Renal Dysfunction in Perinatal Asphyxia & its Correlation with Apgar Score and Hypoxic Ischemic Encephalopathy Stage

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ABSTRACT

Renal involvement is frequent in perinatal asphyxia. The severity of renal involvement and adverse outcome are correlated with severity of asphyxia and HIE stage. The study determined the incidence of renal failure after perinatal asphyxia, to assess comprehensively the renal functions of asphyxiated newborns and to correlate severity and type of renal failure with Apgar Score and HIE stage. This prospective cohort study was conducted on total 50 newborns of >34wks gestational age. All neonates were evaluated clinically and their renal functions were assessed on day 3 and 5. Assessment of fractional excretion of sodium (FeNa) was done to know the type of renal failure. Criteria for labeling an asphyxiated neonate as having renal failure were serum creatinine >1.5mg/dl or oliguria<0.5ml/kg/hr for >6hrs beyond first day of life. HIE staging was done by Sarnat and Sarnat staging system. Results were tabulated and analyzed statistically by student t test, Chi-Square test and Anova test. Acute renal failure was common among asphyxiated newborns with incidence of 57.5%. in our study. Incidence of renal failure increases as Apgar score decreases and as HIE stage progresses. Blood urea and serum creatinine were significantly higher in asphyxiated babies, compared to control group (p value <0.001). Biochemical derangements correlated well with HIE staging and Apgar score and this difference was found significant (p value<0.05). Oliguric renal failure was present in 35% of asphyxiated babies. Incidence of intrinsic renal failure (FeNa>2.5) was more in severely asphyxiated and HIE stage-III babies. Predictors of adverse outcome are intrinsic renal failure, higher HIE stage and severe asphyxia.

KEY WORDS: ARF (acute renal failure), FeNa (fractional excretion of sodium), HIE (hypoxic ischemic encephalopathy), perinatal asphyxia, intrinsic renal failure

INTRODUCTION:

Perinatal asphyxia is one of the most common cause of neonatal mortality and morbidity in developing countries. Hypoxia and ischemia can damage almost every tissue and organ of body, and kidney involvement is seen in about 50%-72% of cases. Milder episodes of ischemia may cause reversible tubular changes, seen microscopically. More severe injury involves the glomerulus and entire nephron may be involved due to corticomedullary necrosis as a result of infarction. This study was performed to determine the incidence of renal failure in perinatal asphyxia, to assess comprehensively the renal function in asphyxiated babies and to correlate the severity and type of renal failure with Apgar score (6) and encephalopathy(HIE) staging of asphyxiated neonates.

MATERIALS AND METHODS:

The study design was prospective cohort study. This study was conducted on total 50 newborns of ≥34wks gestational age, admitted in Neonatology, Department of Pediatrics, M. L. B. Medical College, Jhansi, from January 2009 to June 2010. The study group comprised of 40 neonates, with gestational age ≥34 weeks, born by LSCS or normal vaginal delivery and who were appropriate for their gestational age. Babies with Apgar score of 6 or less at 1 min or babies who needed resuscitation for ≥5 min, were included in study group.
Fractional Excretion of Na
considered as an indicator of intrinsic renal failure. FeNa (fractional excretion of sodium) >2.5% was
potassium was measured on sodium and potassium
alkaline picrate method. Urea estimation was done by
applied for creatinine estimation was modified
done from a peripheral vein. Laboratory method
subjected for creatinine and sodium were also done.
Assessment of fractional excretion of sodium was
done to know the type of renal failure. Criteria adopted
for labeling an asphyxiated neonate as having renal failure
were serum creatinine >1.5 mg/dl (>133
micromol / lit) on 3rd day of life or Urine output < 0.5
ml / kg / hr for >6 hrs beyond 24 hrs of life. In
microscopic urine analysis, presence of granular cast,
hyaline cast, RBC>5/hpf, protein( >1+) and tubular
cells suggest an intrinsic cause.

Severity of asphyxia was determined by
Apgar score (moderate asphyxia is slow gasping
breathing or Apgar score of 4-6 at 1 minute of age and
severe asphyxia is no breathing or Apgar score of 0 -3
at 1minute of age),(NNPD-2000). HIE staging was
done by Sarnat and Sarnat scoring system (1976)[7].
FeNa (fractional excretion of sodium) >2.5% was
considered as an indicator of intrinsic renal failure.

Fractional Excretion of Na =

Urinary Na x Plasma Creatinine
--------------------------------------
Plasma Na x Urinary Creatinine

Proper history with special emphasis on
antenatal, natal and postnatal history, cry status, details
of resuscitation were also recorded. Thorough clinical
examination were done, special emphasis in
neurological examination was given in assessment of
HIE stage of baby like level of consciousness, tone,
posture, convulsion, pupil and neonatal reflexes.
Gestational age assessment was done by LMP and
New Ballard scoring system. Blood sampling was
done from a peripheral vein. Laboratory method
applied for creatinine estimation was modified
alkaline picrate method. Urea estimation was done by
di-acetyld amino oxide method by kit. Sodium and
potassium was measured on sodium and potassium
analyser. Estimation of urine for specific gravity,
sugar, protein and ketones was done by dipstick colour
strips for urine analysis. Microscopic examination of
urine was done to see haematuria (5RBC/hpf).
Statistical analysis was performed by using unpaired
student 't' test, chi-square test and 'Anova' test by using
SPSS software.

RESULTS:
Cases of perinatal asphyxia with renal failure
were kept in group Ia and without renal failure were
kept in group Ib. Control group were kept in group-II.
In this study, incidence of moderate asphyxia was 30%
and that of severe asphyxia was 70%. Incidence of
ARF (Acute Renal Failure) in asphyxiated babies was
57.5%. There was a significant correlation (p value <
0.001) between study and control group when blood
urea and serum creatinine values were compared. This
showed that asphyxiated babies had deranged renal
functions as compared to non-asphyxiated babies.

Incidence of ARF in HIE was 26.7% in stage
I,70% in stage II and 100% in stage III. This showed
that as HIE stage progressed, more renal dysfunction
was seen in asphyxiated babies. This difference in
incidence was found statistically significant (p
value<0.05 done by Chi-square test). Likewise,
incidence of renal failure in moderate asphyxia was
33.33% whereas in severe asphyxia was 67.8%.
This difference in incidence was also statistically
significant (p value<0.05 done by Chi-square test).
Thus renal failure increases as apgar score decreases.

Serum sodium level was almost unaffected in
study and control group except for a slightly lower
level in ARF cases. (Serum sodium level was 132.0±
2.36 and 131±1.65 on 3rd day and 5th day respectively in
ARF cases, while 135±2.15 and 136.6±1.72 on
3rd and 5th day respectively in non-ARF cases. Serum
potassium level in asphyxiated ARF babies was found
to be higher (5.8±0.36 on 3rd day and 6.2±0.43 on 5th
day) than non-ARF asphyxiated babies (4.5±0.4
on 3rd day and 4.4±0.23 on 5th day respectively). Thus
incidence of hyperkalemia (K > 6meq/lit) in ARF
cases was 39.13%. Incidence of haematuria in ARF
cases was 30%, most of them were of intrinsic renal
failure type. Frequency of proteinuria (protein > 1+)
in this study was 47.82%. Incidence of pre-renal renal
failure was 60.9% while of intrinsic renal failure was
39.1%.

High FeNa is more specific for intrinsic renal
tubular damage. Oliguric renal failure was present in
35% of cases and non-oliguric renal failure was
present in 65% of cases of renal failure.
Table 1: Biochemical parameters in moderate and severe asphyxia (according to Apgar score)

<table>
<thead>
<tr>
<th></th>
<th>Blood urea (mean SD)</th>
<th>Serum creatinine (mean SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate asphyxia (n=12) (Apgar 4-6)</td>
<td>29.6±18.3</td>
<td>1.18±0.374</td>
</tr>
<tr>
<td>Severe asphyxia (n=28) (Apgar ≤3)</td>
<td>48.4±24.1</td>
<td>1.66±0.462</td>
</tr>
</tbody>
</table>

Table 2: Co-relation of severity of asphyxia and type of renal failure.

<table>
<thead>
<tr>
<th>Type of asphyxia</th>
<th>pre-renal ARF</th>
<th>Intrinsic ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>%</td>
</tr>
<tr>
<td>Moderate asphyxia (n=4)</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Severe asphyxia (n=19)</td>
<td>7</td>
<td>36.85</td>
</tr>
</tbody>
</table>

Table 3: Urea and creatinine levels correlated with HIE Staging.

<table>
<thead>
<tr>
<th>HIE staging of group I (Study group)</th>
<th>Blood urea (mg/dl) in group I</th>
<th>p-value (between stage I,II,III by Anova test)</th>
<th>Serum creatinine (mg/dl) in group I</th>
<th>p-value (between stage I,II,III by Anova test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>28.5±20.3</td>
<td>p-value &gt;0.05</td>
<td>1.11±0.358</td>
<td>p-value &gt;0.05</td>
</tr>
<tr>
<td>II</td>
<td>47±20.2</td>
<td>p-value &lt;0.005</td>
<td>1.65±0.353</td>
<td>p-value &lt;0.005</td>
</tr>
<tr>
<td>III</td>
<td>68.4±23.2</td>
<td></td>
<td>2.18±0.36</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>42.8±23.9</td>
<td></td>
<td>1.52±0.486</td>
<td></td>
</tr>
</tbody>
</table>

The severity of asphyxia (judged by Apgar score) was correlated with biochemical parameters (blood urea and serum creatinine) and this association was found significant (p value < 0.05), by student t test (Table 1). As severity of asphyxia increased, more cases were found to had intrinsic renal failure (% of intrinsic renal failure in moderate asphyxia was 50% and in severe asphyxia was 63.15%), (Table 2). Thus severely asphyxiated babies were more likely to have intrinsic renal failure. Survival rate in moderate asphyxia was 100%, while in severe asphyxia was 57.24%.

As HIE stage progressed, more babies developed intrinsic type of renal failure, as in HIE stage-I and II, 50% were having intrinsic renal failure, while in HIE- III, this figure was 100%. Mortality was also found to increase when HIE stage progressed, as survival is 100% in stage I, 65% in stage II & 0% in stage III.

Of all ARF cases, 35% babies developed oliguric renal failure (urine output <0.5ml/kg/hr) and 65% had non oliguric renal failure (urine output >0.5/kg/hr).

DISCUSSION:

Perinatal asphyxia is a major cause of neonatal morbidity and mortality, and kidney is very sensitive to oxygen deprivation, occurring as a result of perinatal asphyxia. Within 24 hrs of an ischemic
episode, renal insufficiency and acute renal tubular necrosis may occur and if left untreated, irreversible cortical or medullary necrosis may develop[8].

The definition of perinatal asphyxia was chosen as 1 min apgar score 6 and or need for resuscitation 5 min because need for positive pressure ventilation 5min corresponds to cord pH 7, which is one of the reliable marker of birth asphyxia[9].

In this study, incidence of acute renal failure was 57.5% in asphyxiated babies. This is well matched with earlier studies of chevalier (1984), Perlman (1989), Jayshree (1991) and Nouri(2008).[9,0,5,10]

Hyperkalemia was found in 39.13% of ARF cases. This is also comparable to previous studies. Low GFR in prerenal failure and hypoxic tubular injury in intrinsic renal failure are thus responsible for this hyperkalemia in ARF cases.

30% of babies with ARF developed haematuria and most of them were of intrinsic renal failure type, while 47.82% of babies developed proteinuria (> 1+ protein / HPF) and majority of them were of intrinsic renal failure type. Both of them are related to acute tubular injury[10].

Incidence of oliguric renal failure was 35% of ARF cases. Oliguria, as reported by other authors, ranged from 25% to 69.3% (12,1).Renal parenchymal injury in non-oliguric as well as oliguric renal failure is essentially similar but heterogeneous response of individual nephron and variable damage to tubular epithelium results in anatomical damage in majority of nephrons leading to reduction in single nephron GFR and decreased tubular fluid flow. But if damage to tubular epithelium is less severe, there occurs decrease in fractional reabsorption, which excess the decrease in single nephron GFR leading to polyuria in non oliguric renal failure[2].

In this study, both HIE stage and severity of asphyxia (judged by Apgar score), were correlated with blood urea and serum creatinine and this correlation was found statistically significant (p value < 0.05). As severity of asphyxia increased and HIE stage progressed from stage-I to stage-III, higher values of blood urea and serum creatinine were observed, more number of intrinsic renal failure cases were found and more mortality was observed. Thus renal function assessment using blood urea and serum creatinine seems to be correlated with neurological involvement and degree of asphyxia.

Besides HIE-stage-III & severe asphyxia (as judged by Apgar score), intrinsic renal failure and oliguria are also a predictor of poor outcome. FeNa is an early indicator of tubular dysfunction which differentiates prerenal from intrinsic renal failure. Though from earlier studies, high serum creatinine and high blood urea had 100% sensitivity & negative predictive value to predict adverse outcome[8], these parameter are however poor predictors of adverse outcomes when compared to clinical marker like Apgar score 3 and HIE stage II/III.

Early detection of renal dysfunction in asphyxiated babies can help to prepare guidelines for management of these patients. An early intervention can prevent intrinsic renal failure and thus improve survival of these babies. Lastly the best approach to reduce mortality due to renal failure in asphyxiated neonate is to identify high risk cases for perinatal asphyxia in antepartum and intrapartum stage itself, and prevent this unfortunate event.

CONCLUSIONS:

Transient renal failure is commonly observed in perinatal asphyxia but if hypoxic insults are prolonged, it may lead to irreversible cortical necrosis. Renal function assessment using blood urea and plasma creatinine level is corrected with HIE stage and degree of asphyxia and as HIE stage progresses, more renal dysfunction is observed. Mortality was higher in babies with oliguric renal failure. FeNa is an early indicator of tubular dysfunction which differentiates pre-renal from intrinsic renal failure. Early detection of renal dysfunction in asphyxiated neonates can help to prepare guidelines for management of these patients. An early intervention can prevent intrinsic renal failure and thus improve the survival of these neonates.

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