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ORIGINAL ARTICLE

STUDY OF RENAL OSTEODYSTROPHY IN CHRONIC KIDNEY DISEASE

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ABSTRACT:
The kidney plays an important role in the mineral metabolism; in addition to being a target organ for various hormones involved in calcium and phosphorus metabolism, the kidney is the main organ that activates vitamin D. Thus, it is quite understandable that kidney dysfunction can result in derangement of mineral metabolism. Ever since the first report of severe osteitis fibrosa cystica with parathyroid hyperplasia, this disorder was considered to be a skeletal/bone disease and was named "renal osteodystrophy". The clinical management of renal osteodystrophy, therefore, primarily aimed to maintain parathyroid hormone (PTH) levels appropriate for normal bone metabolism. Traditionally, when defining bone diseases in CKD patients, this group of disorders has been usually termed renal osteodystrophy. However, beside strictly defined, the term renal osteodystrophy means only bone abnormalities. Recently, the KDIGO (Kidney Disease: Improving Global Outcomes) [(1)] conference group agreed that the definition of renal osteodystrophy should be only specific to bone pathology found in patients with CKD. It has been concluded that renal osteodystrophy is one component of the mineral and bone disorders that occur as a complication of CKD. It has been proposed that the evaluation and definitive diagnosis of renal osteodystrophy requires performing a bone biopsy. Histomorphometry is not essential for clinical diagnosis, but should be performed in research studies.
Key words: Chronic kidney disease, Osteodystrophy, Renal

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INTRODUCTION

Kidney is one of the most important organs in the regulation of mineral metabolism.[(1)] Chronic kidney disease (CKD) is a worldwide public health problem that affects 5% to 10% of the world population, with increasing prevalence and adverse outcomes, including progressive loss of kidney function, cardiovascular disease, and premature death.[(1)] The prevalence of chronic kidney disease (CKD) is increasing in the worldwide population.[(2)] The kidney and the skeleton have intimate biological relationships that can affect bone strength as well as renal physiological functions. [(3)]

Both intrinsic primary renal diseases such as diabetic nephropathy, as well as changes in renal function associated with the aging-kidney, affect systemic (including bone) metabolism which, in the case of skeletal interactions with the kidney, can lead to a heterogeneous group of bone diseases all of which are associated with skeletal fragility and increased risk for fractures.[(4)]

Chronic kidney disease, also known as chronic renal failure, chronic renal disease, or chronic kidney failure, is defined as a slow progressive loss of kidney function over a period of several years. Eventually the patient has permanent kidney failure.[(5)] Chronic kidney disease is much more common than people realize, and often goes undetected and undiagnosed until the disease is well advanced and kidney failure is fairly imminent. It is not unusual for people to realize they have chronic kidney failure only when their kidney function is down to 25% of normal. As kidney failure advances and the organ's function is seriously impaired, dangerous levels of waste and fluid can rapidly build up in the body. Mineral and bone disorders are complex abnormalities that cause morbidity and mortality in patients with CKD. In order to raise awareness of the systematic manifestations of mineral and bone disorders, KDIGO established a new term 'chronic kidney disease– mineral and bone disorder' (CKD–MBD) to describe the syndrome of biochemical, bone, and extra-skeletal calcification abnormalities that occur in patients with CKD. The term renal osteodystrophy should be used exclusively to define alterations in bone morphology associated with CKD, assessed by bone biopsy

with or without histomorphometry. The results of the biopsies should be reported based on a classification system that includes parameters of turnover, mineralization, and volume. [7]Based on all of this a new term has been proposed and coined "Chronic kidney disease – mineral and bone disorder (CKD-MBD)" willing to describe the systemic consequences of mineral metabolism disturbances in CKD patients which can no longer be considered restricted only to bone disease. [1]

CKD-MBD defines a triad of interrelated abnormalities of serum biochemistry, bone and the vasculature associated with CKD. The adverse effects of high serum phosphorus and an increase of serum calcium due to calcium overload which are present late in CKD are important component of CKD-MBD as well as vascular changes. Furthermore, to clarify the interpretation of bone biopsy results in the evaluation of CKD-MBD, it has been proposed to use three key histologic descriptors—bone turnover, bone mineralization, and bone volume (so called TMV system)— with any combination of each of the descriptors possible in a given specimen. The TMV classification scheme provides a clinically relevant description of the underlying bone pathology, as assessed by histomorphometry, which, in turn, helps to define the pathophysiology, and, thereby, probably to guide the therapy. [1]

Recent evidence suggests that the traditional syndromes known as renal osteodystrophy, secondary hyperparathyroidism, and vitamin D deficiency are related to mortality in persons with moderate to advanced chronic kidney disease (CKD). The so-called 'kidney bone disease', also known as 'mineral and bone disorders', is defined to include bone disorders, mineral disarrays, and vascular calcification. [8]

AIM

To study renal osteodystrophy in chronic kidney disease patients.

OBJECTIVES

1. To study the changes in serum calcium serum phosphorus, serum alkaline phosphatase levels in chronic kidney disease.
2. To study the bone changes on X-ray in cases of chronic kidney disease.
3. To find out the prevalence and nature of skeletal involvement in chronic renal failure and to associate the severity of skeletal involvement with the duration of chronic kidney disease.

To associate the serum calcium profile changes and bone changes on x-ray with the clinical severity of renal bone disease.

MATERIAL AND METHODS

Study design: It was a observational prospective type of study

Study area: Department of Medicine, D.Y. Patil Medical College and Hospital Kolhapur.

Study setting: Outpatient department of Medicine of tertiary care hospital. Registration of patients was from May 2014 to August 2016. They were registered when admitted under Medicine department. At the time of registration the patients with exclusion criteria were not enrolled for study. The main objective of this study was to study the changes in serum calcium serum phosphorus, serum alkaline phosphatase levels in chronic kidney disease. To study the bone changes on X-ray in cases of chronic kidney disease. To find out the prevalence and nature of skeletal involvement in chronic renal failure and to associate the severity of skeletal involvement with the duration of chronic kidney disease and to associate the serum calcium profile changes and bone changes on x-ray with the clinical severity of renal bone disease. At the time of registration the baseline information was taken especially with respect to sociodemographic factors, clinical findings, and other investigations. Thus each & every patient was followed up in Medicine department till discharge. The data thus collected was analyzed to study of renal osteodystrophy in chronic kidney disease.

Study period: May 2014 to August 2016

Sample size: 50 patients having inclusion criteria were considered.

Study participant: Patients having chronic kidney disease and having inclusion criteria.

Inclusion criteria:

Patients those who are diagnosed to have chronic kidney disease according to National Kidney Foundation.

Willing to participate

Exclusion criteria

1. Patients presenting with acute kidney injury
2. Senile osteoporosis (age > 65 years).
3. K/C/O Parathyroid disease**.**
4. Patients below age of 18 years

Sampling technique: Simple random sampling

Data collection:

Written informed consent was taken from the participants. Patients coming to Medicine department and having inclusion criteria were included in the study. Pre designed Proforma consisting of standard questions related to socio demographic factors, addiction and so on, were interviewed. In addition, questionnaire also included questions on past and present medical history and health seeking behaviour.

Following main domains were covered in questionnaire:

i) Urine analysis
ii) Blood analysis
iii) X ray findings

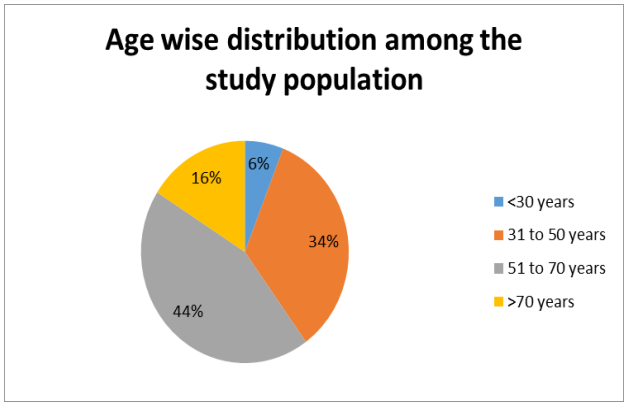
RESULTS

In the present study, CKD patients with grade I medico renal disease had bone changes (22%) compared to patients with grade II medico renal disease (52%). Thus the incidence of bone changes increased with the increase in

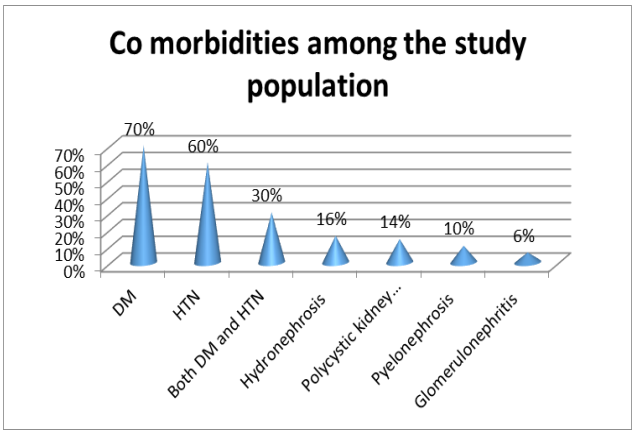
radiological severity of renal disease, which was statistically significant.

Grade I included renal parenchymal disease with small size kidney and among them 7 had unilateral involvement and 13 had bilateral involvement of kidney. Grade II included enlarged smooth kidney with hydronephrosis. Present study showed that as duration of disease increased the severity also increased. P value was statistically significant.

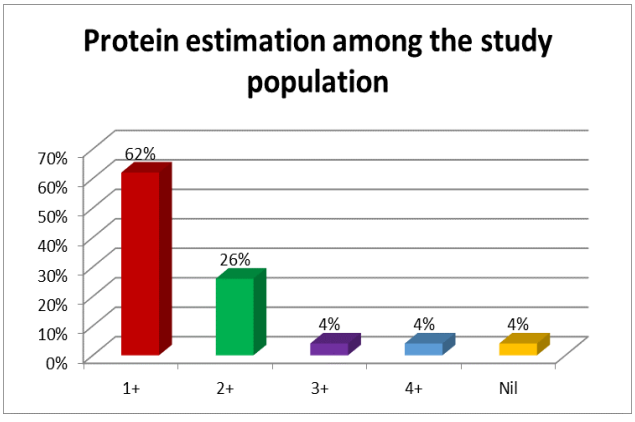
Graph 1: Age wise distribution among the study population



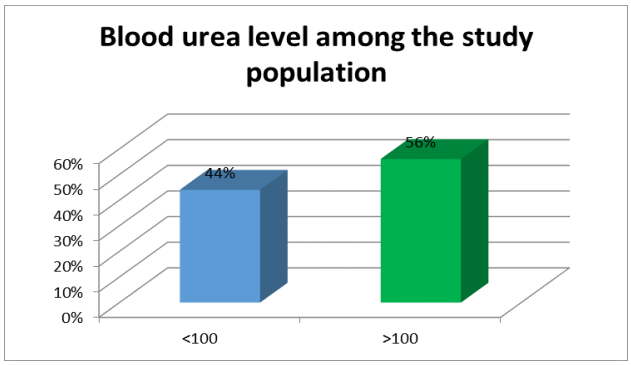
Graph 2: Co morbidities among the study population



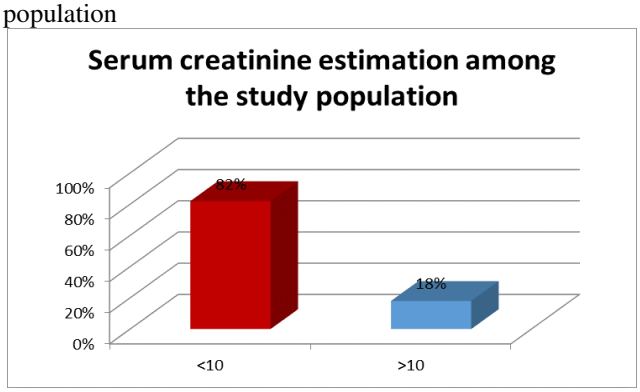
Graph 3: Protein estimation among the study population



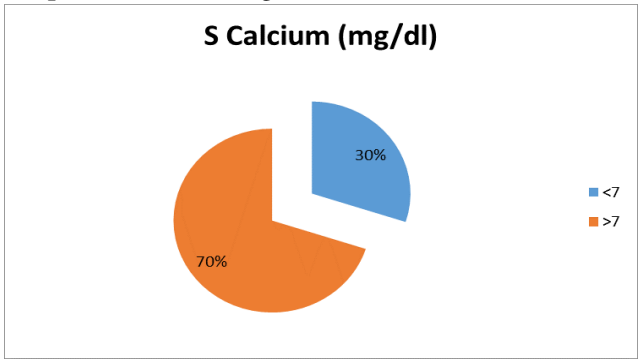
Graph 4: Blood urea level among the study population



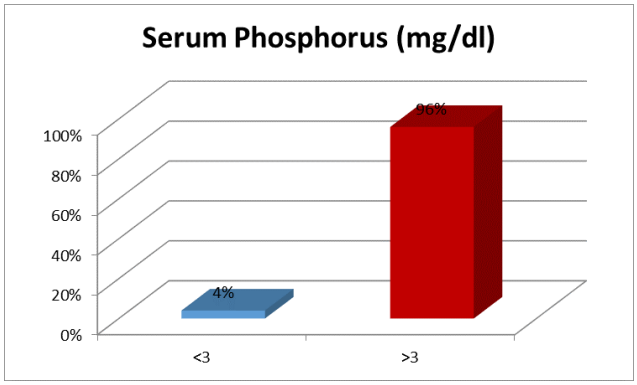
Graph 5: Serum creatinine estimation among the study population



Graph 6: S Calcium (mg/dl)

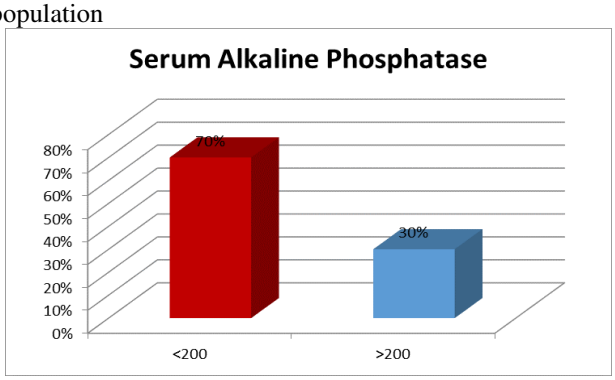


Graph 7: Serum Phosphorus (mg/dl) among the study population

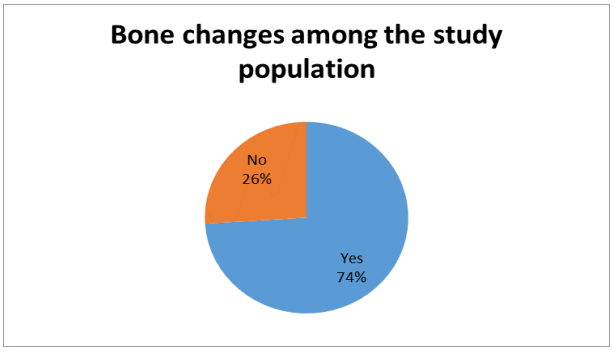


Mean was 167.18 ± 100.7

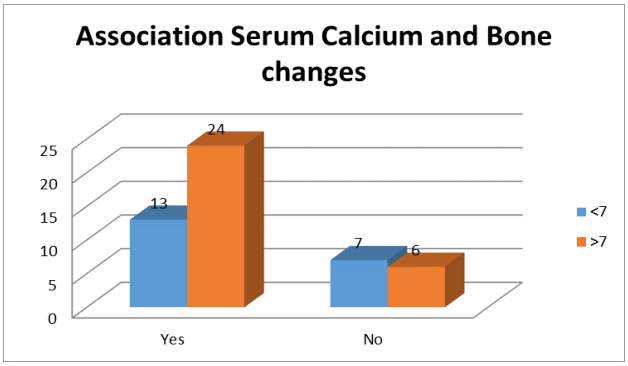
Graph 8: Serum Alkaline Phosphatase among the study population



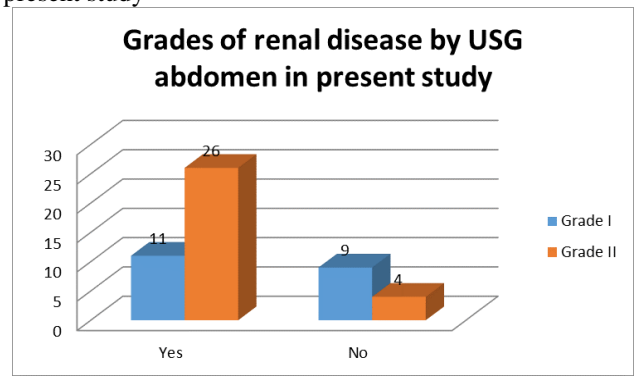
Graph 9: Bone changes among the study population



Graph 10: Association Serum Calcium and Bone changes



Graph 11: Grades of renal disease by USG abdomen in present study



DISCUSSION

Age wise distribution

Mean age was 55.88 ± 14.58 years

In a study by Carlos Perez Gomes et al[9] mean age of the studied population was 61 ± 14 years

Gender wise distribution

In a study by Carlos Perez Gomes et al[9] gender distribution was 54% men and 46% women while this study had 62% males.

Co morbidities

In our study, majority 60% had HTN, 70% had DM, and 30% had both.

In a study by Carlos Perez Gomes et al there was hypertension 39%, diabetes mellitus 23%, polycystic kidney disease 9%, primary glomerulopathy 6%, chronic pyelonephritis 3% and others 5%.

Findings on general examination

In our study, all had pallor and edema.

Bone tenderness among the study population

Study by Rizvi et al showed that 89.55% had bone tenderness.Another Study by Scialla JJ et al showed that 40% had bone pain,while this study found 56% prevalence of bone tenderness in patients.[10, 11]

Investigations:

Study by R.Freethi et al[12] had mean serum creatinine of 4.9 ± 2.23 while this study had higher mean creatinine level of 7.14 ± 4.29 .

Study by R.Freethi et al[12] summarised that there is derangement of mineral metabolism secondary to mineral bone disease in patients with CKD evident from hyperphosphatemia and hypocalcemia in patients. There is also a significant increase in alkaline phosphatase levels in patients with CKD. All these parameters were found to worsen with increase in the stage of CKD highlighting the higher risk of lethal complications secondary to impaired metabolism in patients with poorer renal function.

Mean S Alk Phosph. in a study by Spasovski et al[10] was 91 .

Mean S Alk Phosph. in a study by Coen.et al[9] was 117 ± 38.8 & in a Study by Samina S Khna et al[8] was 269±858.The mean level in the present study were 167.18 ± 100.7.

ALP is a hydrolyze enzyme that dephosphorylates various molecules, most effectively operating in an alkaline environment. ALP is fairly ubiquitous in the human body, but it is especially concentrated in the bone, liver placenta, leukocytes and kidneys. ALP is produced by osteoblasts in bone tissue in response to decreased calcium levels and plays an important role in bone mineralization by hydrolyzing pyrophosphate in the extracellular milieu. ALP is a biochemical marker of bone turnover and is used to monitor the metabolic bone disease associated with renal insufficiency. Elevated ALP levels can be seen with worsening magnitude of bone turnover with the rate of elevation a reliable marker of severity of the high turnover osteodystrophy. The processes of bone absorption and

resorption are closely regulated in healthy individuals. Renal osteodystrophy arises as a consequence of bone remodelling dysregulation.[7- 9] This study showed increased serum calcium with increasing bone changes. Similar findings were present in R. Freethi et al [12] where it was seen that increase in serum calcium level shows increase in bone changes.

CONCLUSION

Clinically evident symptomatic bone disease was noticed in 74% of cases in the present study. Symptomatic skeletal involvement suggests osteomalacia rather than secondary hyperparathyroidism.

Renal bone disease is an important consequence of chronic kidney disease. Frequent monitoring of the plasma concentration of calcium, phosphate and parathyroid hormone is essential to minimize complications. Despite improvement in diagnostic imaging (bone density measurements), determination of biomarkers, mainly parathyroid hormone, still plays a central role. Treatment includes dietary advice and titrated doses of oral phosphate binders such as calcium salts, vitamin D analogues, sodium bicarbonate and cinacalcet. Dialysis is beneficial for patients with end-stage renal failure. Early referral to a nephrologist to guide monitoring and treatment is recommended.

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