal care. Perinatal asphyxia leads to various complications like Hypoxic Ischemic Encephalopathy (HIE), Hypocalcemia, Hyponatremia, Acute tubular necrosis, Metabolic acidosis and Myocardial dysfunction.

Various studies have been done previously correlating Total Serum calcium, Serumsodium, Serum potassium, Serum creatinine and Echocardiographic changes in relation to HIE. In this study by estimating Renal functions, Serum Electrolytes, Serum Total calcium and Echocardiographic measurement of Ejection fraction and Degree of Pulmonary Hypertension in asphyxiated term newborns, we may able to initiate appropriate treatment at the earliest and helps in improving their neurodevelopmental outcome and preventing mortality

Aims and Objectives

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Materials and Methods

Source of data

129 asphyxiated term newborns are followed up by prospective study who are recruited from Special Newborn Care Unit (SNCU) in Department of Pediatrics in Government Villupuram Medical College and Hospital

Type of study

Prospective observational study

Duration of study

One year from January 2020 to December 2020

Sample size

129 asphyxiated term babies who satisfy the inclusion criteria got admitted in the Special Newborn Care Unit of Government Villupuram medical college and hospital.

Inclusion criteria

All Term newborns of 37-42 weeks of gestation who have been admitted in the view of APGAR score <7 at 1 minute of life as per WHO perinatal and Neonatal database

Exclusion criteria

- Newborns <37 weeks or >42 weeks of gestational age
- Newborns with major congenital malformations
- Newborns with congenital structural heart disease
- Newborns left against medical advice
- Newborns born delivered within 4 hours of mother receiving the magnesium sulphate
- Maternal use of anti-convulsants like Sodium valproate and phenobarbitone

Methodology

The study was approved by Ethical committee of Chengalpattu Medical college and Hospital. 129 neonates who are admitted in view of perinatal asphyxia in SNCU of Villupuram Medical college and Hospital as per predefined criteria are recruited into the Study after getting informed written consent from the parents.

Prestructuredproforma was used to obtain the general information regarding Mother details, maternal risk factors and record the parameters. Information regarding the mode of delivery, sex, birth weight, amniotic fluid status were recorded in the proforma. HIE severity status was confirmed bya Radiologist using Neuro sonogram.

Results

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Table 1 Maternal Risk Factors

Maternal Risk Factor	No. of Cases	Percentage
PIH	20	15.5%
GDM	12	9.3%
Anemia	15	11.6%
Teenage Pregnancy	2	1.6%
APH	12	9.3%
Nil	68	52.7%
Total	129	100%

Majority of patients had no maternal risk factor (52.7%). 15.5% of patients had PIH and 11.6% of patients had Anemia. Similarly 9.3% of patients had GDM and 9.3% of patients had APH. Also 1.6% of patients had Teenage Pregnancy as their risk factor

Table 2 Feed Intolerance

Feed Intolerance	No. of Cases	Percentage
Yes	17	13.2%
No	112	86.8%
Total	129	100%

Out of total cases, 17 (13.2%) cases had Feed Intolerance.

Table 3 Blood Urea

Min	Q1	Median	Q3	Max
14.00	32.50	36.00	37.00	78.00

The mean and standard deviation of Blood Urea is 37.047±11.422. The median Blood Urea is 36 and the range is 64 (14-78). The inter-quartile range is 4.5 which we get from Q1 (32.5) and Q3 (37).

Table 4 Serum Creatinine

Min	Q1	Median	Q3	Max
0.20	.60	.70	.80	2.70

The mean and standard deviation of Serum Creatinine is 0.773±0.395. The median Creatinine is 0.7 and the range is 2.5 (0.2-2.7). The inter-quartile range is 0.2 which we get from Q1 (0.6) and Q3 (0.8).

Table 5 Serum Sodium

Min	Q1	Median	Q3	Max
126.00	136.00	137.00	142.00	150.00

The mean and standard deviation of Serum Sodium is 137.938±5.108. The median Sodium is 137 and the range is 24 (126-150). The inter-quartile range is 6 which we get from Q1 (136) and Q3 (142).

Table 6Serum Potassium

Min	Q1	Median	Q3	Max
3.00	3.70	4.20	4.70	5.00

The mean and standard deviation of Serum Potassium is 4.165±0.515. The median Potassium is 4.2 and the range is 2 (3-5). The inter-quartile range is 1 which we get from Q1 (3.7) and Q3 (4.7).

Table 7 Serum Total Calcium

Min	Q1	Median	Q3	Max

The mean and standard deviation of Serum Total Calcium is 8.574±1.329. The median Calcium is 8.7 and the range is 5.7 (5.4-11.1). The inter-quartile range is 1.4 whichwe get from Q1 (8.2) and Q3 (9.6).

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Table 8 Ejection Fraction

Min	Q1	Median	Q3	Max
28.00	65.00	65.00	65.00	68.00

The mean and standard deviation of Ejection Fraction is 60.14±9.407. The median Ejection Fraction is 65 and the range is 40 (28-68). The inter-quartile range is 0 which we get from Q1 (65) and Q3 (65).

Table 9 Pulmonary Hypertension

Pulmonary Hypertension	No. of Cases	Percentage
Nil	94	72.9%
Mild	22	17.1%
Moderate	7	5.4%
Severe	6	4.7%
Total	129	100%

The result shows that majority of cases had no Pulmonary Hypertension (72.9%). 17.1% of cases had Mild Pulmonary Hypertension and 5.4% of cases had Moderate Pulmonary Hypertension. Similarly 4.7% of cases had Severe Pulmonary Hypertension.

Table 10 Outcome

Outcome	No. of Cases	Percentage
Discharged	123	95.3%
Expired	6	4.7%
Total	129	100%

The result shows that majority of cases were discharged (95.3%). Around 4.7% of cases were expired.

Table 11 Correlation between Maternal Risk Factor and HIE Stage

			HIE Stage			Total
			Stage I	Stage II	Stage III	
Maternal Risk Factor	PIH	Count	5	13	2	20
		% within Maternal Risk Factor	25.0%	65.0%	10.0%	100.0%
	GDM	Count	4	7	1	12
		% within Maternal Risk Factor	33.3%	58.3%	8.3%	100.0%
	Anemia	Count	7	6	2	15
		% within Maternal Risk Factor	46.7%	40.0%	13.3%	100.0%
	Teenage Pregnancy	Count	1	0	1	2
		% within Maternal Risk Factor	50.0%	0.0%	50.0%	100.0%
	APH	Count	1	3	8	12
		% within Maternal Risk Factor	8.3%	25.0%	66.7%	100.0%
	Nil	Count	32	30	6	68
		% within Maternal Risk Factor	47.1%	44.1%	8.8%	100.0%
Total		Count	50	59	20	129
		% within Maternal Risk Factor	38.8%	45.7%	15.5%	100.0%

Chi-Square Value = 34.266, P value = < 0.001 Significant

Figure 1 Correlation between Maternal Risk Factor and HIE Stage.

On Correlating the Maternal risk factor with occurrence of HIE, p value significance indicates that maternal risk factors plays significant role in development of perinatal asphyxia

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Table 12 Correlation between Resuscitation and HIE Stage

			HIE Stage			Total
			Stage I	Stage II	Stage III	
Resuscitation	BMV	Count	50	57	0	107
		% within Resuscitation	46.7%	53.3%	0.0%	100.0%
	Intubation and Chest Compressions	Count	0	2	19	21
		% within Resuscitation	0.0%	9.5%	90.5%	100.0%
	Intubation, CC and Adrenaline	Count	0	0	1	1
		% within Resuscitation	0.0%	0.0%	100.0%	100.0%
Total		Count	50	59	20	129
		% within Resuscitation	38.8%	45.7%	15.5%	100.0%

Chi-Square Value = 115.416,P value = < 0.001, Significant

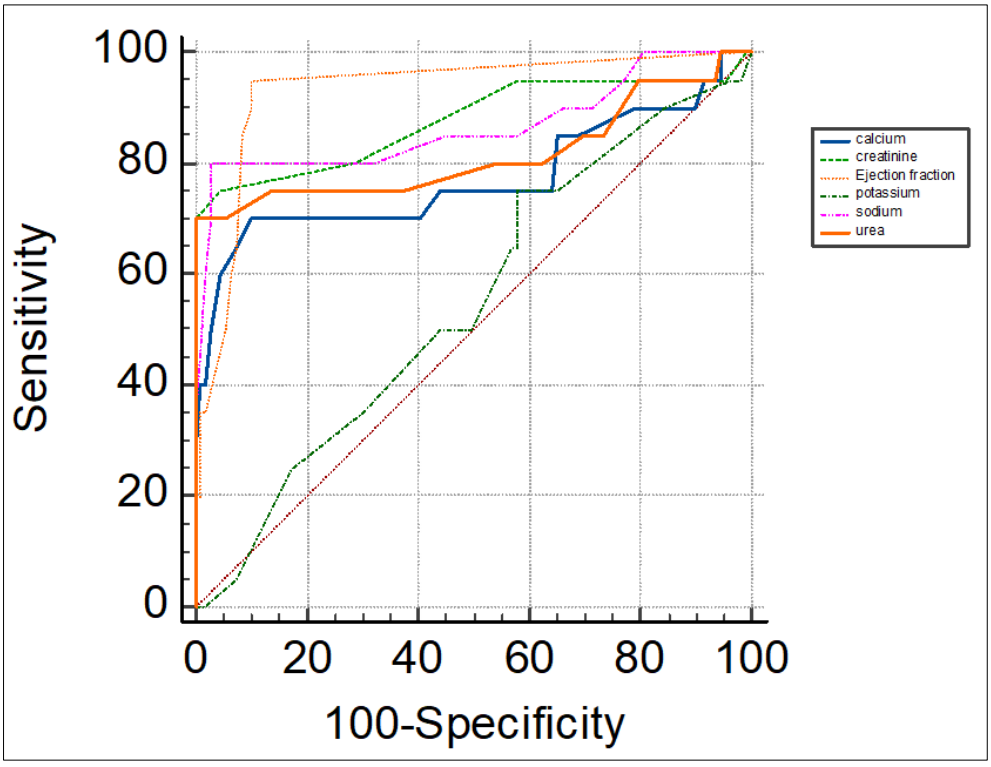

Fig 1:Comparison of ROC curve

Comparison of ROC curves

Sample size	129
Positive group [a]	20 (15.50%)
Negative group [b]	109 (84.50%)

[a]HIE_Severity = 1
[b]HIE_Severity = 0

Variable	AUC	SE [a]	95% CI [b]
Calcium	0.771	0.0777	0.619 to 0.923
Creatinine	0.877	0.0574	0.765 to 0.990
Ejection_fraction	0.931	0.0299	0.873 to 0.990
Potassium	0.549	0.0693	0.413 to 0.685
Sodium	0.866	0.0603	0.748 to 0.984
Urea	0.816	0.0737	0.671 to 0.960

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Ejection fraction, Creatinine, Sodium and Urea biomarkers predict HIE severity with AUC more than 0.80.

Discussion

Around 29% of newborn deaths occurring in the developing countries are due to perinatal asphyxia, despite various treatment guidelines and management the outcome was still not satisfactory resulting in mortality.

The study was conducted in the SNCU of Government Villupuram medical College and hospital, villupuram during the period from January 2020 to December 2020, around 129 asphyxiated neonates who satisfy the inclusion criteria are taken into the study, got admittedin the NICU soon after birth were started on maintainence fluids with 10% dextrose without any electrolyte supplementation in the fluids.

In our study, Maternal risk factors like PIH resulted in 20 cases (15.5%), GDM resulted in 12 cases (9.3%), Maternal Anemia resulted in 15 cases (11.6%) and APH resulted in 12 cases (9.3%), which shows that PIH is a significant maternal risk factor for the development of perinatal asphyxia which correlated with study done by S Chandra *et al*, which showed that most cases of perinatal asphyxia are due to pregnancy complications like Pregnancy induced hypertension and preventable intrapartum complications

In our study, 107 cases resuscitated with Bag and Mask ventilation, out of which 50 cases (46.7%) had HIE I and 57 cases (53.3%) had HIE II. 21 cases resuscitation with Intubation and chest compressions resulted in 19 cases (90.5%) of HIE III, 2 cases of HIE II (9.5%). 1 case resuscitated with intubation, chest compressions and adrenaline injection resulted in HIE III. Proportion of around 20 cases (15.5%) of HIE III occurred which correlated with study done by Gonzalez de DJ and Moya *et al* on relation between resuscitation and perinatal asphyxia

In our study, around 20 cases of HIE III who were resuscitated at birth had significantly low Apgar scores at 1 minute and 5 minute when compared to HIE I, while cases in HIE III showing multiorgan involvement which correlated with study done by Martin Ancel*et al*, identified that Apgar score has significant correlation with the severity of the organs affected.

Our study which done correlation of serum sodium levels and serum total calcium levels with perinatal asphyxia was also similar to the study done by Acharya *et al*, whose mean values of serum sodium and total calcium levels are significantly lower in HIE III when compared to the mean values of HIE I

In our study, various clinical parameters like seizures, shock, respiratory distress, oliguria and feed intolerance are correlated with the increasing severity of HIE which indicates that HIE III babies have multiple organ systems involved when compared with HIE I and HIE II

In our study, around 35 cases (27.2%) had pulmonary hypertension in asphyxiated newborns, out of which 6 cases (4.7%) had severe pulmonary hypertension, this was correlated with the study done by Abdel Mohsen and Amin *et al* and Bakheet*et al* who showed 43.7% and 35.2% cases of persistent pulmonary hypertension had severe birth asphyxia as their risk factor

In our study, out of total cases 50 cases (38.8%) belong to HIE I, 59 cases (45.7%) belong to HIE II and 20 cases (15.5%) belong to HIE III, On comparing the outcome, 6 cases of HIE III expired, while all cases of HIE I and HIE II are discharged. This was correlated with the observational study done by S K Gupta *et al*, who found that HIE I has good outcome when compared with HIE III which is associated with poor outcome

Summary

- The most common maternal risk factor for birth asphyxia is Pregnancy induced hypertension
- Most cases of perinatal asphyxia admitted are delivered by Caesarean section
- All cases of HIE I and most cases of HIE II resuscitated with only bag and mask ventilation, while all cases of HIE III cases required advanced resuscitation
- All cases of HIE II and HIE III are presented with seizures while respiratory distress, shock, oliguria and feed tolerance occurred in most cases of HIE III
- Renal failure occurred predominantly in HIE III cases
- Most cases of HIE II and HIE III showed hyponatremia and hypocalcemia
- Severe myocardial dysfunction occurred in most cases of HIE III cases
- Pulmonary hypertension predominantly occurred in most cases of HIE II and HIE III
- All deaths occurred in neonates belonging to HIE III indicating poor outcome

Conclusion

Among various causes of neonatal deaths, perinatal asphyxia contributes significantly to the mortality. Therefore neonates with significant maternal risk factors should be anticipated for the occurrence of perinatal asphyxia.

It can be concluded from the study that babies born with moderate asphyxia had clinical features like seizures and respiratory distress in most of the cases where as babies with severe asphyxia had severe presentation in the form of Refractory seizures, shock, oliguria and feed intolerance.

Asphyxiated babies had developed elevated blood urea, serum creatinine levels along with lower serum sodium and total calcium levels in proportion to the severity of asphyxia. Babies with severe birth asphyxia had decreased ejection fraction indicating

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significant myocardial dysfunction and increased risk of developing pulmonary hypertension within 24 hours of birth.

With this study, by early recognition of clinical, biochemical and cardiac abnormalities and their effective management at appropriate time will decrease the morbidity and mortality, thereby preventing the development of HIE sequelae and helps in improving the prognosis and neurodevelopmental outcome of the asphyxiated newborns.

Ejection fraction, Creatinine, Sodium andUreabiomarkerspredictHIE severitywithAUC more than 0.80.Thisclearlyindicatesallabove biomarkerswithoptimalcut offwill predictHIE severity

By this study it can be considered that all asphyxiated newborns should be given Close monitoring at early neonatal period will help in early detection and management of clinical, biochemical and cardiac abnormalities.

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