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ORIGINAL ARTICLE

Blood Urea Nitrogen (BUN) levels in renal failure: Unraveling the complex interplay of protein metabolism and kidney health.

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ABSTRACT… Objectives: To evaluate serum calcium, assess creatinine's muscle function marker, and analyze BUN as a protein metabolism indicator in renal failure. **Study Design:** Cross-sectional study. **Setting:** Tehsil Samahni District Bhimber Kashmir. **Period:** April 2020 to July 2020. **Methods:** A total of 90 subjects, including 60 with renal failure and 30 healthy individuals from Tehsil Samahni District Bhimber Kashmir registered with THQ hospital for dialysis, were categorized by age and gender. Blood samples were collected after the written consent of each patient and analyzed for serum calcium, serum creatinine, and BUN using an automated analyzer. Ninety subjects were divided into groups based on age and gender. Blood samples were collected and subjected to serum calcium, serum creatinine, and BUN assays using an automated analyzer to evaluate renal function and calcium homeostasis. **Results:** Serum creatinine levels were significantly elevated in all renal failure groups compared to the healthy group, indicating impaired renal function. However, serum calcium levels remained relatively stable across all groups. Notably, BUN levels were significantly higher in all renal failure groups except for females aged 1-40 years. **Conclusion:** Renal failure is indicated by elevated serum creatinine, highlighting kidney dysfunction, while serum calcium stability may not be indicative of renal failure. Elevated BUN levels imply disrupted protein metabolism, underlining the complex role of these biomarkers in renal health, and necessitating refinement of diagnostic and therapeutic strategies for renal diseases.

Key words: Blood Urea Nitrogen (BUN), Kidney Health Complex Interplay, Protein Metabolism, Renal Failure.

INTRODUCTION

CKD is characterized by gradual loss of the excretory and regulatory functions attributed to functional or structural anomalies with a decreased glomerular filtration rate (GFR) of < 15 ml/min per 1.73 m2 for a minimum of 3 months.[1,2]

Estimating CKD incidence in Pakistan is challenging due to the absence of a centralized renal registry program. However, independent studies indicate a range of 15% to 20%.[3,4]

The kidneys hold a crucial role in upholding and fine-tuning the balance of acids and electrolytes within the body, a fundamental requirement for various metabolic processes and the proper functioning of organs. Chronic kidney diseases, however, undermine these regulatory functions, leading to significant disruptions in the equilibrium of electrolytes and acids, a condition with the potential to pose life-threatening risks.[5]

Chronic kidney disease (CKD) is a global epidemic, often symptomless in its early stages, leading to high morbidity and mortality rates. It imposes a significant economic burden on both developing and developed nations. CKD's estimated prevalence ranges from 8% to 16%, ranking as the ninth leading cause of death, with 9-10 million annual global fatalities. In Pakistan, the lack of a central renal registry program makes estimating CKD incidence challenging, but independent studies suggest a range of 15% to 20%.[6,7]

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Urea nitrogen is a waste product that your kidneys remove from your blood. Higher than normal BUN levels may be a sign that your kidneys aren't working well. Males had higher levels of BUN, Creatinine, and uric acid compared to females. Serum levels of these markers were found to increase significantly ($P<0.05$) from mild to moderate CKD to ESRD patients. Thus, indicating the role of the BUN: Cr ratio as an efficient prognostic marker in the diagnosis of renal failure.

Both BUN and cSosm are independently linked to CKD development. In advanced CKD stages, elevated BUN, but not cSosm, predicts adverse renal outcomes, suggesting BUN's potential as a predictive marker.[8]

The recent literature regarding serum creatinine as a surrogate of muscle mass is summarized, as is the literature concerning the use of other measures of muscle mass, such as plasma gelsolin and actin, and urinary creatinine excretion.[9]

Calcium absorption, primarily in the small intestine, relies on active vitamin D3 (Calcitriol).[10]

A daily calcium intake of 1,000 mg allocates 800 mg for tissue needs and 200 mg for serum calcium maintenance. Excess intestinal calcium is eliminated via urinary excretion. Calcium fluxes between bone matrix, with a flexible reserve of 150-200 mg, but if more is needed, bone calcium is borrowed, not always fully restored.[11,12,13]

METHODS

In this study conducted in Tehsil Samahni District Bhimber Kashmir, 90 subjects of varying ages and genders were divided into two groups: a diseased group consisting of 60 renal failure patients and a controlled group comprising 30 healthy individuals. Blood samples were collected, processed, and analyzed for serum calcium, serum creatinine, and blood urea nitrogen (BUN) levels. Safety precautions were adhered to, and specimens were handled following standard procedures. The tests were conducted using a Chemistry Auto analyzer, with control measures in place to ensure accuracy. The study aimed to assess biomarker variations between the groups to enhance understanding and management of renal diseases after approval from ethical committee (97 THQ/2020-S)

Inclusion Criteria

All patients with chronic kidney disease, No age and Gender limit. Patient oral medication or Dialysis for CKD.

Exclusion Criteria

Patient with liver Cirrhosis, Receiving treatment for any type of Malignancy, Patient receiving immunosuppressed treatment or steroids for any autoimmune condition or transplant.

LABORATORY TESTS

The blood tests in this study included the measurement of three key biomarkers: serum calcium level, serum creatinine level, and blood urea nitrogen (BUN) level. These tests were conducted using a reliable and automated chemistry auto analyzer, specifically the Dimension R X L from Dade Behring USA. To ensure accuracy and consistency, daily calibration was performed using the provided CAL Standards in the kit or Randox Calibration Serum Level 3. This meticulous approach to calibration and analysis helped ensure the precision of the results obtained for evaluating renal health and function in the study's subjects.

Statistical Analysis

Results were analyzed (Mean, Standard Deviation, and Standard error mean) by using SPSS version 20.

RESULTS

Serum Calcium especially and some parameters (Creatinine and BUN) of renal failure were studied in normal renal status and renal failure subjects. A population of thirty subjects with normal renal status and sixty subjects with chronic renal failure (CRF) subject were sampled for the study. The results were analyzed in different genders and in various age groups.

Serum Electrolyte Levels in the Total Male Population provide valuable insights into the

status of serum electrolytes, specifically Calcium, Creatinine, and BUN (Blood Urea Nitrogen), across two distinct groups: Normal and Renal Failure (RF).

In the "Normal" group, the mean calcium level measured was 8.910, with a corresponding standard error of 0.10265. Creatinine levels were relatively low at 0.9233, with a standard error of 0.0533. BUN levels in this group were within the normal range, with a mean of 12.867 and a standard error of 1.0973.

Conversely, the "Renal Failure (RF)" group exhibited significant deviations in their serum electrolyte levels. The mean calcium level dropped notably to 7.4133, with a standard error of 0.09299. Creatinine levels soared to 7.2500, indicating substantial impairment, and this was accompanied by a larger standard error of 0.6056. The most striking difference was observed in BUN levels, which surged to 62.4500, showing a substantial increase from the "Normal" group and underlining the severity of renal dysfunction.

Serum electrolyte levels within the total female population, distinguishing between two groups: "Normal" and "Renal Failure (RF)."

In the "Normal" group, the mean calcium level was measured at 8.747, with a standard error of 0.153. Creatinine levels averaged 0.967, accompanied by a standard error of 0.071, while BUN (Blood Urea Nitrogen) levels showed a mean of 14.600 and a standard error of 1.854.

Conversely, the "Renal Failure (RF)" group displayed substantial variations in serum electrolyte levels. The mean calcium level dropped notably to 7.44, with a standard error of 0.099. Creatinine levels were elevated to 6.937, signifying renal impairment, and this was associated with a larger standard error of 0.765. The most significant contrast was evident in BUN levels, which surged to 63.433, indicating a considerable departure from the "Normal" group and emphasizing the severity of renal dysfunction among this population.

Male populations below 40 years of age (Group 1)

The provided data presents serum electrolyte levels for two distinct groups: "Normal" and "Renal Failure (RF)." In the "Normal" group, the mean calcium level was recorded at 8.98 with a standard error of 0.223. Creatinine levels in this group averaged 0.66, with a standard error of 0.108, while BUN (Blood Urea Nitrogen) levels had a mean of 12.4 and a standard error of 1.639.

Conversely, the "Renal Failure (RF)" group displayed substantial deviations in serum electrolyte levels. The mean calcium level significantly dropped to 6.975, with a standard error of 0.303. Creatinine levels were notably elevated at 7.817, indicating renal dysfunction and accompanied by a larger standard error of 1.499. Most prominently, BUN levels surged to 59.167, signifying a significant departure from the "Normal" group and emphasizing the severity of renal impairment within this population.

Entity	Means± Standard Errors	
	Normal	Renal Failure (RF)
Calcium	8.98±0.223	6.975±0.303
Creatinine	0.66±0.108	7.817±1.499
BUN	12.4±1.639	59.167±11.038

Table-I. Serum calcium, creatinine and BUN levels in males below 40 years of age

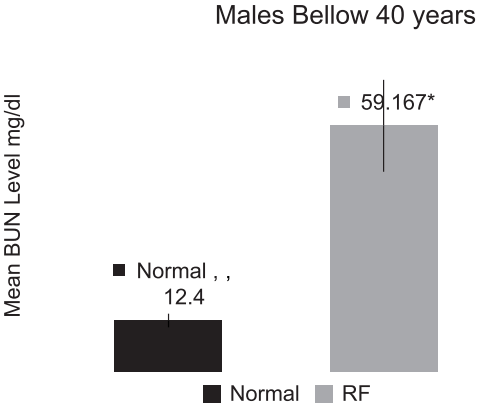

Figure-1. BUN level in males below 40 years of age

Males above 40 years of age (Group-2)

The data presented here reveals the serum electrolyte levels for two distinct groups: "Normal" and "Renal Failure (RF)." Within the "Normal" group, the mean calcium level was

found to be 9.12, with a small standard error of 0.129, suggesting relatively stable calcium levels in this population. Creatinine levels in the "Normal" group averaged 0.99, with a standard error of 0.0781, indicating a typical range for this parameter. In contrast, BUN (Blood Urea Nitrogen) levels in the "Normal" group were observed to be 10.50, accompanied by a standard error of 1.022.

In the "Renal Failure (RF)" group, notable differences emerged. The mean calcium level dropped significantly to 7.661, with a relatively small standard error of 0.124, signalling a decrease in calcium levels compared to the "Normal" group. Creatinine levels in the "RF" group averaged 7.394, with a larger standard error of 1.166, indicating a substantial rise and suggesting renal dysfunction. Most strikingly, BUN levels surged to 63, showcasing a marked increase from the "Normal" group and underscoring the severity of renal impairment within this population.

Entity	Means± Standard Errors	
	Normal	Renal Failure (RF)
Calcium	9.12±0.129	7.661±0.124
Creatinine	0.99±0.0781	7.394±1.166
BUN	10.50±1.022	63±8.627

Table-II. Serum Calcium, Creatinine and BUN levels in males above 40 years of age

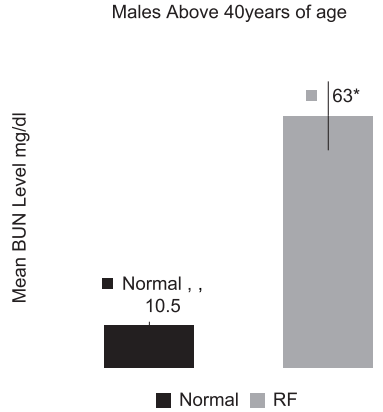

Figure-1. BUN level in males below 40 years of age

Females below 40 years of age (Group-3)

The presented data offers valuable insights into serum electrolyte levels for two distinct groups: "Normal" and "Renal Failure (RF)." In the "Normal" group, the mean calcium level measured was 8.671, with a relatively small standard error of 0.173, suggesting stable calcium levels within this population. Creatinine levels in the "Normal" group averaged 0.986, accompanied by a standard error of 0.119, indicating values within an expected range. On the other hand, BUN (Blood Urea Nitrogen) levels in the "Normal" group were observed at 16.714, reflecting a slightly elevated level compared to typical values, with a standard error of 3.451.

Entity	Means± Standard Errors	
	Normal	Renal Failure (RF)
Calcium	8.671±0.173	7.41±0.354
Creatinine	0.986±0.119	6.81±1.378
BUN	16.714±3.451	57.09±5.909

Table-III. Serum Calcium, Creatinine and BUN levels in females bellow 40 years of age

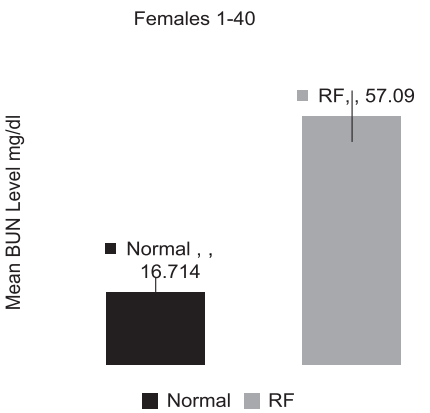

Figure-3. BUN level in females below 40 years of age

In contrast, the "Renal Failure (RF)" group exhibited significant differences. The mean calcium level notably decreased to 7.41, with a higher standard error of 0.354, signifying a drop in calcium levels compared to the "Normal" group. Creatinine levels in the "RF" group were significantly higher, averaging 6.81, with a larger standard error of 1.378, which indicates impaired renal function. Notably, BUN levels were lower in the "RF" group, averaging 57.09, although still relatively high, with a standard error of 5.909.

Female populations above 40 years of age (Group 4)

The table provides a detailed comparison of serum electrolyte levels between two distinct

groups: “Normal” and “Renal Failure (RF).” In the “Normal” group, the mean calcium level was recorded as 8.812, with a standard error of 0.248, suggesting relatively stable calcium levels within this population. Creatinine levels in the “Normal” group averaged 0.95, exhibiting a standard error of 0.083, indicating values within a typical range. Additionally, BUN (Blood Urea Nitrogen) levels in the “Normal” group were measured at 12.75, with a standard error of 1.433, indicating a moderately elevated level compared to normal.

Entity	Means± Standard Errors	
	Normal	Renal Failure (RF)
Calcium	8.812±0.248	7.41±0.141
Creatinine	0.95±0.083	7.01±0.906
BUN	12.75±1.433	67.10±8.266

Table-IV. Serum Calcium, Creatinine and BUN levels in females above 40 years of age

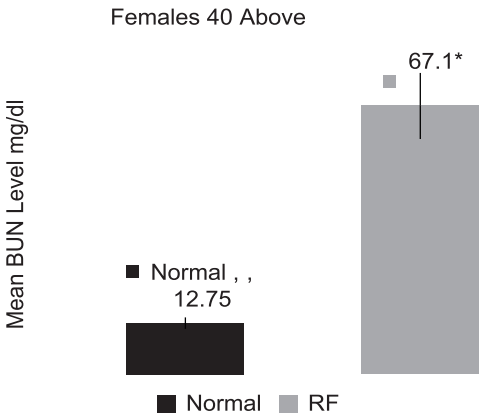

Figure-4. BUN level in Females above 40 years of age

Conversely, the “Renal Failure (RF)” group displayed noteworthy differences in serum electrolyte levels. The mean calcium level in this group was 7.41, with a relatively small standard error of 0.141, highlighting a reduction in calcium levels compared to the “Normal” group. Creatinine levels were substantially elevated in the “RF” group, averaging 7.01, with a standard error of 0.906, signifying impaired renal function. Notably, BUN levels were considerably higher in the “RF” group, averaging 67.10, with a standard error of 8.266, underlining the severity of renal dysfunction within this population.

DISCUSSION

Serum creatinine is found statistically significant in the total population in the present study. It is obvious from this behavior that creatinine does not have a normal level in renal failure patients. The serum Creatinine level was 0.92 mg/dl in normal subjects and 7.25 mg/dl in CRF subjects. In CRF subjects, serum creatinine level was greater than in normal subjects. The difference was found statistically significant. Peter J. et al, 2003[14], have also studied the abnormal behavior of serum creatinine in 1510 patients. In his experiment, he concluded that a serum creatinine level greater than 1.7 mg/dL had a sensitivity of 12.6% and a specificity of 99.9% for the detection of renal failure. The present study shows the same serum creatinine behavior in renal failure patients. In all groups under study, the patients group had significantly higher levels of creatinine as compared to their respective control groups.

The results of the present work illustrate that serum calcium is statistically insignificant in the case of the total population. The serum calcium level was 8.91 mg/dl in all the normal and in renal failure was 7.41 mg/dl. Serum calcium was found to be low in CRF subjects compared to the healthy normal. The difference was found statistically non-significant. Moe SM., 2018 has also studied that in the presence of CKD, most patients will be in positive calcium balance when prescribed calcium-based binders with serum levels of calcium that may be low, normal or high- the result of abnormal calcium homeostasis in kidney disease. However, in present work shows that serum calcium has no significant behavior in renal failure patients when the total population is taken into consideration. All eight groups including control and patients have almost similar behavior for serum calcium levels.

Seki, Makiko, et al. 2019 studied over a median follow-up of 25.8 months, 210 patients reached the renal endpoint. Multivariable Cox analysis revealed hazard ratios (HR) [95% confidence intervals (CI)] for the composite renal outcome: HRs of 1.36 (0.72–2.58), 1.87 (0.95–3.66), and 2.66 (1.23–5.76) in the second, third, and fourth BUN quartiles compared to the first quartile (P for trend < 0.01). Conversely, for calculated serum osmolality quartiles, HRs (95% CIs) for poor outcomes were 1.13 (0.69–1.87), 0.95 (0.58–

1.55), and 1.26 (0.78–2.03), with no significant trend (P = 0.39). Higher BUN quartiles were associated with an increased risk of end-stage renal disease alone, while calculated serum osmolality levels were unrelated to this outcome. Higher calculated serum osmolality levels, but not BUN levels, were associated with adverse renal outcomes independent of the GFR, suggesting that BUN may be a useful marker for predicting kidney disease progression.

The result of the present study serum blood urea nitrogen (BUN) level is found to be statistically significant in the total population except for the 1-40-year-old female age group. In all the normal-status subjects, the serum BUN level was 12.87 mg/dl, whereas in CRF, the concentration of circulatory BUN was 62.45 mg/dl. Serum BUN level was found to be greater in CRF subjects compared to the healthy normal. The difference was found statistically significant except female age group of 1-40 in which the serum calcium level was found 8.671 mg/dl in all the normal status subjects and 7.41 mg/dl in CRF subjects. Serum calcium was found to be low in CRF subjects compared to the healthy normal. The difference was found statistically non-significant in this group.

CONCLUSION

Renal failure correlates with heightened creatinine and BUN levels, highlighting their interconnection as biomarkers. Elevated BUN underscores disrupted protein metabolism in renal health, urging refined diagnostic and therapeutic strategies through further research.

LIMITATIONS

The study's limited, small, and similar sample size may limit applying findings broadly. Future research needs broader assessments with diverse biomarkers and patient profiles to refine renal disease approaches.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	Misbah Batool	Introduction write up.	
3	Najma Majeed	Lab tests.	
4	Zara Shoukat	Proofreading.	
5	Ahmad Munir Qureshi	Result Interpretation.	
6	Muhammad Shoaib	Referencing.	