

## Original Research Article

# Coagulation Profile in neonates with perinatal asphyxia

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### ABSTRACT

**Background:** Perinatal Asphyxia refers to a condition during the first and second stage of labour in which impaired gas exchange leads to fetal acidosis, hypoxemia and hypercarbia. It accounts for about 23 per cent of the four million newborn deaths worldwide.

**Methods:** To estimate the magnitude of coagulation derangement in babies who suffered birth asphyxia and compare it with non-asphyxiated controls.

**Results:** There were 61.9% and 64 % males in both the groups outnumbering females suggesting that the health care seeking behavior for male children is more than for their female counterparts. Birth weight and mode of delivery are comparable in both the groups. PT and APTT were significantly higher in the asphyxiated babies than in their respective control group. It may be noted, however, that PT and APTT values were higher in the control group also, when compared with the reference values. This may indicate that the hemostatic mechanisms are already compromised in the newborns and perinatal asphyxia further augment the situation tilting it in favour of bleeding. Thrombocytopenia is observed in the asphyxiated group which may be due to placental insufficiency. Severe bleeding is significant in asphyxiated group as compared to the control.

**Conclusion:** Dyscoagulation should be considered in all asphyxiated babies, and they may present with clinically significant bleeding, which may require fresh frozen plasma to restore and maintain their coagulation status.

**Keywords:** Coagulation profile, Hemostatic mechanism, Perinatal asphyxia, Thrombocytopenia

### INTRODUCTION

Perinatal Asphyxia refers to a condition during the first and second stage of labour in which impaired gas exchange leads to fetal acidosis, hypoxemia and hypercarbia. It accounts for about 23 per cent of the four million newborn deaths worldwide. In most developing nations, it is the single most important cause of neonatal death, occurring singly or in combination with other morbidities (Ogunfowora and Ogunlesi, 2011; WHO, 2007; Olowu and Azubuike, 1999).<sup>1-3</sup> The American Academy of Pediatrics Committee on Fetus and newborn

has suggested essential criteria for defining perinatal asphyxia.<sup>4</sup>

- Prolonged arterial or mixed acidemia (pH<7.0) on an umbilical arterial blood sample
- Persistence of APGAR Score 0-3 for >5 mins
- Neurological manifestations e.g. seizures, coma, hypotonia or hypoxic ischemic encephalopathy (HIE) in the immediate neonatal period
- Evidence of multiorgan dysfunction in immediate neonatal period.

Perinatal asphyxia can eventually affect every organ of the body, most common ones are renal, cardiovascular, pulmonary, central nervous system, hepatic, metabolic and hematological systems. Most common hematological manifestations are thrombocytopenia due to placental insufficiency and deranged coagulation profile.

Asphyxia predisposes to coagulopathy by enhancing consumption of platelets and some clotting factors as a result of the associated severe hypoxaemia, acidaemia and sepsis.<sup>5</sup> Some reports in developed countries have shown that the levels of vitamin K dependent clotting factors are significantly lower in babies with birth asphyxia than healthy ones, which might be attributed to hepatic dysfunction usually unresponsive to the administration of vitamin K.<sup>6,7</sup>

Thrombocytopenia, alongwith hemostatic abnormalities can predispose to severe bleeding in the neonates, which accentuate morbidity and neonatal mortality in this group of babies.<sup>8</sup> An understanding of association of bleeding with asphyxia can open up opportunities for life saving interventions. Recognizing coagulation status earlier to clinical bleeding may have a role in early intervention to prevent life threatening bleeding. However, the magnitude of this problem has not been well studied. Few of the studies which tried to address this problem have included very few infants to draw any meaningful conclusions. There have been significant advancements in managing asphyxiated neonate over last few decades. This brings us the opportunity to relook at this important problem and formulate management strategy.

Primary objective of this study to estimate the magnitude of coagulation derangement in babies who suffered birth asphyxia and compare it with non-asphyxiated controls.

## METHODS

The study was conducted in the Neonatal ICU of Patna Medical College and Hospital, Patna, Bihar. All neonates (Inborn or Out born) with the history of perinatal asphyxia were included in the study.

### Inclusion criteria

The diagnosis of birth asphyxia was considered if,

- APGAR score <7 at 5 mins
- APGAR score of <5 at one min and later developed Hypoxic ischemic encephalopathy or renal failure or Necrotizing enterocolitis or Respiratory distress needing support. In all these cases sepsis was excluded by blood culture
- There was history of fetal distress and baby needed resuscitation at birth with bag and mask. Later arterial blood gas done within an hour revealed metabolic acidosis/Hypoxia/Hypercarbia or in combination of these, or if the infants developed features of asphyxia as mentioned in criteria 'b'.

This criterion was considered as many babies were referred from peripheral hospitals with no documentation of APGAR scores or APGAR scores were not reliable.

### Exclusion criteria

#### Severe congenital anomalies

Babies developing bleeding before 6 hours of life (this criterion was selected with an assumption that coagulation derangement occurs as cascade of multiple mechanisms following an acute asphyxial event which takes few hours to complete). Babies with perinatal asphyxia on or after day 2 of life were excluded.

### Ethical approval

The study was approved by Institutional Ethical Committee of Patna Medical College and Hospital, Patna, Bihar, India.

### Study type

It is a Case Control study conducted in the Department of Pediatrics, Patna Medical College and Hospital, Patna from May 2018 to May 2019.

### Consent

At admission all the parents were informed of the diagnosis and plan of management. They were updated about various tests including blood tests needed for management. We informed that this sample would be taken along with other blood tests needed for clinical management of the baby. Consent was obtained in the official admission document.

### Data collection

On inclusion, we followed standard procedures in managing birth asphyxia and no new therapeutic intervention has been done at this stage. We obtained blood for coagulation studies between 6 to 24 hours after birth along with other blood sample needed for management of the baby.

### Interpretation of results

PT and INR were reported by the lab. INR of >1.5 was taken as prolonged for further management. APTT reported by the lab was compared to control and considered prolonged if it was greater than control. Platelet counts were obtained from the complete blood count report.

### Statistical analysis

Continuous variables are expressed as mean and standard deviation. Categorical variables were expressed as proportions. Predictive values were computed for

coagulation derangement. Data analysis Data were fed into a computer and analysed using SPSS 20.0. Means of normally distributed data were compared using the independent sample t-test. As indicated, Pearson's chi-square tests, with or without Yates' continuity correction or Fisher's exact tests were used to compare categorical variables. P values of less than 0.05 were considered to be significant.

## RESULTS

Out of 1284 neonates admitted during the study period, 708 had perinatal asphyxia. 484 neonates were excluded based on exclusion criteria. Parents of 98 neonates did not give consent for the study. So, finally, 126 cases with perinatal asphyxia were included in the study. The control group was formed of 150 neonates.

Table 1 compares the socio demographic characteristics of both the cases and control group. The gestational age in both the groups are comparable. There were 61.9% and 64% males in both the groups outnumbering females

suggesting that the health care seeking behavior for male children is more than for their female counterparts. Birth weight and mode of delivery are comparable in both the groups.

**Table 1: Sociodemographic characters of cases and controls.**

Sociodemographic Variables	Cases(n=126)	Controls (n=150)	P value
Gestational age (in weeks)	37.51±1.17	37.56±1.38	0.74*
Male, n(%)	78(61.9%)	96 (64%)	0.80#
Female, n(%)	48(38.1%)	54 (36%)	
Birthweight (in Kg)	2.64±0.53	2.76±0.59	0.07*
Mode of delivery			
CS, n(%)	58(46.03%)	68 (45.3%)	0.90#
NVD, n(%)	68(53.9%)	82 (54.6%)	

CS=Cesarean Section, NVD=Normal Vaginal Delivery, # Done with Pearson's Chi square test, \* done with independent t test.

**Table 2: Comparision of coagulation parameters of cases and controls.**

Coagulation parameter	Reference values	Cases (n= 126)	Controls(n=150)	t	P value
PT (s)	10-12	18.4±3.6	12.4±3.9	13.184	0.0001
APTT (s)	35-45	54.4±4.2	50.2±6.1	6.535	0.0001
Platelet Count (X 10 <sup>3</sup> /mm <sup>3</sup> )	150-450	115.5±56.7	167.8±42.3	8.672	0.0001

Table 2 shows the coagulation parameters in the two groups and its comparison with the normal reference values. PT and APTT were significantly higher in the asphyxiated babies than in their respective control group. It may be noted, however, that PT and APTT values were higher in the control group also, when compared with the reference values.

**Table 3: Clinical bleeding.**

Severity of bleeding	Cases (n=126)	Control (n=150)	P value
No	70	112	0.009
Mild	30	27	0.29
Moderate	14	08	0.11
Severe	12	03	0.007

This may indicate that the hemostatic mechanisms are already compromised in the newborns and perinatal asphyxia further augment the situation tilting it in favour of bleeding. Thrombocytopenia is observed in the asphyxiated group which may be due to placental insufficiency.

Table 3 shows the incidence of bleeding in the two groups. Bleeding, for the ease of categorization for the

study, was divided into mild, which included bleeding from the umbilical stump, and blood stained nasogastric aspirate, not more than 5 ml of volume/ day. Bleeding was considered moderate in cases of hematoma at intramuscular injection site, hematuria, malena, and gastrointestinal losses not amounting to hemodynamic instability. Instances of severe bleeding were intraventricular hemorrhage, pulmonary haemorrhage or bleeding from any site amounting to hemodynamic instability. Severe bleeding is significant in asphyxiated group as compared to the control.

## DISCUSSION

In this study we have noted that significant proportion of babies develop abnormal coagulation status after first few hours of life. Birth asphyxia is an acute event causing enormous hemodynamic rearrangement in the body. The significant change in the hemodynamics is the diving reflex where in the circulation is maintained to vital organs and less vital organs suffer ischemia. This results in liver getting under perfused which may result in impaired function. As the consequence this, the coagulation system gets variably affected. Thus, babies with perinatal asphyxia have more chances of abnormal coagulation parameters.

In this study, platelet count and PT for the controls (apparently healthy babies) were similar to those previously reported in adults and healthy babies by Okunade and Essien in the University College Hospital, Ibadan, Nigeria.<sup>9</sup> However, a PTT of these apparently healthy babies was slightly prolonged than the values expected for older children and adults in our environment. This may indeed reflect a relative hypocoagulable state in healthy newborn babies and may justify the continued routine use of Vitamin K for all newborn babies.

In this prospective case-control study, although estimation of antithrombin III, protein C, protein S, factor V Leiden and individual clotting factors were not done, there were ample laboratory evidences of impaired haemostasis among babies with perinatal asphyxia. All the coagulation screening tests done were significantly prolonged in asphyxiated babies. This is because asphyxia is known to alter the balance between bleeding and clotting cascades, including clotting, fibrinolysis and impairment in platelet interactions. Anoxic tissue damage in birth asphyxia may contribute to intravascular coagulation by releasing tissue thromboplastin into circulation.<sup>10</sup>

Asphyxia has been noted as a cause of thrombocytopenia in the newborn. Increased destruction of platelets appears to be the most plausible pathophysiological mechanism of thrombocytopenia in these cases as thrombocytopenia is present despite normal overall bone marrow cellularity. In addition to this, impaired platelet activation and aggregatory functions, because of hypoxemia and acidosis associated with asphyxia may contribute to bleeding.<sup>11</sup>

## CONCLUSION

Hence, dyscoagulation should be considered in all asphyxiated babies, and they may present with clinically significant bleeding, which may require fresh frozen plasma to restore and maintain their coagulation status. Further studies need to be undertaken for the role of prophylactic administration of fresh frozen plasma.

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