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STUDY ON VITAMIN D LEVELS IN CHRONIC KIDNEY DISEASE PATIENTS.

KEYWORDS

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ABSTRACT

BACKGROUND: *1, 25-dihydroxyvitamin D [1, 25(OH)$_2$D] is the major steroid hormone involved in mineral ion homeostasis regulation. According to various studies published, there is widespread prevalence of varying degrees (50- 90%) of Vitamin D deficiency with low dietary calcium intake in Indian population.*

AIM & OBJECTIVE OF STUDY: *The aim of the study is to estimate the prevalence of vitamin D deficiency in patients with Chronic Kidney disease (e-GFR <60ml/min).*

STUDY DESIGN: *Cross sectional observational study.*

MATERIALS AND METHODS: *Patients attending the outpatient department or admitted to Nephrology ward of Gandhi Hospital in the period between Jan 2015 and Dec 2015 were examined by history, physical examination and the relevant baseline investigations were done. Fifty patients found eligible were enrolled into the study. Chronic Kidney Disease was diagnosed by KDIGO (2012) criteria.[1] In order to eliminate the effect of differences in dietary habits or socioeconomic strata, subjects to the control group were drawn from within the CKD patient family and friends. An informed consent is taken from both cases and controls.*

STATISTICAL ANALYSIS: *Data analysed using the Statistical Package for Social Science (SPSS) software version19.Student T test is applied for comparisons of vitamin D and calcium levels in cases and controls.*

ANOVA test is applied for comparison variable among three CKD cohorts. A P value of < 0.05 is taken as significant.

RESULTS: *Average vitamin D levels among CKD subjects is 15.74 + 7.7ng/ml.Average serum calcium level among CKD patients is 8.74(+ 0.77)mg/dl where as in control it is 8.97 (+ 0.51)mg/dl .In CKD patients serum Phosphorus level and serum Alkaline Phosphatase are 4.8 (+ 1.30) mg/dl and 191.52 (+72.81)mg/dl respectively.*

Average i PTH levels in CKD patients is 230.07 (+ 138.6) pg/ml, which is above normal range.

CONCLUSIONS: *Prevalence of vitamin D deficiency significantly increases as CKD progress. Vitamin D deficiency more prevalent among CKD patients with Diabetes. There is inverse relation between vitamin D and iPTH levels in CKD population*

INTRODUCTION:

Vitamin D and its metabolites are major steroid hormone and hormone precursors rather than vitamins, involved in mineral ion homeostasis regulation since in the proper biologic setting, they can be synthesized endogenously. In response to ultraviolet radiation of the skin, a photochemical cleavage results in the formation of vitamin D from 7-dehydrocholesterol. Cutaneous production of vitamin D is decreased by melanin and high solar protection factor sun blocks, which effectively impair skin penetration by ultraviolet light.

Vitamin D2 (plant source) and vitamin D3 (animal source) have equivalent biologic activity and are activated equally well by the vitamin D hydroxylases in humans. After conversion to calcidiol, there appears to be no difference in the biologic activity of D2 and D3. Calcidiol is then converted in the kidney to 1,25(OH)2D by the action of CYP27B1(1-alpha-hydroxylase) in proximal convoluted tubule cells of the kidney. CYP27B1(1-alpha-hydroxylase) tightly regulated cytochrome P450–like mixed-function oxidase expressed in the proximal convoluted tubule cells of the kidney. PTH and hypophosphatemia are the major inducers of this microsomal enzyme, whereas calcium, FGF23, and the enzyme's product, 1, 25(OH)$_2$D, repress it. This active metabolite is also degraded by another kidney enzyme, 24,25-hydroxylase compound. However, this same 24,25 hydroxylase also hydroxylates 25(OH)D, yielding 24,25(OH)$_2$D. Although more than 40 vitamin D metabolites have been identified, the predominant effects of vitamin D in the body are exerted through the actions of 1,25(OH)2 D (calcitriol).[1,2,3]

There seem to be several mechanisms involved in the decreased levels of 1,25 dihydroxy vitamin D that occur in the course of kidney disease . Decrease in renal mass will obviously limit the quantities of 1-alpha-hydroxylase that are available for production of the active vitamin D metabolite. *The importance of a declining GFR in limiting the ability of the kidney to produce 1 to25-dihydroxyvitamin D was illustrated by the work of Nykjaer et al.*[4,5,6] After glomerular filtration of 25-hydroxyvitamin D, bound to vitamin D–binding protein, undergoes uptake into the proximal tubule cell by the receptor megalin and is the rate-limiting step in the delivery of 25-hydroxyvitamin D to the 1-alpha-hydroxylase enzyme. Accordingly, as GFR declines, there is a limitation of substrate delivery that can compromise the ability of the failing kidney to produce 1,25-dihydroxyvitamin D.[7,8] A reduction in GFR may limit delivery of substrate to the 1-alpha-hydroxylase, which may also limit the ability of the kidney to produce 1,25-dihydroxy vitamin D.

The recent discovery that FGF-23, which increases in the course of kidney disease, can directly suppress 1-alpha-hydroxylase may be an additional contributing factor that limits the ability of the failing kidney to maintain levels of 1,25-dihyroxy vitamin D as kidney disease progresses[9,10]. An additional factor that may be involved is the potential for N-terminally truncated PTH fragments or C-

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terminal PTH fragments to decrease activity of 1-alpha-hydroxylase .

MATERIALS AND METHODS

Patients attending the outpatient department or admitted to Nephrology ward of Gandhi Hospital in the period between Jan 2015 and Dec 2015 were examined by history, physical examination and the relevant baseline investigations were done. 50 patients found eligible were enrolled into the study. Chronic Kidney Disease was diagnosed by KDIGO (2012) criteria.

Inclusion criteria-Patients who were diagnosed to have Chronic Kidney Disease patients with e-GFR < 60ml/min (MDRD formula) in department of Nephrology, Gandhi Hospital and patients with-Cirrhosis of Liver, Morbid obesity- BMI ≥30, Malabsorption, Patients on anti epileptics, Diabetes Mellitus type 1 and 2,taking vitamin D and calcium supplements are excluded.

RESULTS & DISCUSSION:-

In our study 29 (15 deficient+14 insufficient) out of 50 controls had vitamin D deficiency, that accounts for 58% of healthy controls.

The major finding is the extremely high prevalence of vitamin D deficiency in CKD patients and also in controls. In our study incidence of hypovitaminosis D (92%) (insufficient + deficient) among CKD subjects and among healthy controls 58%.

In CKD subjects much lower levels are noted. In CKD group only 8% have normal (>30ng/ml) vitamin D, 68% are vitamin D deficient (< 20ng/ml) and 24% of are insufficient levels. In our study average vitamin D levels among CKD subjects is 15.74 + 7.7ng/ml [table-1].

In healthy controls also only 42% people have sufficient levels of vitamin D (>30ng/ml), 28% of have Vitamin D deficiency (< 20ng/ml) and 30% of control have insufficient levels of Vitamin D (20-30ng/ml).

Overall levels of vitamin D are much lower in CKD subjects compared to their family members and CKD patients are significantly more likely to have severe vitamin D deficiency. The average vitamin D levels among controls is 26.07ng/ml and CKD subjects 15.74ng/ml, which is a statistically significant (<0.001). Among three cohorts of CKD average vitamin D levels are decreasing as CKD stage progresses (21.75ng/ml, 15.89ng/ml, 12.07ng/ml in CKD stage 3, stage 4, stage 5 respectively [table-2]. Among cohorts also difference in vitamin D levels statically significant (<0.001)

In our study CKD population and controls are matched for sexual distribution. Among CKD subjects 5.7% male and 13.3% female subjects have adequate vitamin D levels. 22.9% male and 26.7% female subjects have insufficient levels. 71. 4% male and 60% female have vitamin D deficiency. In controls 42.9% male and 40% female have normal levels. 57.1% male and 60% female have hypovitaminosis D.

As we noted in controls more number of female tend to have hypovitaminosis D. Among CKD subjects in our study more number of male have hypovitaminosis compare to female (94.3% male Vs 86.7% female).

In our study average eGFR in control is 101.82(+ 12.27) and CKD group 22.62 (+16.15) which is statistically significant (p<0.001)

In our study average viatamin D level in Diabetics with CKD is 14.97 +7.93 ng/ml and non diabetics with CKD 16.03 +7.42 ng/ml.

In our study average levels of iPTH in CKD patients is 230.07 +138.6 pg/ml. there is inverse relation between vitamin D and iPTH levels as CKD progresses. In this study iPTH levels among CKD three cohorts are 142.87 +72.78 pg/ml(stage 3), 209.18 +65.46 pg/ml (stage 4) and 309.38 +125.92 pg/ml (stage 5)[table-3].

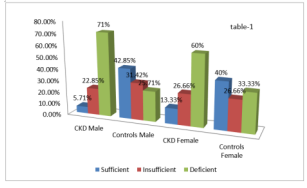
In our study average levels of serum calcium level among CKD patients is 8.74 (+ 0.77)mg/dl and controls is 8.97 (+ 0.51)mg/dl not significant statistically (p<0.081). Average serum Phosphorus level among CKD patients is 4.8 (+ 1.30) mg/dl.Average serum Alkaline phosphatase in CKD subjects is 191.52 (+72.81)mg/dl.

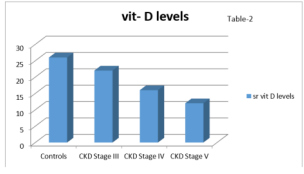
CONCLUSIONS:

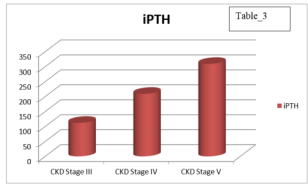
Prevalence of vitamin D deficiency in CKD patients (92%) and healthy population (58%) are significantly higher. Vitamin D deficiency has no significant differences between sexes, though females have more vitamin D deficiency than males, probably because of social factors. Prevalence of vitamin D deficiency significantly increases as CKD progress. Vitamin D deficiency more prevalent among CKD patients with Diabetes.

There is inverse relation between vitamin D and iPTH levels in CKD population

Low serum calcium levels and low Serum Albumin levels in advanced CKD patients, probably because of malnutrition and inflammation. serum Phosphorus and serum ALP increase significantly in advanced CKD.







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