ESTIMATION OF GLOMERULAR FILTRATION RATE BY SERUM CREATININE AND SERUM CYSTATIN C IN BURN PATIENTS FOR PREDICTING ACUTE KIDNEY INJURY

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ABSTRACT

Background: The major complication of burn is acute kidney injury, which carries an extremely high mortality. Creatinine is the most widely used endogenous marker for glomerular filtration. Most of the requirements for a perfect renal filtration marker are fulfilled by Creatinine. Cystatin C (Cys C) is a small 13-kDa protein to fulfill the basic requirements for an endogenous filtration marker.

Objective: To evaluate the estimated glomerular filtration rate by serum creatinine and serum cystatin C in burn patients for predicting acute kidney injury.

Methodology: It was a cross-sectional study, in which 70 subjects were included with burn affecting total body surface area (TBSA) of 20% to 40%. For the estimation of serum Cystatin C the enzyme linked immunosorbent assay (ELISA) was used. Correlation of results was determined by Correlation coefficient. Duration of study: 1st to 30th September 2014. Burns patients having comorbidities like diabetes mellitus, chronic kidney disease, thyroid disease and liver disease were excluded. SPSS version 18 was used for analysis.

Results: The mean age of patients was 31.74 ± 12.55 (range 3-50). There were 41 (58.57%) male and 29 (41.43%) female patients. The mean serum creatinine was 78.3 ± 14.61 umol/L. The average serum cystatin in this study was 6.56 ± 3.48 mg/L. Positive significant correlation was found between both methods of eGFR i.e. r= 0.796 (p-value = < 0.01).

Conclusion: Serum Cystatin C and Serum Creatinine can be used to evaluate impaired renal function effectively at an early stage in burn patients.

Keywords: Burn, Acute Renal failure, Kidney injury, Creatinine, Cystatin C

INTRODUCTION

Patients with burn suffer from many of complications; the most serious of all is the acute renal injury.[1,2] Death rate after acute renal damage is more than 80% despite modern treatment modalities and dialysis, however, incidence of renal damage/ failure is between 1% to 30%.[1] Permanent and complete renal function loss may be caused by Acute Kidney injury (AKI), which reflects a broad spectrum of clinical presentations ranging from mild injury to severe injury in patients with burn.[2] Two types of acute renal damage develop according to time of onset.[3] One is pre-renal occurring within first few days and second type is related to sepsis and multi-organ failure developing later and is most often fatal.[3,4,5]

Serum creatinine is considered as standard representative of glomerular filtration rate due to easy and cheaper availability and is expressed either as its renal clearance or plasma concentration.[4] Being endogenous creatinine fulfils the most but not all of the requirements for a perfect filtration marker. It is not protein bound but low molecular weight substance, which is freely filtered, not metabolized by the kidney and it is physiologically inert.[5] Glomerular filtration rate (GFR) is the total clearance of a specific substance in a unit time to assess the functional capacity of the kidney.[6]

Less than 5% of variation in renal function does not have any effect on the serum concentration of creatinine and it is considered as rough marker of glomerular filtration rate.[7,8] However, age, sex, level of activity and muscle bulk does have definitive effect on serum creatinine level.[7] Cystatin C is not affected by different factors like age, sex, muscle mass and activity level. However, thyroid function disturbance and excessive use of steroids influence its concentration. Reabsorption and metabolism of Cystatin C is performed by proximal tubules at a constant rate throughout life and completely removed from blood.[8]

Cystatin C level is as an endogenous representative of renal level of function in patients with burn, hypovolaemic shock and chronic kidney disease (CKD).[6,7,8] Cystatin C is much more accurate

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diagnostic marker than creatinine level in the differentiation of normal and abnormal renal function especially acute kidney injury.[9] Early detection and response in adjustment of antibiotics after renal injury in suspected patients of major burn can prevent acute renal failure.[10] However, Cystatin C is rarely investigated after burn in early phase for renal status.[11] Therefore the present study was designed to assess the efficacy in terms of correlation of Cystatin C based eGFR in comparison with creatinine.

METHODOLOGY

This cross-sectional study was conducted in Lahore General Hospital, and Post-Graduate Medical Institute, Lahore from 1st January to 30th September 2014. Seventy patients with burn were included in the study from different public hospitals with 6-9 months follow-up. Sample size was calculated by using given formula, by taking risk of acute renal injury in burn patients as 28.1%, at 0.1 margins of error and 95% confidence interval.[12] Patients with 20% to 40% burn of both sexes up to 50 years of age and creatinine clearance between 50 to 80 ml/minute were included in the study by non-probability, purposive sampling technique.

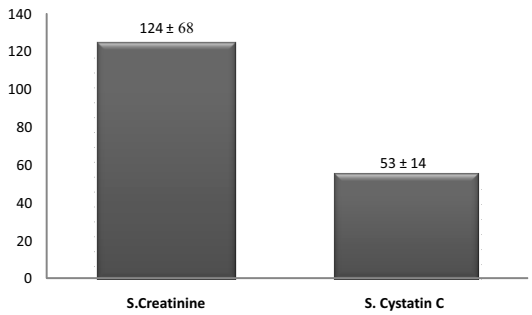
Patients with chronic kidney disease, diabetes mellitus, hypertension, thyroid disease, active liver disease and glucocorticoids intake within 2 weeks prior to burn were excluded from study. After obtaining the informed consent of all the subjects, the personal information of the patient, age, weight and height was recorded on the prescribed proforma. Samples of blood and urine were collected in all the patients on 3rd day post burn. In all the patients 24 hour urine collection was done in sterilized and labeled container. Serum and urinary creatinine was estimated by centrifugation of respective samples. Creatinine clearance was calculated by the specific formula. Serum Cystatin C was estimated in patients with creatinine clearance between 50 to 80 ml/min. Glomerular filtration rate was estimated by serum cystatin and serum creatinine. The data was entered and analyzed by using SPSS version 18. Mean $\pm$ SD was given for normally distributed quantitative variables and Median ± IQR (interquartile range) was given for non-normally distributed quantitative variables. A p-value ≤ 0.05 was considered statistically significant, and correlation of cystatin C and serum creatinine

RESULTS

The mean age of patients was 31.74 ± 12.55 with minimum and maximum age of 3 and 50 years. Seven (10%) patients were < 15 years, 42 (60%) between 16-40 years and 21 (30%) > 40 years of age. There were 41 (58.57%) male and 29 (41.43%) female patients. There were 17 (24.29%) obese and 53 (75.71%) non-obese patients.

The average percentage of burn in the patients was 30.58 ± 5.92 ranging from 20% to 40 %. In this study the mean serum creatinine was 78.30±14.61umol/L from 40 to 101.8umol/L. The average serum Cystatin was 6.56 ± 3.48 mg/l with range of 1.30 – 13.55 mg/l. The average creatinine clearance was 1001.55 ± 298.59 ml/min with range of 500 - 1572.14 ml/min.

Figure I: Mean glomerular filtration rate



The mean glomerular filtration rate by Serum creatinine was 124.30 ± 68.58 (ml/min) with range of 43- 317.13ml/min while mean glomerular filtration rate by Cystatin C was 53.82±14.94 (ml/min) with Pearson correlation coefficient (r) = 0.796 (p-value < 0.001). (Figure I) Significant positive correlation was found between both methods of glomerular filtration rate with r= 0.804 (p-value < 0.01) for males and r= 0.785 (p-value < 0.01) for females.

DISCUSSION

Assessment of acute kidney injury is necessary in burn patients as for as outcome is concerned.[12] In present study, average burn was 30.58 ± 5.92% and majority 58.5% of male patients. This is in contrast to a study reporting mean burn 55.7 ± 23.2% in 86% male and 14 % female patients.[13] Acute renal injury is classified as early occurring within three days mainly due to hypovolaemia and late acute injury is considered as from 4 to 14 days, specifically due to multiple organ failure.[14] However in the present study early and late kidney injuries were grouped as single acute insult. In another recent study carried on 35 patients complicating with renal insult.

Predominantly male patients have on average age of 49.6 years similar to present study.[15]

In current study, there were 41 (58.57%) male and 29 (41.43%) female patients. The higher ratio of male also reported in other study. Because major burn patients pass through multiple specific clinical consequences such as shock, sepsis and multiple organ failure and inflammation which can disturb serum markers, therefore design of studies are used to check the serum for any disturbance of markers at intervals of 5 to 7 days on 3 to 4 times.[16] Cystatin C was constantly in the range of 1.30 – 13.55 mg/L as compared with creatinine having margin from 40 to 101.8umol/L as evidenced by other study to show good renal functional indicator.[17]

In burn, patient's renal function is monitored by 24-hour urine output routinely; however it is a crude measurement. Post-burn early seven day's glomerular filtration rate is altered by derangement of cardiac and vascular output. In present study, mean glomerular filtration rate by Cystatin C was 53.82±14.94 (ml/min) and set to be an excellent renal function indicator as reported in another study.[18] Acute renal disease is a disastrous complication of burn resulting in high morbidity and mortality without any definitive treatment.[19] Therefore, planning an effective prevention is the only cure available at present by investigations such as serum Cystatin C, creatinine and others.[20]

Mortality after acute renal injury in burn patients varies from 19% to 70% in different studies.[21,22] In present study, mortality was not calculated. In a recent study, Neutrophil gelatinase-associated lipocalin (NGAL) was compared with serum Cystatin and serum creatinine as an indicator of acute renal injury in 19 burn patients. It was concluded that Cystatin C is still a better marker of acute renal injury during initial 7 days in severe burn patients as endorsed in the present study.[22]

In present study, the mean serum creatinine was 78.30 ± 14.61 umol/L, the average serum cystatin in this study was 6.56 ± 3.48 mg/l and mean urinary creatinine excretion in this study was 1001.55 ± 298.59 ml/min. The mean eGFR by S Cr method was 124.30 ± 68.58 (ml/min) with minimum and maximum value as 43 and 317.13 (ml/min) while mean eGFR Cys C was 53.82±14.94 (ml/min). Serum Cystatin C is raised in initial 1-2 days followed by serum creatinine for next 5-7 days as a clue to renal injury.[23]

CONCLUSION

It is concluded that serum cystatin C is also a better biomarker of renal function in early stages of acute kidney injury and is less affected by age and gender.

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