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BIRTH ASPHYXIA RELATIONSHIP BETWEEN HYPOXIC ISCHEMIC ENCEPHALOPATHY GRADING AND DEVELOPMENT OF ACUTE RENAL FAILURE IN INDOOR TERM NEONATES AT CHANDKA MEDICAL COLLEGE CHILDREN HOSPITAL LARKANA

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ABSTRACT

INTRODUCTION: *Birth asphyxia usually develops acute renal failure but degree of involvement depends upon severity of asphyxia. In Pakistan birth asphyxia constitutes a large portion of perinatal mortality and leading cause of admission to neonatal intensive care units (NICU).*
OBJECTIVE: *This study was carried out to determine relationship between degree of HIE (Hypoxic Ischemic Encephalopathy) and development of ARF.*
STUDY DESIGIN: *Descriptive cross sectional study.*
SETTING: *Study was conducted in the NICU of children hospital, Chandka medical college Larkana.*
DURATION WITH DATES: *Six months, 20th June 2006 to 25" December 2006.*
MATERIAL AND METHODS: *Fifty term newborns who were admitted in the NICU with history of low Apgar score and fulfilling inclusion criteria were included. Renal functions were assessed using urinary output and biochemical parameters; Chi-squared test was used to assess statistical significance.*
RESULTS: *A total of 50 cases were admitted during the study period, among which37 (74%) were males and 13 (26%) were females. Blood urea and serum creatinine were significantly raise in asphyxiated ARF neonates as compared to without ARF (P< 0.05).*
CONCLUSION & RECOMMENDATION: *Severity of renal failure correlates well with the degree of HIE and signals the early screening of HIE patients for ARF and recommended to improve obstetric services at primary as well as community level to reduce the birth asphyxia and its complication (ARF).*

KEY WORDS: Birth Asphyxia, Hypoxic ischemic encephalopathy, renal failure.

INTRODUCTION

Acute renal failure (ARF) is a common problem in the neonatal intensive care unit[1]. The newborn kidney has a very low glomerular filtration rate (GFR) approximately 1 ml/min/kg of body weight that is maintained by a delicate balance between vasoconstrictor and vasodilator forces[2]. Although sufficient for growth and development under normal conditions, the low GFR of the newborn kidney limits postnatal renal function adaptation to endogenous and exogenous stress[3].

Acute renal failure in newborn is defined as a persistent increased serum creatinine level more than 1.5 mg/dl, two days after delivery[4]. Normal urine output is approximately 1-3 ml/kg/h in newborn and almost all of newborns void within the first 24 hours of life regardless of gestational age[1]. Acute renal failure may be due to pre-renal causes (dehydration, sepsis, asphyxia, etc) renal causes (directed damage to kidneys or congenital anomaly, etc) and post renal causes (posterior urethral valve, prune belly syndrome, neurogenic bladder, etc)[5, 6].

Various studies from Western countries showed that 8-24% of neonates admitted to neonatal intensive care units develop ARF.[5, 7, 8]. Birth asphyxia results in redistribution of blood flow towards the brain, heart and adrenals and away from kidneys, skin and the gastrointestinal tract.[9, 10] Hypoperfusion with concomitant hypercapnia and acidosis

contribute to organ damage.[9, 11] During hypoxic-ischemic events many organs are injured and most vulnerable ones are central nervous system (72%), followed by kidneys (42%), cardiovascular (29%), gastrointestinal tract (29%), and pulmonary (26%).[12, 13] The mortality and morbidity of newborn with acute renal failure is much worse in neonates with multi-organ failure.[12] Birth asphyxia is a major cause of acute renal failure in newborn, 43% to 47% of asphyxiated neonates develop ARF, [14,15] and 40 to 61 % of ARF in newborn was attributed to birth asphyxia.[16, 17]

In Pakistan birth asphyxia constitutes a large portion of perinatal mortality and is a also leading cause of admission to neonatal care services, accounting for 31-50% of all admissions and 25-31% cases fatality rates.[18,19] The neonates who have perinatal asphyxia usually develop acute renal failure but degree of involvement depends upon severity of asphyxia[4] .In Pakistan previously no data is available on relationship between the hypoxic ischemic encephalopathy grading and development of acute renal failure. So keeping in mind the deficiency of scientific data available this study may be considered initial step to determine the close relationship between asphyxia and acute renal failure in neonates.

OBJECTIVES

To determine the relationship between hypoxic ischemic encephalopathy grading and development of acute renal failure in indoor term neonates.

OPERATIONAL DEFINATION

1. **Hypoxic ischemic encephalopathy** (HIE). The degree of Hypoxic ischemic encephalopathy will be graded according to Sarnat's grading system.[20]

Grade I-HIE- Hyperalert (irritable), tone normal, weak Suck, strong moro reflex, mydriasis and tachycardia.

Grade II- HIE- Lethargic, seizures, differential tone legs more than arms, weak moro, absent or weak suck, miosis and bradycardia.

Grade III-HIE- Comatose, flaccid, no suck, no moro reflex, prolonged and frequent seizures, unequal pupils and variable heart rate.

2. **Acute renal failure** will be defined as serum creatinine more than 1.5mg/dl on third day of life.[4]

MATERIAL AND METHODS

SETTING:

This study was conducted in neonatal intensive care unit of tertiary level children hospital,Chandka medical college Larkana.

Table No. 1
AGE AND SEX DISTRIBUTION
(n=50)

Age (Range) Minutes	Sex	No of Patients	%
10-60	Male	37	74
15-60	Female	13	26
Total	Total	50	100

TABLE II

CLINICAL PRESENTATION OF ARF IN ASPHYXIATED NEW BORN WITH ARF

(0=23)

Presentation	No of Patients	Percentage
Oligo-anuria	23	100
Refused to feed	13	59
Respiratory distress	**11**	50
Lethargy	10	45
Dehydration	61	18

TABLE III

UREA AND CREATININE LEVELS (mean ± SD) ON DAY THREE

(n=50)

Investigation	Asphyxiated with ARF (n=23)	Asphyxiated without ARF (n=27)
Blood Urea (mg/dl)	68.19 ±23.54	31.67 ± 6.44
Serum Creatinine (mg/dl)	1.95 ± 0.45	0.83 ± 0.17

TABLE IV

UREA AND CREATININE LEVELS CORRELATED WITH HIE STAGING.

(n=50)

HIE Staging of group A & B	NO: of Patients	Blood Urea (mg/dl) Mean ± SD	S. Creatinine (mg/dl) Mean ± SD
I	11	26.81 ± 4.68	0.69±0.13
II	16	34.82 ± 5.43	0.92 ± 0.14
II+ARF	11	60.53±26.09	1.86±0.23
III+ARF	12	74.58 ± 20.08	2.08 ± 0.58

Both blood urea and serum creatinine were significantly different at Stage I compared to stage III: ($p<0.05$)

DURATION:
Six month duration from 20th June 2006 to 25th December.

SAMPLE SIZE:
50 cases of birth asphyxia.

SAMPLE TECHNIQUE:
Non probability convenience sampling.

SAMPLE SELECTION:
The neonate received in neonatal intensive care unit with history and / or fulfilled criteria for birth asphyxia were included in the study. Inclusion and exclusion criteria were.

Inclusion Criteria
1) All new borns with history of oliguria (anuria) for at least 48 hours with history birth asphysia.
2) Term, appropriate for gestational age (AGA).
3) Evidence of neurological abnormalities suggestive of HIE (altered tone, seizures, depressed level of consciousness).
4) Apgar score at 5 minute of 6 or less in non intubated babies and 7 or less in intubated babies.

Exclusion Criteria
1) Neonates who have received aminoglycosides antibiotics.
2) Congenital abnormalities of kidneys and / or urinary tract.
3) Cardiovascular pathology not related to perinatal asphyxia.
4) Patients who died within 48 hours of admission were excluded because of incomplete investigations.

STUDY DESIGN:
A descriptive cross sectional study.

DATA COLLECTION:
Those neonates were enrolled in this study who were received through obstetric and emergency ward with referral letter about the events happened during delivery and labor. An informed consent was taken from parents of neonate before enrollment and proforma was filled term especially designed for this study. Newborn was labeled by applying Ballard's score and appropriate for gestational age (AGA) by percentile chart (the birth weight between 10th and 90th percentile for sex and gestational age). Diagnosis of birth asphyxia was made an Apgar score of less than 7 at 5 minutes, with one or more of the following criteria[21].
1. Presence of meconium stained liquor.
2. Subsequent convulsions occurring with in 4th hours or birth.
3. Need for assisted ventilation by facemask and oxygen or endotracheal intubation.
On the basis of apgar score at 5 minutes the asphyxiated were further grouped into mild (score of 6 or 7) moderate (score 5 or 4) and severe asphyxia (score 3 or less). All neonates with clinical features of HIE were staged by Sarnat and Sarnat grading system.[22] The criteria of acute renal failure (ARF) in an asphyxiated neonate as having renal failur were urine output less than 0.5 ml/kg/hr, blood urea more than 40mg/dl, serum creatinine more than 1.5 mg/dl, presence of significant hematuria or proteinurea .These criteria were applied on day 3 of life and any three of four when fulfilled were considered as indication of renal failure. This can be explained on the fact that in the first 48 hours of life, these levels are reflections of maternal renal functions. In normal babies there is a subsequent fall in the blood urea and serum creatinine, whereas in case with renal damage, these levels rise above normal. The HIE grading and development of acute renal failure were correlated. All neonates were catheterized to maintain strict input output chart. The 24 hours fluid intake and daily body weight were recorded. Collected urine was analyzed for PH, blood, glucose, protein by multistix method and microscopically for pus cells and casts. The blood urea was estimated by glutamate dehydrogenase enzyme method, serum creatinine by kinetic Jaffe's method and electrolyte by flame photometer. Further investigations were done like blood glucose, serum calcium, cerebrospinal fluid analysis and renal radionuclide scanning, ECG were done as and when required.
All investigation were sent to a single laboratory i.e, Zulfiqar Ali Bhutto laboratory Chandka medical college and hospital Larkana specially assigned for the study: The renal function parameters were monitored within 24 hours of birth and then on day 3 of life. After three days those babies having abnormal renal functions had their laboratory parameters monitored every alternate day till recovery. To differentiate prerenal from intrinsic renal failure fluid challenge 20 ml/kg of normal saline were given as intravenous bolus (excluding patients having hypervolemia) to increase urine output. If no response furosemide 2 mg/kg intravenously were given. If there were still no increase in urine output intrinsic renal failure was diagnosed after excluding postrenul causes by doing ultrasound. In neonates ARF were managed conservatively as per hospital NICU protocol. Asphyxiated babies with impaired renal functions were grouped as A and remaining babies with normal renal function were grouped as B.

TABLE V
HIE STAGING LEADING TO ARF
(n=50)

HIE Staging	No of Patient	ARF in HIE Stage	%
I	11	-	-
II	27	11	40.7
III	12	12	100

TABLE VI
RESPONSE TO FLUID CHALLENGE
NO=23

No. of patient given fluid challenge	NO: of patient Given response to challenge	NO: of patient not given response to challenge
23	6	17
%	27% '	73.9 %

DATA ANALYSIS:
Data were analyzed with help of SPSS soft ware (ver 10.0). Frequency and percentage was computed for categorical variables like sex, clinical grading of hypoxic ischemic encephalopathy, apgar score and investigation. Mean and standard deviation was computed for quantitative variable age. The Chi- square test was used to assess statistical significance of relationship between the degree of hypoxic ischemic encephalopathy and acute renal failure.

RESULT
Fifty (50) neonates enrolled, 74% male and 26% were female (Table 1). Group A consists of asphyxiated neonates with ARF and group B without ARF. The age ranging from ten minutes to sixty minutes and weight ranging from 2.6 to 3.9 kg. The mean weight was 2.5 kg and mean gestation 39.5 weeks.

Twenty nine babies (58%) were delivered in the hospital while twenty one (42%) babies were delivered at private centre/clinic. Most common presentation in asphyxiated ARF were oligo-anuria, refused to feed, respiratory distress and lethargy as shown in Table II. Apgar score at five minutes of 50 asphyxiated babies was 0-3 in 19 (38%), 4-5 in 18 (36%) and 6-7 in 13 (26%). Asphyxiated babies (n=50) had hypoxic ischemic encephalopathy with 22% in stage I and 54% babies in stage II while 24% had stage III.

Oliguria was detected in (46%) of neonates, difference in urine output was observed in newborn with varying grading of asphyxia. Blood urea, serum creatinine values significant rises in asphyxiated ARF babies as compared to without ARF on day 3 ($P < 0.05$), (Table III).

A rising trend in concentration of blood urea and creatinine was observed as HIE staging of neonates progressed and difference was statistically significant between babies with HIE I and those with HIE III ($p<0.05$), (Table IV), as well as severity of ARF was correlated with HIE staging (Table V).Similar correlation was observed when blood urea and creatinine level were categorized according to Apgar score at 5 minute i.e, higher values of urea and creatinine were seen with lower Apgar scores.

Twenty three oligo-anuric neonates were given f1uid challenge and observing the response as indicated in (tableVI). Of the 23 neonates with ARF 4 (18.1 %) expired, 14 (63.6%) improved on day 7-12 and 4 still had abnormal function on discharge. Four babies who died three were having HIE grade III and one had HIE grade II.

DISCUSSION

Acute asphyxia is a common problem in newborn. The low glomerular filtration rate of newborn kidneys limits postnatal renal function adaptation to endogenous and exogenous stresses. As kidneys are very sensitive to oxygen deprivation, renal insufficiency may occur within 24 hours of a hypoxic ischemic episode, which if prolonged, may even lead to irreversible cortical necrosis. However renal injury in birth asphyxia is a potential consequence of adaptive mechanism. Amongst the recognized complications of birth asphyxia, ARF is the commonest and carries a poor prognosis may even result in permanent renal damage in up to 40% of survivors.[23] Twenty Three (46%) of our patients presented with oliguria, which is comparable to other studies (42-69%) [24, 25] and significant increase was seen with increase in severity of asphyxia. It was observed that blood urea and serum creatinine levels were significantly increased in our patients (46%) on day three of life, and results are comparable to western as well as regional studies from India (43_68%).[14,15,26,27] Obstruction of tubular lumen and back leak mechanism contributed to increase in urea and creatinine levels in asphyxiated neonates with renal damage[28]. In our study we found rising in concentration of blood urea and serum creatinine of asphyxiated neonates with acute renal failure. No case was found in HIE I, 40.7% in HIE IT whereas all case of HIE III developed acute renal failure. Similar increase was noted in other studies[14, 15] with HIE staging as well as with low Apgar score.[4, 14]

We had not found hematuria or gross proteinuria as observed by others in HIE II or III with acute renal failure, [14,25] because we already eliminate such cases that showed any congenital anomalies clinically and or on ultrasound.

Fluid challenge were given to 23 neonates, 6 patients responded to fluid challenge by increased urine output and hence were called prerenal failure (27%). Remaining 17 patients did not respond and were called intrinsic renal failure (73.9%), Gupta, et al found (21.2%) pre-renal (FENa 1-2.5 % 7/33 cases).Over all pre-renal failure is the most common cause of acute renal failure in new born (60- 70%),[29, 30] where as in our study intrinsic renal failure were more common because we put the patient on maintenance fluid from first day of admission. Over all mortality rate in our HIE cases with acute renal failure was (18%) which is closer to other result (15%).

CONCLUSION

We concluded that birth asphyxia is a significant cause or acute renal failure in neonates and the degree of hypoxic ischemic encephalopathy as well as low Apgar score correlates with the severity of acute renal failure.

RECOMMENDATION

All neonates with birth asphyxia admitted in neonatal intensive care units should be screened for acute renal failure because:

(a) Early recognition of renal injury is important for maintenance of fluid and electrolyte homeostasis.

(b) To avoid the nephrotoxic drugs.

(c) To monitor renal function.

1. Improve obstetric services at primary and community level to prevent neonatal death due to birth asphyxia and its common complications like HIE and ARF.

2. There is close relation between HIE and ARF, such patients should be monitored for developmental delay and renal functions.

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