INTRODUCTION

Biochemical markers play an important role in accurate diagnosis and also for assessing risk and adopting therapy that improves clinical outcome. Creatinine is a breakdown product of creatine phosphate in the muscles. Creatinine is transported through the bloodstream to the kidneys. Serum creatinine is the most commonly used test to assess renal function. The National Kidney Disease Education Program recommends calculating glomerular filtration rate (GFR) from serum creatinine concentration. The diagnosis of renal failure is usually suspected when serum creatinine is greater than the upper limit of normal. In chronic renal failure, an eventual reduction occurs in the excretion of creatinine by both the glomeruli and the tubules. Creatinine values may alter as its generation may not be simply a product of muscle mass but influenced by muscle function, composition, activity, diet and health status. The increased tubular secretion of creatinine in some patients with kidney dysfunction could give false negative value.

The impaired renal functions are mainly reflected by the laboratory detection of serum creatinine, which is not sensitive enough to detect early change of renal function, when active management is important. Creatinine reflects renal filtering capacity, which is not sensitive to acute or chronic kidney injury until it is substantial enough to compromise the filtering ability. Recently it has been postulated that a substantial number of patients have evidence of tubular

ORIGINAL ARTICLE

CORRELATION OF BETA 2 MICROGLOBULIN WITH SERUM CREATININE AND CREATININE CLEARANCE IN PATIENTS WITH DIFFERENT LEVELS OF RENAL FUNCTION

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ABSTRACT

Background: Chronic kidney disease is a major health problem in Pakistan. Serum creatinine is the most common test used to assess renal function. This study was aimed to evaluate the levels of β2 Microglobulin and creatinine in individuals with different levels of renal function and to see the correlation between these biomarkers.

Material & Methods: Total subjects included in the study were 88; 50 males and 38 females, of 30-60 years age, selected randomly from Sheikh Zayed Hospital Lahore. Creatinine clearance was calculated from serum creatinine and 24 hours urinary volume and urinary creatinine for all study subjects and they were divided into 4 groups on the basis of creatinine clearance.

Results: Serum and urinary β2 Microglobulin levels were found to be raised in both male and female patients of all groups, while serum creatinine levels were in normal range in patients with creatinine clearance above 60 ml/min. Both β2 Microglobulin and serum creatinine levels were increased in parallel with the severity of renal disease. It was found that serum and urinary β2 Microglobulin had a positive correlation with serum creatinine in all groups. β2 Microglobulin showed negative correlation with creatinine clearance in all groups.

Conclusion: β2 Microglobulin correlates more closely with different levels of renal functions. It shows positive correlation with serum creatinine and negative correlation with creatinine clearance.

KEY WORDS: β2 Microglobulin, Serum creatinine, Creatinine clearance, Renal function.
Creatinine clearance (Cr.Cl) is the volume of plasma cleared of creatinine per unit time and is a useful measure for approximating the GFR. However, the creatinine clearance systematically overestimates the GFR due to secretion of creatinine by the renal tubules. By measuring the amount of creatinine excreted in the urine over 24 hours and serum creatinine, the creatinine clearance may be calculated by the formula.

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\text{Cr.Cl} = \frac{(uCr \times uV)}{(sCr \times 1440)}. \]

\( \text{Cr.Cl} \) is Creatinine clearance in ml/min, \( uCr \) is Urine Creatinine in mg/dl, \( sCr \) is Serum creatinine in mg/dl, \( uV \) is 24 hour urine volume in ml and 1440 represents number of minutes in 24 hours.

\( \beta_2 \) Microglobulin is a non-glycosylated protein. In the system, it possesses the negative charge. \( \beta_2 \) Microglobulin is a component of MHC class 1 molecules, which are present on almost all cells of the body except red blood cells. \( \beta_2 \) Microglobulin is generally required for the transport of MHC class I heavy chains from the endoplasmic reticulum to the cell surface. \( \beta_2 \) Microglobulin is filtered by the glomerulus, absorbed and catabolised by the proximal tubules. Clinically the appearance of significant amount of this protein in urine is one of the earliest sign of almost all renal diseases. Serum creatinine is affected by factors other than GFR, in particular muscle mass and meat intake. \( \beta_2 \) Microglobulin is released at constant rate in normal subjects, readily filters through the glomerular capillary wall, over 99.9% being reabsorbed and catabolised in proximal tubules with virtually no return of the filtered protein to the circulation. \( \beta_2 \) Microglobulin is therefore theoretically a highly suitable biomarker of renal dysfunction.

The current study was designed to determine the values of these biomarkers in patients with different levels of renal functions and find out the correlation between serum and urinary \( \beta_2 \) Microglobulin, serum and urinary creatinine, blood urea nitrogen and creatinine clearance in patients with different levels of renal function.

MATERIAL AND METHODS

It was a cross-sectional study. Both male and female (88 in number), subjects between the ages of 30 to 60 years; suffering from different levels of renal dysfunction were selected from the Sheikh Zayed Hospital, Lahore. Diagnosed cases of end stage renal disease (ESRD), patients on mainte-
### Table 2: Comparison of serum creatinine, $\beta_2$ Microglobulin (MG) blood urea nitrogen (BUN) and creatinine clearance in male patients of different groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Serum creatinine (mg/dl)</th>
<th>Serum $\beta_2$MG (µg/ml)</th>
<th>BUN (mg/dl)</th>
<th>Creatinine clearance (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=10)</td>
<td>1.25±0.06</td>
<td>5.77±0.29</td>
<td>17.70±0.97</td>
<td>110.09±3.49</td>
</tr>
<tr>
<td>Group 2 (n=4)</td>
<td>1.43±0.28</td>
<td>6.24±0.14</td>
<td>20.50±4.05</td>
<td>69.90±3.56</td>
</tr>
<tr>
<td>Group 3 (n=10)</td>
<td>1.88±0.30</td>
<td>6.29±0.15</td>
<td>26.70±3.96</td>
<td>44.80±1.65</td>
</tr>
<tr>
<td>Group 4 (n=26)</td>
<td>4.75±0.62</td>
<td>9.63±0.58ab</td>
<td>79.50±8.58</td>
<td>11.22±1.40</td>
</tr>
</tbody>
</table>

Values are Mean± SEM.

### Table 3: Comparison of serum creatinine, $\beta_2$ Microglobulin, blood urea nitrogen and creatinine clearance in female patients of different groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Serum creatinine (mg/dl)</th>
<th>Serum $\beta_2$MG (µg/ml)</th>
<th>Blood urea nitrogen (mg/dl)</th>
<th>Creatinine clearance (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=6)</td>
<td>0.90±0.13</td>
<td>5.08±0.76</td>
<td>13.00±1.91</td>
<td>124.38±4.35</td>
</tr>
<tr>
<td>Group 2 (n=6)</td>
<td>0.98±0.07</td>
<td>5.84±0.20</td>
<td>14.00±1.53</td>
<td>71.12±2.61</td>
</tr>
<tr>
<td>Group 3 (n=12)</td>
<td>1.01±0.07</td>
<td>5.88±0.12</td>
<td>14.25±1.07</td>
<td>48.22±1.77</td>
</tr>
<tr>
<td>Group 4 (n=14)</td>
<td>2.12±0.25</td>
<td>6.19±0.45</td>
<td>41.07±4.73</td>
<td>18.04±1.76</td>
</tr>
</tbody>
</table>

Values are Mean± SEM.

### Table 4: Comparison of urinary $\beta_2$ Microglobulin and urinary creatinine in male patients of different groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urinary $\beta_2$ MG(µg/ml)</th>
<th>Urinary Creatinine(mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=10)</td>
<td>1.82±0.51</td>
<td>114.86±17.86</td>
</tr>
<tr>
<td>Group 2 (n=4)</td>
<td>2.63±0.48</td>
<td>54.00±5.80</td>
</tr>
<tr>
<td>Group 3 (n=10)</td>
<td>5.56±0.71</td>
<td>45.14±7.78</td>
</tr>
<tr>
<td>Group 4 (n=26)</td>
<td>6.91±0.43</td>
<td>42.77±3.74</td>
</tr>
</tbody>
</table>

Values are Mean± SEM

### Table 5: Comparison of urinary $\beta_2$ Microglobulin and urinary creatinine in female patients of different groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urinary $\beta_2$ Microglobulin(µg/ml)</th>
<th>Urinary Creatinine((mg/dl))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=6)</td>
<td>1.05±0.07</td>
<td>83.62±10.68</td>
</tr>
<tr>
<td>Group 2 (n=6)</td>
<td>2.58±0.27</td>
<td>86.88±14.78</td>
</tr>
<tr>
<td>Group 3 (n=12)</td>
<td>3.03±0.15</td>
<td>47.36±8.04</td>
</tr>
<tr>
<td>Group 4 (n=14)</td>
<td>4.91±0.46</td>
<td>31.74±3.25</td>
</tr>
</tbody>
</table>

Values are Mean± SEM.
DISCUSSION

Various studies have been conducted to find out the biochemical markers which could play an important role in diagnosis of different renal diseases, assessment of the associated risk and adopting therapy. From these studies, it has been speculated that the appearance of significant amount of proteins in urine is one of the earliest sign of almost all renal diseases. The current study is unique that it was conducted on 88 individuals (50 males and 38 females) between the ages of 30 to 60 years with different levels of renal function and suffering from different renal problems. It may be interpreted from these results that serum creatinine is a poor marker in assessing early renal damage as it is influenced by muscle mass, gender, age, race and medications and is often not elevated until the injury is well established. Moreover, serum creatinine level reflects renal filtering capacity, which has a lot of reservation and is therefore not sensitive to acute or chronic kidney injury until it is substantially enough to compromise the filtering ability. Serum creatinine also does not reflect any renal damage in early stage of diabetes when kidneys are hyper functional due to initial hyperglycemia, leading to increase in the kidney size and higher glomerular filtration rate. Mean serum creatinine in both male and female patients showed inverse correlation to creatinine clearance in all groups. In group 3 and 4, serum creatinine was above the normal, showing renal injury. From these results, it is obvious that serum creatinine is a late marker of renal injury. It does not show early renal damage. In contrast to creatinine, both serum and urinary β2 Microglobulin values were above the normal in both male and female patients of group 1 and 2. These results indicate that β2 Microglobulin is more sensitive and accurate biomarker for the assessment of renal functions as compared to serum creatinine. The most probable reason for this could be that South Asians have different diet and muscle mass as compared to Caucasians and creatinine is influenced by these factors. Tazeen et al.16 reported similar results. High values of β2 Microglobulin in group 1 patients could also be due to any subclinical acute phase disease, as β2 Microglobulin is released in high amount in acute inflammatory conditions. It was depicted that β2 Microglobulin correlates more closely to glomerular filtration rate in all different levels of renal functions in different groups of patients as compared to creatinine. β2 Microglobulin showed positive correlation with creatinine and blood urea nitrogen in all groups of patients while both β2 Microglobulin and creatinine showed inverse correlation to creatinine clearance in both male and female patients of all four different groups. The consistent negative correlation between β2 Microglobulin and creatinine clearance, indicates the importance of β2 Microglobulin in diagnosing renal damage at any level. Measuring β2 Micro-globulin concentrations is a simple and accurate method of detecting minor degrees of renal damage and monitoring the effects of treatment.

CONCLUSIONS

Serum and urinary β2 Microglobulin has highly significant positive correlation with both serum creatinine and blood urea nitrogen in all groups of patients. A negative correlation exists between serum and urinary β2 Microglobulin and creatinine clearance in both male and female patients in all groups.

It is suggested to plan a population based study with larger numbers of individuals having specified race, gender, body mass index and nutritional parameters, so that β2 Microglobulin can be identified as independent biomarker for the assessment of renal functions.
REFERENCES


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