

Original Research Article

Immediate complications of hypoxic-ischemic encephalopathy in term neonates with resistive index as prognostic factor

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ABSTRACT

Background: Hypoxemia, a decreased arterial concentration of oxygen, frequently results in hypoxia, or decreased oxygenation to cells or organs. Hypoxic-ischemic encephalopathy (HIE) is a leading cause of neonatal brain injury, morbidity, and mortality globally. In the developed world, incidence is estimated at 1-8 per 1,000 live births, and in the developing world, estimates are as high as 26 per 1,000. The objective of the study is use of resistive index as prognostic factor for immediate neonatal outcome by Doppler ultrasound in birth asphyxia.

Methods: 50 babies were subjected to neurosonogram between 12-24 hours of life admitted to tertiary care centre. Resistive index (RI) was measured for all enrolled neonates within 24 hours of life using pulse wave Doppler ultrasound. RI was calculated as: $RI = (S - D)/S$, where S=peak systolic velocity and D=end diastolic velocity. RI was measured for all enrolled neonates within 24 hours of life using pulse wave Doppler ultrasound with 3.5 MHz transducer. RI was calculated as: $RI = (S - D)/S$. A RI between 0.56 and 0.90 was considered normal and neonates were classified as having either normal or abnormal RI.

Results: The study conducted states that the mean age taken is 17.12 hours with a p value of 0.82 and the cord pH of mean 6.88 with p value of 0.70 which is suggestive of adverse outcomes in birth asphyxiated babies while the resistive index of cerebral arteries and renal arteries is 0.66 with p value of 0.115 which is statistically significant. The lesser the resistive indices the more severe is the adverse outcome.

Conclusions: The immediate consequences of HIE like death, seizures, acute kidney injury which are the parameters in my study has a positive co relation with resistive indices of the cerebral arteries and renal arteries measures respectively.

Keywords: Birth asphyxia, Cranial ultrasound, Seizures, Resistive index, Term neonates, Flow velocities

INTRODUCTION

Among neonates with hypoxic ischemic encephalopathy (HIE), 15-20% die and nearly 25% develop permanent neurological deficits. Apgar scores and cord blood acidosis have been used to predict long term outcomes of neonates with HIE with limited usefulness. More sensitive techniques like neuroimaging are limited by cost and expertise. It is, therefore, essential to have evidence based prognostic tools to inform families regarding possible long term sequelae.³

HIE occurring during the perinatal period is one of the most commonly recognized causes of severe long-term neurologic deficits in children. The severity of the encephalopathy predicts the risk of death and long-term neurodisability.³ The central nervous system is disturbed in 70% of neonates after severe birth asphyxia; however, asphyxia is likely to cause disturbances in a number of organ systems other than the brain.³

In neonates with hypoxic-ischemic encephalopathy, high levels of cerebral blood flow measured at 12-24 hours of life have been associated with more severe brain injury.³

A substantial proportion of asphyxiated infants (35–85%) exhibit predominantly cerebral deep nuclear neuronal involvement, and injury to these areas has been associated with unfavourable neurologic outcome. Therefore, measurements of brain perfusion with dynamic color Doppler sonography during this period may provide information that correlates with reperfusion injury.³

Resistive index (RI), calculated from the cerebral arteries by cranial Doppler ultrasonography, reflects cerebral hemodynamic changes in asphyxia and has been evaluated as a bedside marker of risk of subsequent neurodevelopmental impairment in HIE.⁴ Studies from high income countries have found decreased cerebral RI to differentiate asphyxiated neonates from healthy controls and to reasonably predict the risk of subsequent neurodevelopmental impairment.⁶

METHODS

This is a cross sectional analytical study including all term (37-40 weeks of gestation) neonates born with perinatal asphyxia with Apgar score <6 at 5' min of birth with term neonates with cord blood pH<7.1 and term neonates with seizures excluding metabolic causes. The study has been conducted in a rural area with 50 babies admitted to tertiary care centre with birth asphyxia satisfying my inclusion criteria were included for my study after taking written informed consent. Ethical committee clearance was taken. These babies were subjected to neurosonogram between 12-24 hours of life.

After viewing cranial structures with the grey-scale US colour Doppler is switched on to screen vascular structures. Colour, spectral, and power Doppler imaging were performed in the coronal and transverse plane via the anterior or the temporal fontanels, respectively. Power Doppler is used to screen for regions of hyper- or hypovascularity. Colour Doppler abnormalities include changes in the RI on spectral tracings and abnormalities of flow velocity in the venous sinuses and arteries. The choice which fontanel is used is based on convenience as well as which vessels the operator wishes to visualize.

RBF was evaluated on the 1st day of life with Doppler ultrasonography utilizing a Duplex with a 5 Mz sector probe. All measurements were done by the same observer. Neonates were examined when clinically stable, in a resting state, lying in a supine position. The probe was positioned on the left flank of the baby. Systolic velocity (SV), mean velocity integrated over the complete cardiac cycle (MV) and diastolic velocity (DV) were measured; RI and pulsatility index (PI) were calculated according to the following formula:

$$RI = (SV)DV/SV \text{ and } PI = (SV)DV/MV$$

RI was measured for all enrolled neonates within 24 hours of life using pulse wave Doppler ultrasound with 3.5 MHz transducer. Resistive index was calculated as:

$$RI = (S - D)/S$$

Where S=peak systolic velocity and D=end diastolic velocity.

A RI between 0.56 and 0.90 was considered normal and neonates were classified as having either normal or abnormal RI.

Renal blood flow in neonates were examined when clinically stable, in a resting state, lying in a supine position. The probe was positioned on the left flank of the baby, visualizing sample volume directly in the proximal portion of the left renal artery that was insonated at an approximately angle of 30°. RI and PI were calculated according to the following formula:

$$RI = (SV)DV/SV \text{ and } PI = (SV)DV/MV$$

Renal function was investigated as follows: daily measurement of urine output, plasma creatinine, BUN, electrolytes and osmolality in the 1st week of life. Plasma creatinine >1.2 mg/dl, blood urea >100 mmol/l and oliguria <1 ml/kg/24 hours were considered for acute kidney injury.

For early onset sepsis daily measurement of blood counts and C reactive protein was done. Total leucocyte counts >20,000 cells/cumm and C reactive protein >10 mg/dl within 72 hours of life were considered as early onset of sepsis and the appropriate treatment was started.

Outborn neonates and neonates with congenital anomalies were not included in my study.

Statistical software

The statistical software namely statistical package for the social sciences (SPSS) 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, and tables.

RESULTS

The study was done for a period of one and half years between January 2019 to June 2020 and we found to have a total of 50 patients in total.

Table 1: Age distribution of patients studied.

| Age in hours | No. of neonates | % |
|--------------|-----------------|-------|
| 11-20 | 42 | 84.0 |
| 21-30 | 8 | 16.0 |
| Total | 50 | 100.0 |

The present study is carried out on a population of 50 babies in total satisfying my inclusion criteria. Most the babies were studied between 12-20 hours of life i.e. 42

babies (84%) and 8 babies (16%) between 21-24 hours of life.

In the present study male babies were more 31 out of 50 babies while the female babies were 19 with male to female ratio of 1.73 making male babies more susceptible.

Table 2: Gender distribution of patients studied.

| Gender | No. of neonates | % |
|--------------|-----------------|--------------|
| Female | 19 | 38.0 |
| Male | 31 | 62.0 |
| Total | 50 | 100.0 |

In the present study, the RI is normal between 0.56-0.9 which is 72% and the number less than 0.56 and more than 0.9 are abnormal which together in both cerebral arteries is 28%.

While for both renal arteries 0.56-0.9 is normal which is 80% and the abnormal values <0.56 is 20% with severe consequence.

Table 3: RI distribution of patients studied.

| RI | No. of neonates (n=50) | % |
|--------------|------------------------|------|
| ACA | | |
| <0.56 | 10 | 20.0 |
| 0.56-0.9 | 36 | 72.0 |
| >0.9 | 4 | 8.0 |
| MCA | | |
| <0.56 | 10 | 20.0 |
| 0.56-0.9 | 36 | 72.0 |
| >0.9 | 4 | 8.0 |
| RA RT | | |
| <0.56 | 10 | 20.0 |
| 0.56-0.9 | 40 | 80.0 |
| >0.9 | 0 | 0.0 |
| RA LT | | |
| <0.56 | 10 | 20.0 |
| 0.56-0.9 | 40 | 80.0 |
| >0.9 | 0 | 0.0 |

Amongst the 48 babies survived acute kidney injury and early onset sepsis was seen in 10% of the babies each, 16% had seizures while 30% of them improved.

In the current study, total leucocyte count 20000 is 58% and CRP is 88% which shows early onset sepsis and blood urea >100 is 10% and serum creatinine >1.2 is 10% which suggests acute kidney injury.

Table 4: Neonatal outcome distribution of patients studied.

| Neonatal outcome | No. of neonates (n=50) | % |
|------------------|------------------------|------|
| Death | 2 | 4.0 |
| Survivors | 48 | 96.0 |
| AKI | 5 | 10.0 |
| EOS | 5 | 10.0 |
| Improved | 30 | 60.0 |
| Seizures | 8 | 16.0 |

Table 5: Blood investigations.

| Blood investigations | No. of neonates (n=50) | % |
|---------------------------------|------------------------|------|
| Total count | | |
| <4000 | 0 | 0.0 |
| 4000-20000 | 21 | 42.0 |
| >20000 | 29 | 58.0 |
| Blood urea | | |
| <20 | 12 | 24.0 |
| 20-100 | 33 | 66.0 |
| >100 | 5 | 10.0 |
| Serum creatinine (mg/dl) | | |
| <1.2 | 45 | 90.0 |
| >1.2 | 5 | 10.0 |
| CRP | | |
| 0-10 | 44 | 88.0 |
| >10 | 6 | 12.0 |

The RI values of anterior cerebral arteries is p value of 0.115, middle cerebral artery is 0.328 p value and of right renal artery is 0.001 and left renal artery is 0.021 p value which is all statistically significant.

In the present study, the total count p value is 0.002 while that of CRP is 0.001 which of the both are statistically significant for early onset sepsis and the p value of blood urea is 0.014 while that of serum creatinine is 0.002 which are both statistically significant for correlation with acute kidney injury.

Table 6: RI - a comparison in patients studied according to neonatal outcome of neonates studied.

| RI | Neonatal outcome | | Total | P value |
|--------------|------------------|--------------------|-----------|---------|
| | Improved | Not improved/death | | |
| ACA | 0.69±0.09 | 0.61±0.22 | 0.66±0.16 | 0.115 |
| MCA | 0.68±0.07 | 0.64±0.21 | 0.66±0.14 | 0.328 |
| RA RT | 0.70±0.10 | 0.59±0.13 | 0.66±0.12 | 0.001** |
| RA LT | 0.71±0.12 | 0.63±0.13 | 0.68±0.13 | 0.021* |

Table 7: Comparison of blood investigations according to neonatal outcome of patients studied.

| Variables | Neonatal outcome | | Total | P value |
|-------------------------|------------------|--------------------|------------------|---------|
| | Improved | Not improved/death | | |
| Total count | 18562.97±5002.98 | 24437.25±7770.94 | 20912.68±6832.27 | 0.002** |
| Blood urea | 30.53±13.07 | 48.25±34.67 | 37.62±25.38 | 0.014* |
| Serum creatinine | 0.89±0.28 | 1.38±0.76 | 1.08±0.58 | 0.002** |
| CRP | 4.82±1.52 | 8.65±4.12 | 6.36±3.40 | 0.001** |
| Birth weight | 2.79±0.44 | 2.90±0.50 | 2.84±0.46 | 0.427 |

+Suggestive significance (p value: 0.05<P<0.10), *moderately significant (p value: 0.01<P≤0.05), **strongly significant (p value: P≤0.01)

DISCUSSION

Despite birth asphyxia being preventable cause of preventing death and other comorbidities still it poses a significant amount of risk for the new-born babies. Even with recent improvements in early identification and intervention there is considerable morbidity and mortality. Most the babies were studied between 12-20 hours of life i.e. 42 babies (84%) and 8 babies (16%) between 21-24 hours of life. male neonates (62%) exceeded the female neonates (38%) and 38% of POG 39 weeks while maximum being delivered through vaginal route compared to caesarean and assisted deliveries. 74% of the neonates were under 2.5–4 kg birth weight. 22% of the neonates had a birth weight of less than 2.5 kg and 4% of the neonates had greater than 4 kg birth weight.

Mild (68%) cases of Sarnat staging were found to be least affected than moderate (28%) and severe (4%) cases which maximum pH being affected in 4% of 7. As per our study higher number of neonates (>55%) were found lie in 0.56-0.9 RI distribution which indicates normal category. Whereas less than 20% of the neonates were found to lie below 0.56 and 8% of the neonates >0.9 RI distribution which indicates higher morbidity and mortality. While RI of renal artery <0.56 were 20% who presented with acute kidney injury.

According to our study 96% of the neonates were survivors and 4% of the neonates suffered deaths. Among the survivors 60% neonates were under improved category whereas 16% neonates were under seizures category. 10% of the cases were under AKI and EOS categories each.

CONCLUSION

In conclusion, RI studied in between 12-24 hours of birth asphyxiated babies carries a significant value to predict the immediate neonatal outcomes in babies like death, seizures, sepsis, AKI in a resource limited setting, we need more studies which outlook the need for studying resistive indices for prognosticating the immediate effects of neonatal outcome in asphyxiated babies. The present study adds that presence of abnormal resistive index <0.56 and >0.9 significantly increases the risk of death, AKI, sepsis and seizures in term asphyxiated babies.

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