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RESEARCH ARTICLE

FREQUENCY OF HYPOCALCAEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: Chronic kidney disease is a major public health problem worldwide. Kidney failure is becoming increasingly common and is associated with poor health outcomes and high medical expenditures.
Objective: To determine the frequency of hypocalcemia among patients with chronic kidney disease.
Setting: Department of General Medicine, Hayatabad Medical Complex, Peshawar.
Duration of study: Six months 6/5/2019 to 6/11/2019.
Study design: Cross sectional study.
Materials and Methods:
Total 194 patients were included in the study. Detail history, clinical examination and laboratory investigation was preformed for the confirmation of CKD. From all the patients at admission, 3cc of blood was obtained under strict aseptic technique and was immediately sent to hospital laboratory to detect hypocalcaemia and hypocalcaemia was considered positive if the serum corrected calcium level <8.5mg/dL.
Results: Stages of CKD was analyzed as 17(9%) patients had CKD stage 1, 29(15%) patients had stage 2, 54(28%) had stage 3, 51(26%) had stage 4, 43(22%) had stage 5 respectively. More over 50(26%) patients had hypocalcemia while 144(74%) patients didn't.
Seventy four 74(38%) patients had duration of CKD ≤ 6 months while 120(62%) patients had duration of CKD >6 month. Mean duration of CKD was 7 months with standard deviation ± 3.78. One hundred and forty 140 (72%) patients had weight ≤80 Kgs while 54(28%) patients weight >80 Kgs. Mean weight was 76 Kgs with standard deviation ± 15.29.
Conclusion: Frequency of hypocalcemia was found about 26% in patients with chronic kidney disease.

Introduction:-

Chronic kidney disease (CKD) is defined as a slow and progressive kidney damage leading to Glomerular filtration rate below 60 mL per minute per 1.73 m^2 for three months or more[1]. It is a major public health problem worldwide. In the United States, kidney failure is becoming increasingly common and is associated with poor health outcomes and high medical expenditures.[2] The number of patients suffering from chronic kidney disease in United States is

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growing rapidly and is expected reach 71 million by 2030[3]. A study conducted in Karachi Pakistan showed a prevalence of moderate CKD (GFR <60) to be 5% among people aged 30 years or above[4].

The most common causes of CKD are diabetes mellitus, hypertension, and glomerulonephritis. Together, these cause approximately 75% of all adult cases[5]. Other rare causes are Infective, obstructive and reflux nephropathies, family history of CKD or hereditary kidney disease e.g. polycystic kidney disease, hypercalcemia and multisystem diseases with potential kidney involvement like systemic lupus erythematosis, neoplasms and myeloma accounts for 15-20% .[6] The presence of chronic kidney disease confers a markedly increased risk of cardiovascular disease, and people with CKD often have other risk factors for heart disease, such as hyperlipidemia.[7]

Intuitively, it would be expected that high serum calcium concentrations contribute to rapid kidney function deterioration, due to precipitation of calcium-phosphorus product in vessels causing vascular calcifications, or to acute effects of hypercalcemia. Preceding studies used a composite outcome of progression (50% decline or eGFR slope >−5 mL/min/1.73 m2 plus initiation of renal replacement therapy [RRT]), and did not investigate the absolute change in kidney function for each CKD stage. In one study the frequency of hypocalcemia was 23.8% in patients with CKD.[8-10]

The frequency of hypocalcaemia in chronic kidney disease may vary due to different socioeconomic status, living standard, residence of the patients so as no such study has been conducted in our population. The aim of this research is to determine the frequency of hypocalcaemia among patients with chronic kidney disease (CKD) and the results of our study will open more ways towards research about the risk factors of hypocalcaemia among CKD patients and effect of its supplementation.

Materials And Methods:-

This cross sectional study was carried out at Department of General Medicine, Hayatabad Medical Complex Peshawar from 6-5-2019 to 6-11-2019. Total 194 patients having age ranged 30-60 years presenting with chronic kidney disease of stage 1-5 with duration >3 month were included in the study. Patients with known hypoparathyroidism, pancreatitis and those who underwent total thyroidectomy (on the basis of history and lab investigations) were excluded from the study. Written informed consent was obtained from all patients after explaining them the purpose and benefits of the study. At the time of admission, 3cc blood was obtained from all patients under strict aseptic technique and was immediately sent to hospital laboratory to detect hypocalcaemia. All the above mentioned information was recorded on pre design proforma. Exclusion criteria were strictly followed to control bias in study results.

All the data was analyzed in SPSS version 27.0. Mean + standard deviation were calculated for continuous variables like age, weight, duration of CKD. Frequency and percentages were calculated for categorical variables like gender, stages of CKD, hypocalcemia. Hypocalcemia was stratified among the age, weight, gender, duration of CKD and stage of CKD to see the effect modifications. Post stratification chi square test was applied. P value of < 0.05 was considered significant.

Results:-

Total 194 patients were included. Age ranged between 30-60 years, mean age 45 years with standard deviation of ± 11.90. Out of 194, 114(59%) patients were male and 80(41%) were females.

Age distribution was analyzed as 35(18%) patients were in age range 30-40 years, 81(42%) patients were in age range 41-50 years and 78(40%) patients were in age 51-60 years.

Stages of CKD was analyzed as 17(9%) patients had CKD stage 1, 29(15%) patients had stage 2, 54(28%) had stage 3, 51(26%) had stage 4, 43(22%) had stage 5 respectively. (Figure I). More over 50(26%) patients had hypocalcemia while 144(74%) patients didn't. (Figure II)

Seventy four 74(38%) patients had duration of CKD ≤ 6 months while 120(62%) patients had duration of CKD >6 month. Mean duration of CKD was 7 months with standard deviation ± 3.78. (Table 1).

One hundred and forty 140 (72%) patients had weight ≤80 Kgs while 54(28%) patients weight >80 Kgs. Mean weight was 76 Kgs with standard deviation ± 15.29. (Table II)

Figure 2:- Stages of Chronic Kidney Disease (CKD) (n=194).

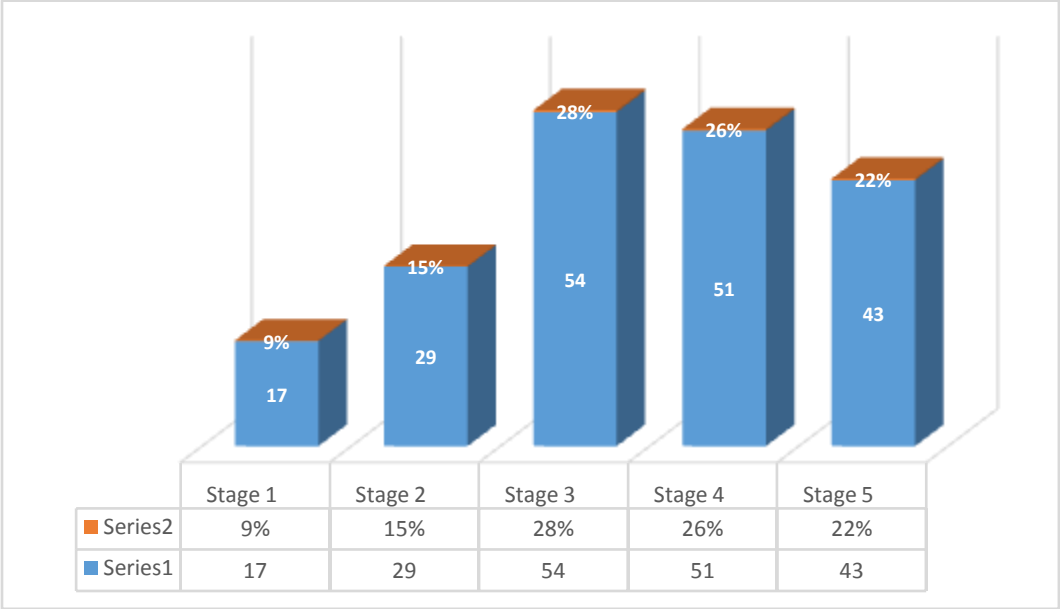

Figure II:- Hypocalcemia status.

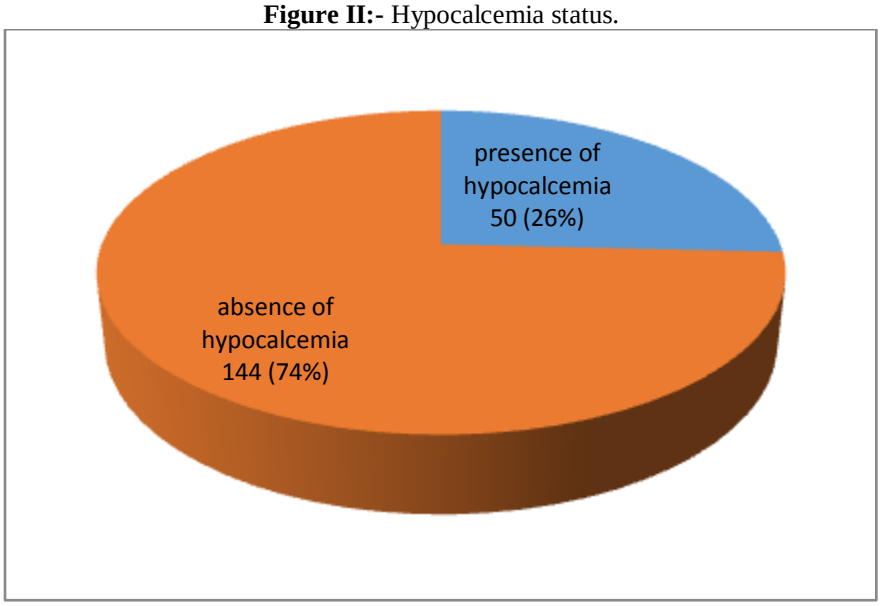

Table I:- Duration of chronic kidney disease (CKD) n=194.

Duration	Frequency	Percentage
≤ 6 month	74	38%
>6 month	120	62%
Total	194	100%

Mean duration ± SD = 7 months ± 3.78

Table II:- Weight distribution of chronic kidney disease (CKD) patients (n=194).

Weight	Frequency	Percentage
≤ 80 Kgs	140	72%

>80 Kgs	54	28%
Total	194	100%

Mean weight ± SD = 76 Kgs ± 15.29

Discussion:-

Chronic kidney disease leads to a decrease in the conversion of 25-hydroxyvitamin D to its active form 1,25-dihydroxyvitamin D, particularly when the glomerular filtration rate (GFR) falls below 30 mL/min. This results in an increase in PTH.[11] Ultimately, the increased absorption of phosphorus and calcium can lead to calcium-phosphorus mineral deposition in the soft tissues. In the early stages of renal failure, hypocalcemia can occur because of the decrease in calcitriol production and a subsequent decrease in the intestinal absorption of calcium.[12]

Our study shows that more over 50% patients had hypocalcemia while 74% patients didn't had hypocalcemia. Similar results were observed in another study conducted by Vikrant S et al in which a total of 462 patients of CKD Stage 3–5D were studied.[13] The frequency of various biochemical abnormalities was hypocalcemia (23.8%), hypercalcemia (5.4%), hypophosphatemia (2.8%), hyperphosphatemia (55.4%), raised alkaline phosphatase (56.9%), secondary hyperparathyroidism (82.7%), and hypoparathyroidism (1.5%).

Nondiabetic CKD patients as compared to diabetic CKD had a higher alkaline phosphatase (**P** = 0.016), a higher iPTH (**P** = 0.001) a higher proportion of patients with iPTH above KDOQI target range (**P** = 0.09), and an elevated alkaline phosphatase (**P** = 0.004).[13,14] The 25OHD levels were suggestive of severe Vitamin D deficiency in 33.7%, Vitamin D deficiency in 45.4%, and Vitamin D insufficiency in 11.3% patients. There was a significant positive correlation between iPTH with alkaline phosphatase (**r** = 0.572, **P** = 0.001), creatinine (**r** = 0.424, **P** = 0.001), and phosphorus (**r** = 0.241, **P** = 0.001) and a significant negative correlation with hemoglobin (**r** = −0.325, 0.001). On multivariate logistic regression analysis, an elevated alkaline phosphatase was a significant predictor of hyperparathyroidism (odds ratio 9.7, 95% confidence interval 4.9–19.2, **P** = 0.001).[15,16]

Schwarz et al found no association between calcium and CKD progression in CKD stage 1–5 patients.[17] Lim et al reported low serum calcium to be associated with a faster kidney function decline in a pooled cohort of CKD stage 3–4 patients.[18] Another study conducted by Jalleh R et al had reported that eight patients (52-85 years of age) with stage 4-5 CKD developed clinically significant hypocalcaemia (corrected calcium 1.45±0.21mmol/L) following denosumab therapy for osteoporosis.[19] Seven of the eight patients required inpatient management with three patients requiring intravenous calcium replacement and cardiac monitoring in a high dependency unit. Our study also identified additional factors that could potentially contribute to hypocalcaemia such as lack of calcium supplementation, use of non-calcium based phosphate binders, absence of or use of lower doses of calcitriol supplementation, low vitamin D levels, concomitant treatment with loop diuretics, history of parathyroidectomy, or presence of acute medical illness. Multiple cases of severe hypocalcaemia in CKD patients following denosumab exposure were encountered after TGA warnings, resulting in considerable morbidity and intensive healthcare interventions in CKD patients.[20]

We advocate greater awareness amongst the medical profession, careful consideration before using denosumab in CKD patients, and close follow-up after administration to prevent morbidity.

Conclusion:-

Chronic renal failure are most frequently associated with hypocalcemia in our setup. Hypocalcemia is also associated with other disorders like infectious diseases, acid-base disorders, maliganancies, and miscellaneous diseases which include acute pancreatitis, magnesium deficiency, aplastic anaemia, diabetes mellitus and hypertension. The lowest calcium levels were found in hypoparathyroidism and there was significant difference in means of the calcium levels in various disorders causing hypocalcemia

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