ORIGINAL ARTICLE

The Significance of Proteinuria and its Associations in Patients Having Acute Renal Failure

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ABSTRACT

Aim: To determine the significance of proteinuria and its associations in pts having acute renal failure.

Method: The type of study is a prospective observational study conducted for a period of three months from January 2014 to March 2014, at a tertiary care centre in Karachi Pakistan. A total of n= 40 patients who presented to our department with acute renal failure or acute chronic renal failure were included in the study. Proteinuria was analyzed with gel electrophoresis in the patients and its predictive value for requirement of renal replacement therapy was noted.

Results: A total of n= 40 patients were included in the study, having a mean age of 58.6 +/- 27 years and a male to female ratio of 24 : 16. Mortality of patients was 15(37.5%), the non survivor population was in critical condition at the time of referral having an APACHE II score of 29 +/- 5, they also had lower values for baseline creatinine and a higher tubular to glomerular ratio which points towards acute tubular necrosis. Among those who had survived 25(62.5%) a total of 7(17.5%) patients were those who did not recover and 19(47.5%) were those who recovered and returned towards normal renal functioning. Those who did not recovered had increased levels of tubular proteinuria and went into end stage renal disease.

Conclusion: According to the results from our study the gel electrophoresis analysis for proteinuria is a cost effective and reliable method, when it comes to determining the tubular or glomerular proteinuria in patients with acute renal failure requiring renal replacement therapy in the intensive care unit. Presence of tubular proteinuria correlates with duration of dialysis support and the mortality rate, and the presence of glomerular proteinuria indicates glomerular damage and its severity.

Keywords: Acute renal injury, Dialysis, proteinuria, tubular proteinuria, glomerular proteinuria.

INTRODUCTION

The incidence of acute renal injury or chronic renal injury in 20 to 50% in the intensive care unit[1], the cause of this injury is commonly acute tubular necrosis, it is associated with adverse outcomes and increased mortality rate[2]. Serum creatinine levels are poor indicators and have poor specificity and sensitivity[3], according to a series of clinical trials urine protein levels are a better marker for acute renal injury and to determine the course of end stage renal disease[4]. But this association is less certain. Some specific indicators have received more attention in the scientific community for their association with unfavorable outcomes as reflected by the requirement of renal replacement therapy, such indicators include, Neutrophil Gelatinase Associated Lipocalin, Kidney injury molecule and cystatic-c[5,6]. But quantifying these indicators is very limited and they are not available at all centers, in contrast a

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technique of SDS PAGE, for the quantitative analysis of proteinuria is promising as it is inexpensive and convenient[7], it separate molecules according to their size, and staining properties determine the amount, and presence of low molecular weight bands reveal tubular loss of protein, where as high molecular weight bands reveal more larger protein molecules like albumin and globulin indicating glomerular damage.

The aim of our study is to determine the significance to proteinuria both of tubular and glomerular variety as determined by the gel electrophoresis in patients with acute renal injury/ chronic renal injury.

MATERIALS AND METHODS

The type of study is a prospective observational study conducted for a period of three months from January 2014 to March 2014, at a tertiary care centre in Karachi Pakistan. A total of 40 patients who presented to our department with acute renal failure or chronic renal failure were included in the study. All the patients were referred from the intensive care unit, as they were unresponsive on medical treatment, the patients were referred to our department for the administration of renal replacement therapy which included hemodialysis and venovenous hemofiltration. The choice for using the specific modality was determined by the patient's

status, hemodynamic, nutritional and metabolic. All the patients were in the FAILURE stage of the Rifle criteria. A fresh urine sample was collected via the indwelling catheter and which was then sent for gel electrophoresis, as recommended by the manufacturer of the machine used for analysis[7]. Two scores were used to analyze the proteinuria, using the tubular score and the glomerular score. A single trained laboratory scientist analyzed the samples using a visual score on a scale which marked 0,0.5,1,2,3 and 4 respectively. Dilution factor was duly applied where it was applicable. Tubular injury and hence the use of tubular score was determined by the presence of low molecular weight bands above albumin, and the higher molecular bands below albumin were used to determine glomerular damage and the hence the use of glomerular score. The intervention was not at all affected by this study. Patient survival was defined as when the patient is alive at discharge, and renal recovery is defined as that renal function has returned to baseline upon discharge. Renal non recovery is defined as a deteriorating renal function having an estimated glomerular filtration rate of less than 15ml per min. Statistical analysis was done using SPSS version 20, mean and standard deviations are used for descriptive data, while categorical data was analyzed as frequency and percentages, student t test and Pearson chi square test was used to comparing the data.

RESULTS

A total of n= 40 patients were included in the study, having a mean age of 58.6+/-27 years and a male to female ratio of 24:16 having either acute renal failure or acute chronic renal failure having a ratio of 22:18 respectively, the mortality of patients was 15(37.5%), the non survivor population was in critical condition at the time of referral having an APACHE II score of 29+/-5, they also had lower values for baseline creatinine and a higher tubular to glomerular ratio which points towards acute tubular necrosis see table 1. Among those who had survived 25(62.5%) a total of 7(17.5%) patients were those who did not recover and 19(47.5%) were those who recovered and returned towards normal renal functioning. Those who did not recovered went into end stage renal disease. Both the groups of those who recovered and those who did not had low APACHE II scores at the time of presentation, the renal non recoverers also had higher values for baseline creatinine 414+/-327 versus 125+/-18 for those who recovered. And the group that did not show any signs of recovery also had higher values for tubular/glomerular scores and higher total scores from combined tubular and glomerular proteins, reflecting a severe and irreversible damage to the renal glomeruli refer to table 1. There were 8 patients who required dialysis for less than two days while 10 patients required dialysis for more than 2 days before returning to normal renal function. The group which required more days of dialysis also had higher values for tubular and glomerular scores suggesting more injury.

Table 1: Summary of demographic data in different groups of patients.

Variables	Survivor	Non survivor	P value
Number	25 (62.5%)	15 (37.5%)	
Age in years	64 +/- 15	64 +/- 10	Not Significant
APACHE II Score	20 +/- 4	29 +/- 5	<0.001
Creatinine (baseline) in umol/L	335 +/- 300	120 +/- 48	<0.02
Creatinine (Intradialytic) in umol/L	403 +/- 208	354 +/- 127	Not Significant
Dipstick score	1.4 +/- 0.8	1.3 +/- 0.9	Not Significant
Glomerular score	2.3 +/- 2	1.5 +/- 1	Not Significant
Tubular score	1.4 +/- 1.3	1.5 +/- 1.1	Not Significant
Tub/Glom ration	75 +/- 36	114 +/- 59	<0.05
Tub + Glom total score	3.8 +/- 2.5	3.1 +/- 1.8	Not Significant
	Renal Recoveries	**Renal Non Recoveries**	
Number	19 (47.5%)	7 (17.5%)	
Age in years	60 +/- 7	65 +/- 9	Not Significant
APACHE II Score	19 +/- 4	21 +/- 6	Not Significant
Creatinine (baseline) in umol/L	125 +/- 18	414 +/- 327	<0.01
Creatinine (Intradialytic) in umol/L	331 +/- 89	429 +/- 237	Not Significant
Dipstick score	0.5 +/- 0.0	1.8 +/- 0.9	<0.001
Glomerular score	0.6 +/- 0.1	3.0 +/- 1.9	<0.002
Tubular score	0.6 +/- 0.2	1.7 +/- 1.0	<0.02
Tub/Glom ration	100 +/- 0.5	65 +/- 40	<0.01
Tub + Glom total score	1.2 +/- 0.5	4.6 +/- 2.4	<0.005

Table 2: Duration of dialysis and comparison of various variables. Excluding patients who underwent end stage renal disease or those who died.

Variables	Dialysis for less than 2 days	Dialysis for more than 2 days	P value
Number	8	10	
Days dialyzed	1.5 +/- 0.4	10 +/- 9	<0.05
Apache II score	19 +/- 4	22 +/- 6	Not Significant
Creatinine (baseline) in umol/L	159 +/- 80	163 +/- 74	Not Significant
Gender M:F	5:1	4:4	Not Significant
Age in years	64 +/- 9	64 +/- 10	Not Significant
Dipstick	0.8 +/- 0.5	1.7 +/- 1.1	0.059
Tubular score	0.7 +/- 0.2	2.0 +/- 1.2	<0.02
Glomerular score	1.0 +/- 1.0	3.1 +/- 2.1	0.059
Tub/Glom ratio	89 +/- 26	73 +/- 44	Not Significant
Tub + Glom Total score	1.7 +/- 1.1	5.0 +/- 2.9	<0.02

DISCUSSION

Scientists have developed many markers to assess the renal function which include NGAL, KIM-1 and Cystatin-C[8]. But these markers are not widely available, and hence a need for an easier to manage and administer method for the assessment of renal function for the management of acute renal failure. Many nephrologists use serum creatinine levels as gold standard which is also a hindrance towards the use of these new biomarkers[8]. The combined assessment with biomarkers and urinary protein levels has shown higher accuracy[9]. Acute tubular necrosis is characterized by secretion of urinary protein and enzymes[10], the most susceptible sites of the nephron are the proximal tubules and the thick ascending limb of the loop of henle, these sites are most susceptible to ischemic damage, due to their low blood supply, and high energy requirements. Routine dipstick method is not efficient in detecting tubular proteinuria, gel electrophoresis is one of the methods which detects and is affordable and reliable[7]. Tubular proteinuria comprises of low molecular weight proteins such as beta 2 microglobulin, KIM-1, Cystatin C, NGAL and alpha 1 microglobulin, which are filtered across the glomerulus and are normally reabsorbed by the proximal tubular cells, but disruption of the proximal tubular cells cause these proteins to be secreted into the urine pathologically[11]. This proteinuria can also help identify which patients required renal replacement therapies, according to the results of our study those who required longer duration of dialysis had increased levels of tubular proteinuria. Tubular proteinuria often precedes glomerular proteinuria as reflected by this study[6]. Tubular proteinuria is a more reliable test as compared to glomerular proteinuria when it comes to the prediction of length of renal replacement therapy that would be required by the patients who have acute renal failure[13]. Tubular proteinuria is also associated with increased mortality[1], which is due to the fact that severely ill patients have sever acute tubular necrosis. In our study we found lower levels of baseline creatinine in those patients who did not survive, indication their previously health predisposition, and due to multi organ failure they were not able to survive. Increased mortality has always been associated with middle and high molecular weight proteins in the urine, such as albumin[14], but its value in predicting the acute renal failure is not reported. In our study we found that those who did not recover their renal function they had higher levels of baseline creatinine and also higher glomerular proteinuria scores, and this is associated with poor rates of renal dysfunction, which is also found in the study of Matthew et al who also showed glomerular proteinuria to be an indicator of severe renal injury.

CONCLUSION

According to the results from our study the gel electrophoresis analysis for proteinuria is a cost effective and reliable method, when it comes to determining the tubular or glomerular proteinuria in patients with acute renal failure requiring renal replacement therapy in the intensive care unit. Presence of tubular proteinuria correlates with duration of dialysis support and the mortality rate, and the presence of glomerular proteinuria indicates glomerular damage and its severity.
The authors have no conflict of interest.

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