

Comparison of the Efficacy of Serum Creatinine and Microalbuminuria in Early Diagnosis of Renal Injury in Asphyxiated Infants in Calabar, Southern Nigeria

Sunny Oteikwu Ochigbo*, Jacob Jackson Udo, Anthony Chidibere Nlemadi, Kudirat Omololuolaniyo

Department of Pediatrics, University of Calabar, Teaching Hospital, Calabar, Nigeria

ABSTRACT

Background: Microalbuminuria and serum creatinine are the specific markers of acute renal injury. Perinatal asphyxia is responsible for 50% of all neonatal deaths and nonoliguric acute renal injury is one of its complications. This study was undertaken to determine the efficacy of serum creatinine and microalbuminuria for early diagnosis of renal injury in severely asphyxiated neonates in Calabar, Nigeria.

Methods: This prospective cross-sectional study was performed among severely asphyxiated newborns admitted into the neonatal wards of the University of Calabar Teaching Hospital (UCTH). Standard methods for the determination of blood urea and electrolyte were executed. Micral-test strips have been applied using urine dipstick and the result of the test was negative only for albumin. The developed colors have been compared five minutes after the first test.

Results: Fifty full-term newborns were enrolled and their serum electrolytes, creatinine and the creatinine clearance were essentially normal. Six neonates demonstrated positive results in the microalbuminuria assessment, while the rest were negative in this regard. The test has 0% sensitivity and 100% specificity, while the positive and negative predictive values were 0% and 88%, respectively.

Conclusion: Microalbuminuria is not a useful marker for early diagnosis of acute renal failure in the newborns with severe prenatal asphyxia, but further studies are recommended.

Keywords: Acute kidney injury, Apgar, Birth asphyxia, Micral test strip, Newborn

Introduction

Microalbuminuria is an early marker of certain diseases affecting the urinary system. Creatinine clearance test determined the overall large reserve of glomerular filtration rate (GFR), therefore it is not sensitive enough for detecting acute or chronic kidney injuries unless the damage is significantly substantial to compromise the filtration ability. There is continuous positive relationship between urinary albumin excretion and the adverse clinical outcomes (1). Estimated prevalence of acute kidney injury (AKI) is dependent to the definition and the setting, with some degree of renal insufficiency noted in 7.1% of hospital admissions (2) and in 30% of patients admitted to an intensive care unit (ICU) (3). Although most of the patients with renal disorders

are asymptomatic, it is noteworthy that routine screening of all patients who has the risk factors of developing renal diseases is necessary. For incurable acute renal diseases, specifying the severity of renal dysfunction enhances the quality of selecting appropriate chemotherapeutic adjustment and provided valuable prognostic information. The identification of AKI leads to prompt referring to the nephrologists, thus the prognosis of the disease is reported much better (4). Above all, it is expected to improve an appropriate intervention by instant identification of AKI.

The conventional methods of plasma creatinine measurement may be seducing and it plays a crucial role, especially in the neonate's

* Corresponding author: Sunny Oteikwu Ochigbo, Department of Pediatrics, University of Calabar, Teaching Hospital, Calabar, Nigeria. Email: ochigbosunny@gmail.com

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longevity. Although the reliability of this method is not rather confirmed, but the best way to convince the primary diagnosis of AKI is to measure the levels of the proteins (albumin) found in the urine using the Micral-test strips. The normal range of urine albumin is considered less than 20 mg/dl. When the albumin level raised to 20 to 300 mg/dl, the physician should note that albumin is spilling into the urine beyond an acceptable range due to a renal injury.

The comparison of the efficacy of microalbuminuria and routine use of serum creatinine as a marker of renal failure in severely-asphyxiated newborns has not been executed in Calabar, yet. Therefore, this study aimed to evaluate a diagnostic approach using urine albumin as an affordable and less invasive method.

Methods

This prospective cross-sectional study was conducted during April to September 2014. All the severely asphyxiated full-term neonates admitted into the newborn units of the University of Calabar Teaching Hospital (UCTH) participated in this study. These units, previously described by Udo et al (5), admit both inborn and outborn infants.

In this study, Apgar score of three or less at five minutes of life was considered as severe birth asphyxia. Some data such as the age, gender, birth weight, signs and symptoms at the time of delivery, mother's age, duration of the labor, place and the method of delivery, and the other relevant neonatal and maternal history were obtained delicately for all the participated infants. Meticulous physical examination and anthropometric measurements were compared to the standard values. Exclusion criteria included preterm neonates, febrile infants (Temperature > 37.50° Celsius), infants with a past history of congenital or otherwise renal disease, and history of antibiotic use.

The standard method for determination of blood urea, creatinine, and other electrolytes was performed. The serum creatinine clearance was calculated using a simple and reliable recipe (modified Schwartz formula). The urine samples were collected with the use of urine bags; When was hard to do especially for the female infants, a suprapubic aspiration was safely performed and the samples were transferred into pre-labeled universal containers for the assessments. The urinalysis was executed for each subject using the multi-strip known as Combi-10. Only the urine samples with negative test of albuminuria were selected for further investigations for microal-

buminuria (MA) using the Micral-test strips (Roche diagnostics Quebec, Canada) (6).

Since a minute, the observed color was compared to the manufacturer "Micral" pad inscription. The comparison of the reaction with a color scale was also done five minutes after the first test as the color is usually stable for that period. The results were considered positive when at least two urine samples produce a reaction color corresponding to 20 mg/dl (threshold for microalbuminuria) or more of albumin. All infants were under care with the routine program for perinatal asphyxia until were discharged. The study was terminated if a patient requested for transfer to other centers, discharge against medical advice, voluntary withdrawal of the consent after initial approval, and death of the patient.

The required data were obtained and standard statistical analysis was performed using SPSS version 20. The quantitative variables were summarized using means, median, and ranges as appropriate. The proportions were compared using Chi-square test. A probability (P-value) less than 0.05 was considered statistically significant.

Ethical committee of the hospital approved this study.

Results

A total of 50 neonates were enrolled into the study with male-female ratio of 1.8:1. The mean age of the newborns was 30.3±36.2 hours. The mean ages for males and females were 26.91±38.2 and 36.4 ±32.6 hours, respectively with no statistical significance (P=0.382).

Generally, male infants had higher total mean anthropometric parameters. The weight (with the average of 3.05±0.57) and OFC (34.6±1.77) were not statistically significant. The mean length of the male subjects were 50.3±3.51 and for the females newborns was 47.5±5.0 centimeters. This parameter was found to be statistically significant between genders (P=0.045) (Table 1).

The serum electrolytes, creatinine and creatinine clearance were essentially normal for both groups of the patients with and without microalbuminuria. Though within range, the patients who reported negative microalbuminuria had a slightly higher value; however, it demonstrated no statistical disparity between both groups. (Table 2).

Six of the neonates (12 % of total) reported positive and 44 of them (88%) reported negative for microalbuminuria. Hence the sensitivity was 0%; specificity was 100%, while the positive and

Table 1. Anthropometric Characteristics of the Subjects

Age(hrs)	OFC(cm)					
	Wt(kg)		Stature(cm)		OFC(cm)	
	M	F	M	F	M	F
≤ 6	3.9±1.5	2.79±0.5	52.4±3.8	44.3±11.6	35±1.4	36.2±0.29
>6- ≤12	3.55±0.6	0	46.5±2.1	0	35.5±0.7	0
>12 - ≤24	2.99±0.46	2.67±0.51	50.4±2.9	49±3.0	34.7±1.8	34.3±1.5
>24 - ≤48	2.90±0.45	3.02±0.6	50.4±3.6	46.5±0.7	34.7±0.88	33±0
≥ 48	2.8±1.43	2.55±0.35	47±1.7	46±5.7	34.7±1.5	31.5±4.9

Total Mean: 3.15±0.54, 2.86±0.58, 50.3±3.51, 47.5±5.02, 34.89±1.52, 34.14±2.1

Mean of all Subjects: 3.05 (±0.57), * 49.3±4.29, 34.6±1.77

*Pvalue=0.045

Table 2. Relationship between microalbuminuria and serum electrolytes, urea, creatinine, and creatinine clearance in the subjects

Parameter	MA Positive (n=50)	MA Negative (n=50)	T	P value
	Mean ±SD	Mean ±SD		
Sodium(mmol/l)	133.2±5.7	134.5±5.2	0.58	0.56
Potassium(mmol/l)	4.0±0.47	4.3±0.8	1.24	0.24
Bicarbonate(mmol/l)	18.3±3.4	18.1±3.5	-1.71	0.87
Chloride(mmol/l)	100.3±2.4	102.6 ±6.1	1.68	0.12
Urea(mg/dl)	3.62±2.15	5.18±3.04	1.21	0.23
S. Creatinine (umol/l)	100±7.13	109.3±25.1	1.83	0.08
Creatinine Clearance	0.21±0.03	0.22±0.03	0.95	0.35

Table 3. Serum creatinine and microalbuminuria in the detection of renal impairment

Serum Creatinine	Microalbuminuria		Total
	Yes (%)	No (%)	
Elevated	0	0	0
Normal	6(12%)	44 (88%)	50
Total	6 (12%)	44 (88%)	50 (100%)

negative predictive values were 0% and 88%, respectively. (Table 3).

Discussion

Birth asphyxia is a cause of morbidity and mortality worldwide and is responsible for 23% of the four millions neonates' deaths globally (7). Studies have demonstrated that it was the reason for 50% of all newborn's deaths (7). Acute renal failure is a complication of severe perinatal asphyxia, which commonly presents with nonoliguric kidney injury (8, 9).

The majority (30% and 26% in groups) of the newborns in this study were full-term neonates aged below 6 and 48 hours, respectively. The biochemical laboratory results of the newborns in the first few days of life are not trustworthy, though the study conducted by Cuzzolin et al. (10) exhibited no dissimilarity in the levels of electrolytes and serum creatinine among the neonates with low birth weight (LBW), very low birth weight (VLBW), and normal birth weight.

Our study revealed that anthropometric parameters such as weight, OFC, and length did not influence microalbuminuria. None of the growth parameters showed any statistically significant distinctness between the male and

female subjects except the mean length. This is confirmed by Byung et al. (11) who observed the correlation between microalbumin and creatinine ratio with the age, height, weight, and body surface area among normal Korean children. This is against the findings reported Gould et al. (12), which confirmed that the lengths of the babies were correlated with microalbuminuria.

The serum sodium and bicarbonate concentrations were at the lower limit of normal. These are expected findings in severe birth asphyxia patients. It is likely related to the disequilibrium from fractional excretion of sodium probably associated with the effect of rennin angiotensin system (RAS), circulatory catecholamine, atrial natriuretic peptide, and prostaglandins. This phenomenon may also be secondary to the dilution effect of inappropriate anti-diuretic hormone (ADH) secretion. It is already known that tissue hypoxia also may lead to metabolic acidosis. These values were not below the critical levels thus urgent adjustment was not needed. The slightly high potassium levels could be attributed to in vitro hemolysis. This observation was confirmed by Basu et al. (13).

The serum creatinine and creatinine clearance were not insane for the both groups; this was expected because creatinine remains normal except in severe renal injury. Serum creatinine concentrations may not alter until 25 to 50 percent of the kidney function is lost, therefore significant rise in serum creatinine occurs several days after renal failure. Serum creatinine in the first few days of the neonate's life reflects the mother's and not

the infant's renal function. All the patients though had reported severe perinatal asphyxia but none of them showed clinical or paraclinical signs of renal failure. This was against the findings confirmed by Aggarwal et al. (14) who showed that the incidence of AKI in infants with Apgar score of five was more frequent compared to the control group. They noted that clinical markers of asphyxia predicted the prognosis more accurately than the renal function tests.

In view of the non sensitivity and positive predictive value in this study, it was signified that microalbuminuria when compared with serum creatinine as an early predictor of renal derangement is a poor marker, though none of the current study patients presented with established renal disease. This is corroborated by Abbulimhen-Iyoha et al. in Benin among patients with sickle cell anemia (15-17).

According to the results, early detection of acute renal injury by measuring microalbuminuria was not valuable. Besides, the performance of microalbuminuria as a predictor of early renal impairment versus serum creatinine in newborns with severe birth asphyxia was not reliable though further studies with larger sample size are advised.

Conclusion

Microalbuminuria is not beneficial in early detection of acute renal failure in neonates with severe birth asphyxia. Further studies with larger sample size are recommended.

Conflicts of interests

None declared.

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