ASSOCIATION OF BIRTH ASPHYXIA WITH CORD BLOOD NUCLEATED RED BLOOD CELL

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ABSTRACT

BACKGROUND

Asphyxia can lead to severe hypoxic ischaemic organ damage in new-borns which may cause postnatal manifestation of hypoxic-ischaemic encephalopathy. Studies have found that the Apgar score failed to predict specific neurologic outcomes of the infants. Increased cord blood nucleated red blood cell in term neonates is an indicator of chronic intrauterine hypoxia. We set out to assess the role of nucleated RBC as a non-invasive, easy, cheap and at the same time early biochemical means of asphyxia diagnosis in our clinical setting.

MATERIALS AND METHODS

All inborn babies with Apgar scores <7 at 1 and 5 minutes of life were reviewed. Relevant information from mother case sheet were obtained. Cord blood samples was drawn and sent for blood gas analysis and number of NRBCs/100 white blood cells (WBC) was determined using Leishman stain.

RESULTS

Our study proves the relevance of increase nucleated RBC in terms of early detection of birth asphyxia. Most common cause of birth asphyxia found was meconium aspiration. No co-relation was found with chorioamnionitis or maternal obstetrical history.

CONCLUSION

Many specific biomarkers are being investigated now a day for early detection of birth asphyxia. Umbilical cord pH is costly and may be underestimated in birth asphyxia. In our study, the elevated cord blood nRBC count was shown to be a good predictor of perinatal asphyxia. Since, it is cost-effective and does not require any special expertise or any high-tech facilities, it may be a useful, reliable, inexpensive and easily available marker to evaluate perinatal asphyxia. Hence, increase nucleated RBC has an important role in diagnosing and predicting the outcome of perinatal asphyxia.

KEYWORDS

Birth Asphyxia, Cord Blood P^H, APGAR Score, Nucleated RED Blood Cell.

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BACKGROUND

Asphyxia-insufficient oxygen supply-can lead to severe hypoxic ischaemic organ damage in new-borns followed by a fatal outcome or severe life-long pathologies. Although birth asphyxia is not always distinguishable as the cause of perinatal and postnatal death, its pronounced impact on the mortality of new-borns is well-documented, representing profound deficits in current healthcare systems worldwide. Secondary to birth asphyxia, a postnatal manifestation of hypoxic-ischaemic encephalopathy (HIE) is frequently observed being associated with either mild or severe organ damage in asphyxiated new-borns, both leading to the development of chronic pathologies. The severe insults often cause neurodegenerative diseases, mental retardation and epilepsies.

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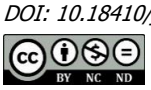

Birth asphyxia (BA) is one of the leading causes of new-born mortality.[1] Each year approximately 23% of neonatal deaths occurred due to birth asphyxia with an equal number of survivors with serious neurological squeals, such as cerebral palsy, mental retardation and epilepsy leading to detrimental long-term consequences for both child and family.[2]

There is ample literature available that has improved our understanding of the mechanisms that lead to birth asphyxia, but early indicators of tissue damages due to birth asphyxia are lacking and not widely studied. Currently a categorisation of perinatal complications is still not well classified. Therefore, absolute necessity required to optimise currently used diagnostic systems by utilising innovative non-invasive technologies and creating reliable approaches capable to provide information for follow-up personalised treatments.

Apgar score is a measure of the vitality of the new-born infant on the basis of heart rate, respiration, colour, muscle tone and reflex irritability. An association between low Apgar score and cerebral palsy was first thoroughly described in 1981, but has since been debated.[3,4] In recent years, doubts have been cast on the value of the Apgar score. Studies found that the Apgar score failed to predict specific

neurologic outcomes of the term infants. Furthermore, the Apgar score also has its own limitations. A number of factors may influence an Apgar score such as drugs, trauma, congenital anomalies, infections, hypoxia, hypovolemia, and preterm birth.

The count of umbilical cord nRBC for every 100 white blood cells has been introduced as a marker of perinatal asphyxia.[5] Increased counts of foetal nRBC have been reported in hypoxic foetal situations such as IUGR and foetal distress.[6] The nRBC, which are in fact premature precursors of the red blood cells, are released from the fetal bone marrow in response to the increased erythropoietin caused by hypoxia. Researchers have mentioned that an increase in nRBC in term neonates is indicator of chronic intrauterine hypoxia. This rise has been reported to start as early as 2 hours after hypoxia; the longer the duration of asphyxia, the more intense will be the rise in nRBC.

We set out to assess the role of nucleated RBC/100 WBC in relation to Apgar score and arterial blood gas analysis, as non-invasive, easy and cheap and at the same time early biochemical means of asphyxia diagnosis in our clinical setting.

Objectives

1. To assess cord blood nucleated red blood cells as an early marker of perinatal asphyxia.
2. Comparison of Apgar score in relation to cord blood ph and cord blood nucleated red blood cell in perinatal asphyxia.

MATERIALS AND METHODS

This was a hospital-based case control study conducted at Kempegowda Institute of Medical Science, Bengaluru, and Karnataka. The study population included 60 term new-borns of which 30 are cases and 30 controls with perinatal asphyxia delivered in KIMS over a period of 15 months. The data was analysed using EpiData analysis V2.2.2.186 and Stata 12.0 software.

Inclusion Criteria

1. Term babies with birth weight of >2.5 kg with Apgar score of <7 at 5 minutes
2. Need for PPV for more than 1 minute.
3. pH of cord blood <7.0.

Exclusion Criteria

1. Prematurity.
2. Receiving general anaesthesia pethidine, phenobarbitone and other drugs likely to cause depression in babies
3. Infant of diabetic mother.

Sampling Technique- All the asphyxiated babies were attended by a paediatric resident trained in neonatal resuscitation protocol designed by American Academy of Paediatrics. After initial resuscitation Apgar scores at 1 and 5 were determined. This was the criteria used to define birth asphyxia. All inborn babies (term and post term) with Apgar scores <7 at the 5th min of life were reviewed.

For determining the blood gas level, 1 cc of heparinzed blood was taken and ran in automated EPOC blood analyser.

Mixed cord blood samples were taken from the placental side of the cut cord by milking method& a drop was put on a glass slide. The smears were stained with Leishman stain and number of nRBCs/100 white blood cells (WBC) was determined.

All reports collected were compiled and send for statistics analysis.

RESULTS

Total 60 newborns were evaluated of which 30 were cases and 30 control.

Group	Mean (SD) of Umbilical Cord pH	P value #
Control	7.3 (0.04)	<0.001
Case	6.8 (0.2)	

Table 1. Comparison of Mean (SD) of pH of Umbilical Cord among Cases and Controls, N=60

#unpaired t test

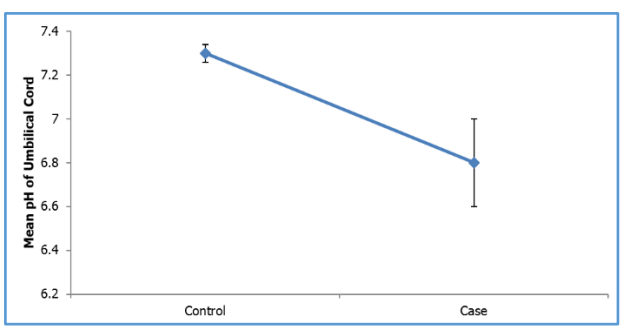

Figure 1. Comparison of Mean (SD) of pH of Umbilical Cord among Cases and Controls, N=60

Group	Mean (SD) of Umbilical cord Lactate Level	P value #
Control	3.9 (1.4)	<0.001
Case	9.1 (1.7)	

Table 2. Comparison of Mean (SD) of Lactate Level of Umbilical Cord among Cases and Controls, N=60

#unpaired t test.

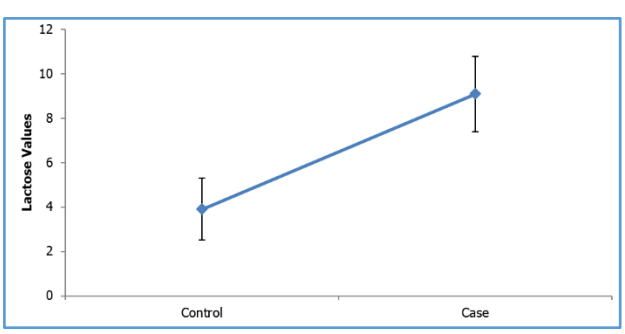

Figure 2. Comparison of Mean (SD) of Lactate level of Umbilical Cord among Cases and Controls, N=60

Group	Mean (SD) of base Excess	P value#
Control	- 5.5 (2.2)	<0.001
Case	-15.2 (2.6)	

Table 3. Comparison of Mean (SD) of Base Excess among Cases and Controls, N= 60

#unpaired t test.

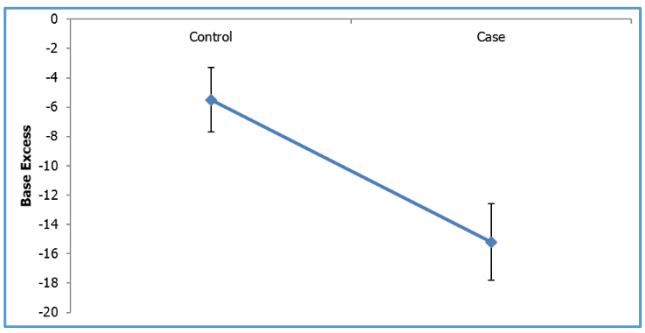

Figure 3. Comparison of Mean (SD) of Base Excess among Cases and Controls, N=60

APGAR Score at 1 Minute	Case n (%)	Control n (%)	P value *
0-3	27 (90.0)	0 (0.0)	<0.001
4-6	3 (10.0)	0(0.0)	
≥7	0 (0.0)	30 (100.0)	
Total	**30 (100.0)**	**30 (100.0)**	

Table 4. Comparisons of APGAR score at 1 minutes among cases and controls, N=60

* Fishers exact test.

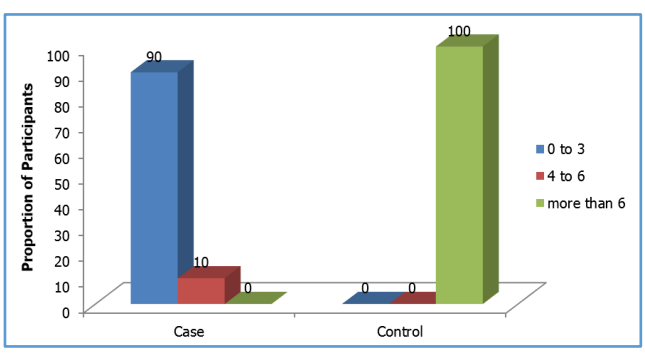

Table 4. Comparisons of APGAR Score at 1 Minutes among Cases and Controls, N=60

APGAR Score at 5 Minute	Case n (%)	Control n (%)	P value *
0-3	1 (3.3)	0 (0.0)	<0.001
4-6	29 (96.7)	0 (0.0)	
≥7	0 (0.0)	30 (100.0)	
Total	**30 (100.0)**	**30 (100.0)**	

Table 5. Comparison of APGAR Scores at 5 Minutes among Cases and Controls, N=60

* Fishers exact test.

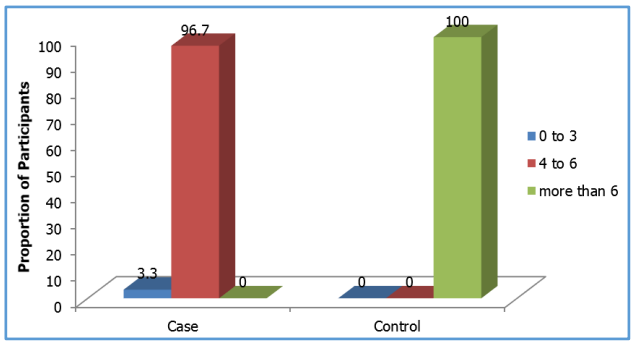

Figure 5. Comparison of APGAR Scores at 5 Minutes among Cases and Controls, N=60

PPV	Case n (%)	Control n (%)	P value *
Given	30 (100)	0 (0.0)	<0.001
Not given	0 (0.0)	30(100.0)	
Total	**30(100.0)**	**30 (100.0)**	

Table 6. Comparisons of Positive Pressure Ventilation (PPV) among Cases and Controls, N=60

*Fishers exact.

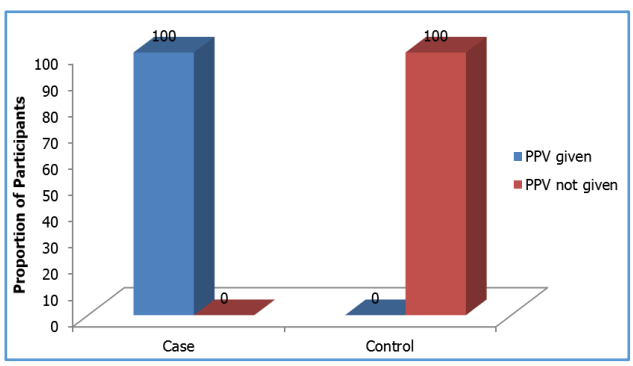

Figure 6. Comparisons of PPV among Cases and Controls, N=60

Group	Mean (SD) of Nucleated RBC per 100 WBC	P value §
Control	6.4 (1.2)	<0.001
Case	13.4 (2.4)	

Table 7. Comparison of Mean (SD) of Nucleated RBC per 100 WBC among Cases and Controls, N=60

§unpaired t test.

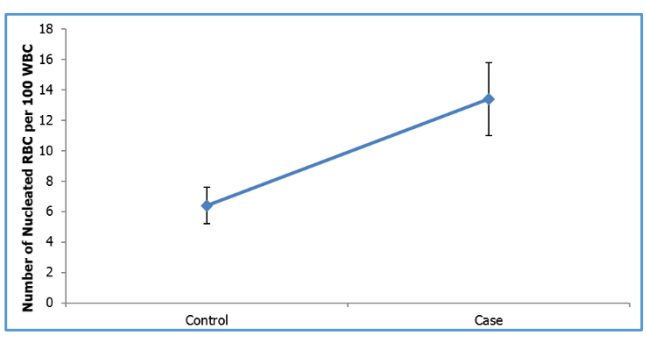

Figure 7. Comparison of Mean (SD) of Nucleated RBC per 100 WBC among Cases and Controls, N=60

DISCUSSION

According to WHO, 4–9 million new-borns develop birth asphyxia each year and at least the same number develop severe consequences such as epilepsy, cerebral palsy and developmental delay. Major manifestations of asphyxia are produced as a result from a combination of hypoxia and ischemia of the brain and other vital organs. An English study demonstrated that 80% of term infants without congenital malformation who had symptoms of NE, had evidence of perinatally acquired insults.[7]

Our analysis of the relationship between five-minute Apgar scores and infant survival indicates that the Apgar score shows the predictive value for infant death of term infants in post-neonatal period.

The Apgar scores at 1 and 5 minutes were significantly lower in the asphyxiated infants compared to the control group. The same result was detected by Boskabadi et al that found a lower Apgar score at 1 and 5 minutes postpartum, which is considered as an indicator of exposure to perinatal asphyxia.[8] However, Freeman and Nelson reported that an Apgar score at 1 minute indicates neither substantial hypoxia nor ischemia.[9] Despite all these results, a low Apgar score is still not specific for perinatal asphyxia.

In our study the mean pH in cases was 6.8 while control had mean pH of 7.3. Bretscher.[10] suggested an umbilical cord artery pH of 7.20 as the lower limit of normality. Umbilical artery pH <7.00 was detected to be of bad prognostic criteria.[11]

In the present study, the cord blood pH, base excess were significantly lower while lactate level were higher in asphyxiated infants compared to controls.

Nucleated red blood cells are primarily produced in the fetal bone marrow in response to erythropoietin and are stored in the marrow as precursors mature erythrocytes. Studies have shown decreasing nRBCs as the gestational age increases, except that post-term infants have higher counts than term infants.[12] Tissue hypoxia results in increased levels of erythropoietin, which in turn leads to stimulation of erythropoiesis and increased numbers of circulating nRBCs.

In present study, the mean nRBC/100WBC count in control and case group was and 6.4 ± 1.2/100WBCs and 13.4 ± 2.4/100 WBCs respectively, which is comparable to the study by Tung lag et al where the mean nRBCs in asphyxiated neonates was 11.36 ± 10.7 when compared to 4.83 ± 3.01 in non-asphyxiated neonates.[13] Gupta et al also in their study found nRBC/100 WBC count of 5.7 ± 2.33212 in control group and 10.34 ± 3.87883 in asphyxiated group.[14] Also, Phelan et al observed in their study that the nRBC count was significantly higher in newborns with birth asphyxia than the control group.[15]

CONCLUSION

Currently diagnosis of perinatal insults relies on adequate documentation of general medicine and obstetrics factors and on radiological and laboratory assessments. But early identification of infants at highest risk for developing seizures to hypoxic ischemia is critical, so that therapeutic strategies can be facilitated. Many specific biomarkers are being investigated now a day to assess damage such as Apgar Score which has its own limitation like it cannot be measured in out born babies or home delivered babies. It is also influenced by various drugs. Umbilical cord pH is also one good parameter for diagnosis of birth asphyxia, however in a poor resource countries like ours, blood gas analysis facilities are not available in majority of places. Also, some studies have proven that in severe birth asphyxia umbilical artery pH can be grossly under-estimated in birth asphyxia due to poor umbilical perfusion.

In our study, the cord blood nRBC count was shown to be a good predictor of perinatal asphyxia

Since, it is cost-effective and does not require any special expertise or any high-tech facilities, it may be a useful, reliable, inexpensive and easily available marker to evaluate perinatal asphyxia.

Hence, we conclude that nucleated RBC increases considerably with birth asphyxia. Hence it might have an important role in diagnosing and predicting the outcome of perinatal asphyxia. However, more investigation and studies are required for better understanding of perinatal asphyxia and its outcome.

SUMMARY

Birth asphyxia is one of the most common causes of mortality in neonatal period. Not only this, birth asphyxia also leads to severe complication in later life like, HIE, cerebral palsy. Hence, its early detection is important for an early intervention.

Apgar score was considered as an important parameter for detection of birth asphyxia, but it can be influenced by several factors like drugs, anaesthesia. It also cannot be assessed in out born babies or babies born at home.

Umbilical cord pH is also one of good parameters for diagnosis of birth asphyxia, however it is costly and grossly under- estimated in birth asphyxia due to poor umbilical perfusion.

Hence, we need to find an early, cost effective way of detection of birth asphyxia.

In our study, we found that nucleated RBC/ 100 WBC in all babies with APGAR score <7 was increased in asphyxiated babies as compared to normal babies which was statistically significant.

Thus, we conclude that nucleated RBC/100 WBC is a good indicator for early detection of birth asphyxia.

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