A Study on Correlation Between Serum Creatinine, Estimated Glomerular Filtration Rate (EGFR), Calcium, Phosphorus, Uric Acid, Vitamin D, Parathyroid Hormone, and Alkaline Phosphatase in Patients with Chronic Kidney Disease

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ABSTRACT: Chronic kidney disease (CKD) is associated with abnormalities of mineral bone metabolism. These changes start early in early stages and they get worse with disease progression. The aim of the study was to understand the correlation between serum creatinine, eGFR, serum calcium, phosphorus, uric acid, vitamin D, PTH and alkaline phosphatase in CKD patients.

KEYWORDS: CKD, eGFR, PTH.

I. INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem and its management, by either dialysis or transplantation, imposes a considerable economic burden to health systems. Its prevalence is high and continues to increase, especially in developing countries. Studies have suggested that early diagnosis and treatment of modifiable CKD risk factors are important to prevent the progression to renal replacement therapy. Established predictors for development of CKD include high blood pressure and diabetes mellitus. Chronic kidney disease (CKD) is a known risk factor, not only for end-stage kidney diseases, but also for cardiovascular mortality and all-cause mortality. (7) Globally, the number of deaths from CKD has increased by more than 80% over the past 20 years. (8) Many factors, including low estimated glomerular filtration rate (eGFR), elevated proteinuria, diabetes, and hypertension have been identified as risk factors for the development and progression of CKD.

Kidney damage for 3 months as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, that can lead to decreased GFR, manifest by either:
• Pathological abnormalities; or
• Markers of kidney damage, including abnormalities in imaging tests
• GFR <60ml/min/1.73m² for 3 months, with or without kidney damage

Phosphorus is a mineral which combines with calcium to form the hard structure of your bones and teeth. It comes from the food that you eat. It is found in all cells in your body and is absorbed with help from Vitamin D. Calcium is
stored in your bones, and is essential along with phosphorus, vitamin D and PTH for building and keeping your bones healthy and strong.

Kidneys control the balance between calcium and phosphate in your body. It is important that the levels of phosphate and calcium in your blood remain normal. Patients with chronic kidney disease (CKD) have marked disruption in bone and mineral metabolism resulting in a complex disorder that has been termed CKD-mineral bone disorder (CKD-MBD).

II. RELATED WORK

The concept of biochemical alterations of CKD-MBD include elevated serum phosphate, and decreased serum calcium as well as heterogeneous bone disease and excessive vascular and soft tissue calcification. CKD-MBD is associated with an increased fracture risk and higher rate of cardiovascular events and cardiovascular-related deaths. Both negative and positive calcium balance pose potential health threats in CKD-MBD: negative balance may increase risk for osteoporosis and fracture, and positive balance may increase risk for extra skeletal calcification and cardiovascular events.

Calcium balance is relatively simple: it is whole-body calcium retention or deficit calculated by subtracting total body calcium losses from total calcium inputs. However, the physiological processes controlling calcium balance make it more complex, particularly in CKD. Decreased renal function interferes with the kidney’s ability to maintain fluid and electrolyte homeostasis. The ability to concentrate urine declines early and is followed by decrease in ability to excrete phosphorus, uric acid and potassium. Many studies have demonstrated that as renal function declines, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus, calcium and alkaline phosphatase.

Present study aims to evaluate the correlation between creatinine, calcium, phosphorus, uric acid, vitamin D, PTH and alkaline phosphatase in patients with chronic kidney disease presented to laboratory department of Ruby Hall Clinic.

III. AIM AND OBJECTIVES

1) To estimate serum creatinine in study subjects (cases and controls) and categorize them into various stages according to estimate glomerular filtration rate (eGFR) by using MDRD equation.
2) To estimate calcium, phosphorus, uric acid, vitamin D, PTH and alkaline phosphatase in chronic kidney disease patients and healthy individuals (controls).
3) To study correlation of creatinine, estimate glomerular filtration rate eGFR, calcium, phosphorus, uric acid, Vitamin D, PTH and alkaline phosphatase

IV. MATERIAL AND METHODS

Patient Group
In this study 50 patients with chronic kidney disease patients irrespective of cause were selected. Subjects for this study were randomly selected from patients coming to laboratory from January 2018 to February 2018 for investigations as prescribed by clinicians/nephrologists at Ruby Hall Clinic, Pune. Measurements of serum creatinine, calcium, phosphorus, uric acid, vitamin D, PTH and alkaline phosphatase were easily accepted by patients with chronic kidney disease.

Clinical information and data of these subjects were obtained like age, gender, weight, registration number, duration of disease and associated clinical conditions, etc. Among that both Males and Females were included. Total 25 healthy subjects were selected randomly to represent the control group with no history of any renal disease or symptoms.
Equipment:
1. Vitros5600 System
2. Cobas 6000 System
3. Pipettes
4. Sample dispensing tips
5. Sample cups

Serum Creatinine
1) COBAS 6000
This kinetic colorimetric assay is based on the Jaffé method. In alkaline solution, creatinine forms a yellow – orange complex with picrate. The rate of dye formation is proportional to the creatinine concentration in the specimen. The assay uses “rate -blanking” to minimize interference by bilirubin. To correct for non – specific reaction caused by serum/plasma pseudo – creatininechromogens, including proteins and ketones, the results for serum or plasma are corrected by 0.3 mg/dL.

Reaction Sequence
2) Vitros 5600
Method: Enzymatic (creatinineamidohydrolase).
The vitroscreat Slide is a multi-layered, analytical element coated on a polyester support.
A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. Creatinine diffuses to the reagent layer, where it is hydrolyzed to creatine in the rate-determining step. The creatine is converted tosarcosine and urea by creatineamidino hydrolase. The sarcosine, in the presence of sarcosine oxidase, is oxidized to glycine, formaldehyde, and hydrogen peroxide. The final reaction involves the peroxidase-catalyzed oxidation of a leuco dye to produce a colored product.
Following addition of the sample, the slide is incubated. During the initial reaction phase, endogenous creatine in the sample is oxidized. The resulting change in reflection density is measured at 2 time points.

V. RESULTS

1) Gender wise distribution of study cases and controls:
Total 75 subjects (case and controls) were included in the study, out of which 52 were males and 23 were females

2) Age wise distribution

<table>
<thead>
<tr>
<th>AGE IN YEARS</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>31-40</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>41-50</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>51-60</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>61-70</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>71-80</td>
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<td>3</td>
</tr>
<tr>
<td>81-90</td>
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<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>23</td>
</tr>
</tbody>
</table>

Table 1. Age and Gender Wise Distribution

Figure 1. Age and Gender Wise Distribution of Study Cases and controls
Maximum number of cases were of stage 5 (G5) i.e 29 (17 males and 12 females) as compared to G3 and G4 stages. It was 7 and 14 respectively.

<table>
<thead>
<tr>
<th>CKD stage</th>
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<tbody>
<tr>
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</tr>
<tr>
<td>G4</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>G5</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>21</td>
</tr>
</tbody>
</table>

Table No.2 Distribution of study cases as per CKD stages

This table shows distribution of cases and control subjects as per age and study parameters

Mean age in control group was 48.84 years and case group was 55.38 years
Mean serum creatinine in control group was 0.8 mg/dl and in case group was 5.5 mg/dl
Mean eGFR in control group was 98.6 whereas in case group it was 16.3 i.e on lower side.
Mean Calcium in control group was 9.47 as compared to 8.78 in case group.
Mean Phosphorus in control group was 3.31 as compared to 4.86 in case group.
Mean uric acid level in control group was 5.81 as compared to 7.69 in case group.
Mean vitamin D in control group was 27.64 whereas 19.45 in case group.
Mean PTH value in control group was 25.02 as compared to 441.9 in case group, means on higher side.
Mean alkaline phosphatase value in control group was 78.56 as compared to 172.4 in case group.

Statistical significane was noted in creatinine, eGFR, calcium, phosphorus, uric acid, PTH and alkaline phosphatase, though vitamin D showed no significance in between case and control group.

VI. CONCLUSION

Abnormalities of mineral bone metabolism are common in CKD patients. These abnormalities start in early stages of CKD and worsen with disease progression. In the present study the changes in the serum levels of phosphorus and PTH were significant in relation to the progression of the disease. There was not significant changes in calcium, uric acid and vitamin D in all study cases as patient may on treatment or maybe on supplements rich of calcium and vitamin D. Though in our study statistical significance was not noted with alkaline phosphatase, it was seen that it is increased in all 3 stages and it can be used as prognostic marker to guide treatment in patients with CKD and drug development to reduce vascular wall calcification to reduce morbidity due to cardiovascular disorder in CKD patients.

VII. FUTURE SCOPE

In developing countries, due to lack of proper infrastructure and laboratory setups, most of the patients lack proper diagnosis. Physicians have to rely on clinical findings for diagnosis. With development of cost effective estimate of calcium, phosphorus, alkaline phosphatase, uric acid, PTH and vitamin D and their usefulness in in diagnosis and prognosis of kidney disease can be found out. This can prevent morbidities and mortality due to kidney disease and
associated conditions. Though its proven fact, with modification of diet, lifestyle and proper nutrition the effect of chronic kidney disease can be prolonged which can reduce dependence of patient on dialysis.

REFERENCES


