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Original article

ACUTE RENAL FAILURE IN TERM NEWBORN FOLLOWING PERINATAL ASPHYXIA

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Abstract: **Introduction:** Perinatal asphyxia (PA) results in hypoxic damage to almost all organs, kidneys being most frequently (40%) affected.

Objectives: was to determine the incidence of acute renal failure (ARF) in term neonates with PA and to correlate it with severity of hypoxic ischemic encephalopathy (HIE).

Materials and methods: This prospective study of 54 term neonates with PA was performed in tertiary level neonatal intensive care unit at Pediatric Clinic Sarajevo from June 2014 to June 2016. The severe PA was defined as 5. minute Apgar score < 3 and moderate PA as 5. minute Apgar score 4-6. Criteria adopted for ARF were serum creatinine > 1.5 mg/dl (> 133 micromol/L) on 3rd day of life or urine output < 0.5 ml/kg/hr for > 6 hrs beyond 24 hrs of life.

Results. Out of 54 neonates with PA, 22 (40.74%) had ARF. Most of them (63.6%) had non-oliguric ARF with mean renal output of 2.2 ± 0.5 ml/kg/h. Eight neonates (36.4%) had oliguric ARF with mean renal output of 0.35 ± 0.6 ml/kg/h. Most of the neonates with oliguric ARF (63.4%) had severe PA while in those with non-oliguric ARF moderate PA was predominant. ARF was highest in the neonates with HIE III (85.71 %) (Figure 1). This showed that as HIE stage progressed, more renal dysfunction was seen in asphyxiated babies and this difference in incidence was found statistically significant ($p < 0.05$).

Conclusions. Neonates with severe PA had more frequent ARF and the predominant type of renal involvement was non oliguric. Neonates with HIE stage II and III had significantly higher incidence of ARF.

Keywords: perinatal asphyxia, acute renal failure, HIE staging, oliguria.

INTRODUCTION

Perinatal asphyxia (PA) is the major cause of neonatal mortality and long term neurological morbidity with an estimated incidence of 1-10/1000 live births (1). It results in hypoxic damage to almost all organs of the neonate; with kidneys being most frequently (40%) involved (1). The neonatal kidney is anatomically and functionally immature. Renal insufficiency manifests as early as 24 hours of life leading to irreversible cortical necrosis when prolonged. Detection of renal failure is vital in neonates with hypoxic ischemic encephalopathy (HIE) to sustain a stable biochemical milieu and initiate appropriate treatment (2). Neonatal acute renal failure (ARF) is a diagnostic and therapeutic challenge as clinical and laboratory parameters are not strictly defined yet (2). PA and birth injuries together contribute to almost 29% of neonatal deaths. World Health Organisation (WHO) defined birth asphyxia as "failure to initiate and sustain breathing at birth" with Apgar score of < 7 at 1. minute of life (1, 3). American College of Obstetrics and Gynecologists (ACOG) and American Academy of Pediatrics (AAP) have laid down essential criteria to diagnose PA which include, prolonged metabolic or mixed acidemia (pH < 7.0 on cord arterial blood sample), persistence of an Apgar score of < 3 for 5 min or longer, clinical neurologic manifestation as seizures, hypotonia, coma or HIE in the immediate neonatal period coupled with multiorgan dysfunction (1, 3).

METHODS

This prospective study was conducted in a tertiary level neonatal intensive care unit at Pediatric Clinic Sarajevo from June 2014. to June 2016. Consecutive 54 term (37-42 weeks) neonates with perinatal asphyxia

(PA) (5. minutes Apgar score (AS) < 7) were enrolled in the study. Neonates with factors that can alter renal function such as septicemia, respiratory distress syndrome, necrotizing enterocolitis or major congenital anomalies were excluded from the study. Neurological status was assessed using Sarnat and Sarnat staging (4). All the neonates were evaluated clinically and their renal functions were assessed on 3rd day. Renal profile was done by estimation of serum creatinine, urea, sodium and potassium. Assessment of fractional excretion of sodium was done to differ intrinsic from extrinsic renal failure. Criteria adopted for ARF 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 hours of life. Statistical analysis was conducted using statistical products and services solutions (SPSS) software version 17.0.

RESULTS

The mean birth weight in studied neonates was 3352 g (SD = 427.3), length 51,3 cm (SD = 2.1), clinical gestation 38,9 weeks (SD = 0.87) and head circumference 34,4 cm (SD = 1.6). Most of the neonates were delivered by the vaginal route (59%), 39% via caesarian section and 2% via vacuum extraction. Only 11,1 % (6/54) of the neonates had a very low 5. minutes Apgar score of 0–3, while 88,9% (48/54) had a moderate 5. minute Apgar score of 4–6. Nine neonates (16.6%) were intubated and mechanically ventilated, 5 of them during primary resuscitation and others later within first three days of life (Table 1).

Staging of hypoxic ischemic encephalopathy (HIE) by Sarnat and Sarnat system was done on admission. Nineteen neonates (19/54; 35.19%) had HIE I, twenty-eight (28/54; 51.85%) had HIE II and 7 (7/54; 12.96%) HIE III. Out of 54 neonates with PA, 22 (22/54; 40.74%) had ARF. Most of neonates with ARF (14/22; 63.64%) had non-oliguric ARF with mean renal output of 2.2 ± 0.5 ml/kg/h. In those neonates with oliguric ARF (8/22; 36.36%) the mean renal output was 0.35 ± 0.6 ml/kg/h. Out of eight neonates with oliguric ARF, five (5/8; 62.5%) had severe PA while in those with non-oliguric ARF moderate PA was predominant and present in 8 out of fourteen neonates (8/14; 57.14%). This difference in a type of ARF (non-oliguric/oliguric) in a correlation with a degree of PA was found statistically significant ($p < 0.05$), with oliguric type more frequent in neonates with more severe PA. Sixteen out of twenty-eight neonates (16/28; 57.14%) with HIE II and five out of seven neonates (5/7; 71.43%) with stage III had ARF. Only one out of nineteen neonates (1/19; 5.26%) with HIE I had ARF.

Table 1. *Basic characteristics of neonates included in our study*

Subjects	Value
Gender (male)	35 (54.7%)
Birth weight < 2,5 kg (LBW)	15 (27.8%)
Mean birth weight (kg)	3,35 ± 0.42
Positive CPR	13 (24.1%)
Ventilator requirement	9 (16.6%)
Acute renal failure present	22 (40.74%)

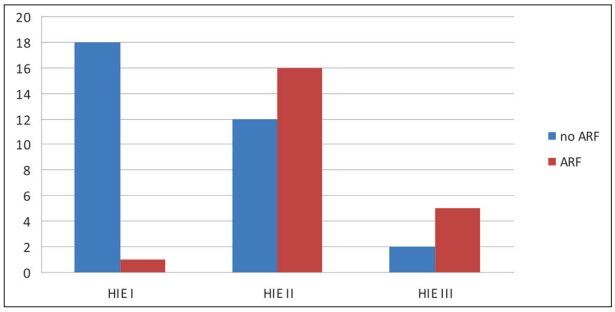

Figure 1. *Incidence of ARF in correlation to a degree of HIE*

ARF was highest in the neonates with HIE III (85.71%). (Figure 1). This showed that as HIE stage progressed, more renal dysfunction was seen in asphyxiated babies and this difference in incidence was found statistically significant ($p < 0.05$). The mean values of serum values of urea, creatinine, Na and K are shown in Table 2.

Table 2. *Urea, creatinine, Na and K levels correlated with HIE staging*

HIE staging	N	Blood urea (mg/dl) Mean SD	P value (between stage I, II, III by Anova test)	Serum creatinine (mg/dl) Mean SD	P value (between stage I, II, III by Anova test)	Serum Na (mmol/l) Mean SD	P value (between stage I, II, III by Anova test)	Serum K (mmol/l) Mean SD	P value (between stage I, II, III by Anova test)
I	19	27.4 ± 19.2	P < 0.05	10.10 ± 0.25	P < 0.05	131.65 ± 2.15	P < 0.05	4.4 ± 0.23	P < 0.05
II	28	46 ± 19.1		1.55 ± 0.24		132.45 ± 2.35		5.8 ± 0.36	
III	7	67.3 ± 22.1		2.17 ± 0.36		136.65 ± 1.72		6.2 ± 0.43	
Total	54	41.7 ± 22.8		1.52 ± 0.46		132.65 ± 2.25		4.5 ± 0.4	

FeNa (fractional excretion of sodium) >2.5% was considered as an indicator of intrinsic renal failure.

$$\text{Fractional Excretion of Na} = \frac{\text{Urinary Na x Plasma Creatinine}}{\text{Plasma Na x Urinary Creatinine}}$$

Incidence of pre-renal renal failure was 13/22 (59.09%) while of intrinsic renal failure was 9/22 (40.91%).

DISCUSSION

PA is an insult during the intrauterine or immediate extrauterine period to the fetus or the newborn due to hypoxic and/or ischemic damage to various organs of greater magnitude which leads to transitory or permanent functional and biochemical changes. Hypoxia and ischemia can result in impairment of every tissue and organ of the body, kidneys are extremely sensitive to oxygen deprivation. Neonates are more susceptible to acute kidney injury because they have low glomerular filtration rate, high renal vascular resistance, high plasma renin activity and decreased reabsorption of sodium in the proximal tubules. Renal insufficiency can manifest within 24 hours of a hypoxic ischemic episode, and if prolonged, may even lead to irreversible cortical necrosis (4). Difficulties in serum creatinine interpretation make it more difficult to achieve a consensus regarding ARF definition (3, 5). Recent studies recognize that even small increments in serum creatinine levels increase morbidity and mortality (6, 7, 8). Studies by Jayshree (9), Nouri (10) and Gupta (2) chose the cut-off level of 90 ìmol / l for serum creatinine at 48 hours of life. We took the cut-off of 133 ìmol / l for creatinine at 72 hours of life.

In our study, incidence of ARF was 40.74% in asphyxiated babies. This is well matched with earlier studies (2, 9, 10).

The presence of PA and its severity significantly correlated with increasing incidence of ARF (4.5). Our study noted a 13.5 fold increase risk of developing ARF in HIE III compared to HIE I. ARF was the highest in the neonates with HIE III (71.43%) and the lowest in the neonates with HIE I (5.26%). The higher degree of HIE was also statistically significantly associated with oliguric type of ARF in comparison to non-oliguric type of ARF. This is also concordant to earlier studies (2, 9, 10).

CONCLUSION

Neonates with severe PA had more frequent ARF. The predominant type of renal involvement was non oliguric. Neonates with HIE stage II and III had significantly higher incidence of ARF. The most of the neonates with oliguric ARF had severe PA.

Abbreviations

ARF — acute renal failure
HIE — hypoxic-ischaemic encelopathy
PA — perinatal asphyxia
SD — standard deviation

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

Sažetak

AKUTNA BUBREŽNA INSUFICIJENCIJA KOD NOVOROĐENČADI KAO POSLEDICA PERINATALNE ASFIKSIJE

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Uvod: Perinatalna asfiksija (PA) rezultuje hipoksičkim ostećenjima skoro svih organa, među kojima je bubreg najčešće zahvaćen (40%).

Cilj: Cilj rada je da se utvrdi incidenca akutne bubrežne insuficijencije (ARF) kod donešenih neonatusa sa PA i da se napravi korelacija sperinatalne asfiksije i težine hipoksično ishemijske encefalopatije (HIE9).

Materijal i metode: Ova prospektivna studija obuhvatila je 44 donešena neonatusa sa PA i izvedena je u tercijarnoj ustanovi neonatalne intenzivne nege na Pedijatrijskoj klinici u Sarajevu od juna 2014. do juna 2016. godine. Težina PA je definisiana kao 5.ominutni Apgar skor; 3 i umereni PA kao 5.ominutni Apgar skor 4-6. Kriterijumi koji su uzeti u obzi za ARF su bili se-

rumski kreatinin: 1.5 mg/dl (:133 mikromol/lL) trećeg dana života ili uzlučivanje urina; 0.5 ml/kg/sat na preko 6 sati u okviru prvih 24 sata života.

Rezultati: Od 54 neonatusa sa PA, 22 (40,74%) su imali ARF. Većina njih (63,6%) su imali neoliguričan oblik ARF sa srednjim bubrežnim izlučivajem u vrednosti od 2.2 ± 0.5 ml/kg/h. 8 neonatusa (36,4%) je imalo oliguričan oblik ARF sa srednjim bubrežnim izlučivanjem 0.35 ± 0.6 ml/kg/h. Većina neonatusa oliguričnog oblikom ARF (63,4%) je imala ozbiljnu PA, dok kod onih sa neoliguričnim oblikom ARF, umerena PA je bila predominantna. ARF je bio najviši kod neonatusa sa HIE III (85.71%) (Fig. 1). Možemo zaključiti da HIE progredira, više je zahvaćena renalna disfunkcija, koja je bila zabeležena kod beba sa asfiksijom i ova razlika u incidenci je bila statistički značajna.

Zaključak: Neonatusi sa ozbiljnim PA su imali češće izraženu ARF i to neoligurični tip. Neonatusi sa HIE stadijuma II i III su imali visoko značajnu incidencu ARF.

Ključne reči: perinatalna asfiksija, akutna bubrežna insuficijencija, HIE gradiranje, oliguria.

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