The Prevalence of Acute Kidney Injury in Neonates with Asphyxia

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Introduction: As defined by the World Health Organization, perinatal asphyxia is respiratory insufficiency due to impaired gas exchange, hypoxia, hypercarbia, anaerobic glycolysis, and metabolic acidosis [1]. Asphyxia is a common cause of mortality and morbidity among neonates. Its incidence is about 1-10% per 1000 live births [2]. Following severe asphyxia and ischemia, reperfusion occurs in different organs including the brain, heart, and adrenals which damages organs like the kidneys, gastrointestinal tract, and skin [3]. The kidneys are most commonly involved in ischemia [3]. While there are globally adopted definitions for acute kidney injury (AKI) in adults and children, defining AKI is complex in newborns. Most studies have defined it as a serum creatinine level higher than 1.5 mg/dL in neonates with asphyxia.

Materials and Methods: This retrospective study was performed in Ali-Asghar and Shahid-Akbar-Abadi Hospitals, Tehran, Iran in a period of one year. The medical documents of all newborns diagnosed with asphyxia were studied. The asphyxia grade was determined according to the asphyxia Sarnat criteria. The kidney function was evaluated based on the serum creatinine level.

Results: Thirty-eight cases met the inclusion criteria. There were 13 Sarnat grade-1 cases (34.2%), 19 grade 2 cases (50%), and 6 grade 3 patients (17.6%). Three (7.8%) patients (2 patients in grade 3 and one patient in grade 2 of the Sarnat grading scale) developed AKI. AKI was detected in 33% of the patients in grade 3 and 5.2% of the patients in grade 2 of the Sarnat grading scale. Nine patients (23%) died, of whom 83% were in grade 3 and 16.9% in grade 2 of asphyxia.

Conclusions: AKI developed in 7.8% of the cases, of whom 33% were in grade 3 and 5.2% were in grade 2 of the Sarnat grading scale. The low rate of AKI development in our study might be due to the small sample size and patient mortality in the first 3 days of life.

Keywords: Acute kidney injury; Neonates; Asphyxia.
determine the prevalence of AKI defined as a serum creatinine level higher than 1.5 mg/dL, in neonates with asphyxia.

**Materials and Methods**
This retrospective study was performed in Ali-Asghar and Shahid-Akbar-Abadi Hospitals, Tehran, Iran in a period of one year from September 2012 to September 2013. Medical documents of all newborns diagnosed with asphyxia were studied. Demographic characteristics including sex, weight, gestational age at birth, and type of delivery were obtained. The asphyxia grade was determined according to the Sarnat criteria [13]. The kidney function was evaluated based on the serum creatinine level. The patient was included in the study if any of the following criteria was present: an Apgar score ≤ 7 at 10 minutes, using positive pressure ventilation (PPV) for >1 minute, or delay of the first cry > 5 minutes, and prolonged (>1 hour) antenatal acidosis.

**Statistical analysis:** Data was analyzed using SPSS software version 20 (Chicago, IL, USA). To describe continuous variables, mean and standard deviation (SD) were calculated. Frequency (percentage) was used in order to describe categorical variables. A two-tailed p-value less than 0.05 was considered significant in order to reject the corresponding null hypothesis.

**Results**
Fifty medical documents of newborns diagnosed with asphyxia were reviewed of which 38 met the inclusion criteria. Boys and girls comprised 56 and 44% of the study population with a mean weight of 2770 gr and a gestational age of 36 weeks. About 91% of the neonates were delivered by Cesarean section and 9% by natural vaginal delivery (NVD). Out of 38 cases, there were 9 Sarnat grade-1 cases (23.7%), 19 grade 2 cases (50%), and 6 grade 3 patients (17.6%). Three (7.8%) patients (2 patients in grade 3 and one patient in grade 2 of the Sarnat grading scale) developed AKI. AKI was seen in 33% of the patients in grade 3 and 5.2% of the patients in grade 2 of the Sarnat grading scale. Nine patients (23%) died of whom 83% were in grade 3 and 16.9% in grade 2 of asphyxia.

**Discussion**
Perinatal asphyxia can lead to the dysfunction of multiple organs. Reperfusion mostly damages the kidneys. There is not a uniform definition for AKI in children. The incidence of AKI in perinatal asphyxia has been reported 11% to 100% in various studies based on different definitions. Some definitions include a decreased renal function as a creatinine level≥ 1.5 mg/dL during 48 hours after birth, a daily creatinine level increase more than 0.3 in the first 48 hours after birth or a 50% increase from its baseline level, and a decreased urine output or oliguria (<0.5 cc/kg/hour) for 6 hours.

Generally, creatinine is not an appropriate marker to determine AKI, especially in neonates. The creatinine level in the first 3·4 days of life is a reflection of maternal creatinine. Some neonates who have severe asphyxia at the time of delivery will expire. The GFR level in the first days of life is low and major changes in GFR does not necessarily lead to changes in the creatinine level. More than 50% of the cases of AKI do not present with oliguria. However, the prognosis is poor and the mortality rate is high if oliguria develops. In order to diagnose and treat these cases earlier, evaluation of more sensitive markers like KIM-1 and NGAL are required. The indication is controversial and more studies should be conducted in this field.

In our study, 3 (7.8%) cases (2 patients in grade 3 and 1 patient in grade 2 of the Sarnat grading scale) developed AKI. In other words, 33% of patients in grade 3 and 5.2% of patients in grade 2 of the Sarnat grading system developed AKI. None of the cases in grade 1 developed AKI. Asphyxia was more seen in grade 3.

Dan et al [6] reported that the overall prevalence of asphyxia based on the clinical diagnosis was 11.7%. They defined AKI as a creatinine level≥ 1.5 mg/dL on the 2nd and 3rd days of life. In this study, the prevalence of AKI was 42.9% in grade 3 and 4.6% in grade 1 of asphyxia. The results are rather similar to our findings.

Nouri et al [7] defined AKI as a creatinine level> 1.2 mg/dL the in first 48 hours after birth. AKI was detected in 17.9% of the patients, 2/3 of whom had asphyxia grade 2 while most of the cases that developed AKI were in grade 3 of the Sarnat grading scale in our study.

M-gray et al [8] defined asphyxia as an APGAR score 6 at 5 minutes and AKI as a creatinine level more than 1.5 mg/dL with normal function of the kidneys of the mother. In this study, the prevalence of ARF was 60% in severe asphyxia and zero in moderate asphyxia. Moreover, 60% of all AKI cases were non oliguric, 25% were oliguric, and 15% were anuric.
In a study by Jayash et al [9], asphyxia was defined as an Apgar score less than 7 at 1 minute and a need for resuscitation for more than 1 minute. ARF was defined as oliguria, a creatinine level more than 1 mg/dL, and BUN higher than 40 mg/dL with no improvement by hydration and the use of diuretics. In this study, 43% of the cases had asphyxia and 69% had oliguric renal failure.

In a study by Ginercol et al, asphyxia was defined as an arterial blood PH level< 7. In this study, 50% of the cases developed renal failure [10]. Perlm J et al [11] reported oliguria in 40%, beta 2 micro globulin changes in 57%, and azotemia in 11% of asphyxiated newborns.

In a study by Gupta et al [12], renal failure was detected in 47% of the asphyxiated newborns, 78% of whom were non oliguric and 22% were oliguric. The inclusion criteria in this study were 5th minute Apgar score< 7 and AKI development on the 3rd day of life based on the presence of 3 of the following criteria: 1- urine output < 5 cc/Kg/hour, 2- BUN> 40 mg/dL, 3- creatinine level> 1 mg/dL 4-marked hematuria or proteinuria.

Ambar et al [13] evaluated the development of AKI in newborns with asphyxia. They defined AKI as oliguria (urine output< 1 cc/Kg/hour) and creatinine> 1.5 mg/dL. AKI was detected in 61.66% of the cases, of whom 81% were nonoliguric and 18% were oliguric.

Based on the definition of Asphyxia as an Apgar score ≤ 6 at 5 minutes and a need for resuscitation more than 5 minutes and AKI defined by Acute Kidney Injury Network criteria, Kaur et al [14] reported AKI in 56% of the cases with severe asphyxia, and tubular dysfunction persisted until 96 hours of age among AKI newborns. The low rate of AKI development in our study might be due to our small sample size and patients mortality in the first 3 days of life. More case-control studies with larger sample sizes are required in this regard.

Conclusions
In conclusion, AKI was seen in 7.8% of the cases, of whom 33% were in grade 3 and 5.2% were in grade 2 of the Sarnat grading system

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The abstract of this paper was orally presented in the 4th International Congress of Iranian Society of Pediatric Nephrology held on 11-13 February 2015, Tehran, Iran [15].

Conflict of Interest
Authors have no conflict of interest to declare.

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References