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Research Article

FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH CHRONIC KIDNEY DISEASE PRESENTING AT SIUT KARACHI

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Abstract:

OBJECTIVE: To conclude the frequency of Calciferol (Vitamin D) insufficiency in subjects with CKD (Chronic Kidney Disease) presenting at SIUT Karachi.

METHODOLOGY: One hundred patients of both genders visiting Department of Nephrology, SIUT (Sindh Institute of Urology and Transplantation), Karachi, from January 2015 to July 2016, aged above eighteen years with chronic kidney disease underwent Vitamin D levels investigation, and 5 ml of venous blood sample was sent to pathology laboratory for the analysis of Vitamin D, and patients with a level of less than 20 ng/ml was taken as deficient. The data was collected at pre-designed pro forma and SPSS (version 20.0) was used for data analysis. Chi-square test connected as the trial of noteworthiness.

RESULTS: 83% out of total 100 patients with CKD have Vitamin D deficiency.

CONCLUSION: Chronic kidney disease is the usual cause of Vitamin D insufficiency (83%); low socioeconomic status (63%) composes a significant number of cases.

Key Words: Vitamin D deficiency, Chronic Kidney Diseases, Rickets, Osteomalacia.

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INTRODUCTION:

Vitamin D is one of the fat-soluble vitamins that are present in foods such as milk, dairy foodstuffs, and in many other foods. Calciferol or Vitamin D is also formed in our body subsequent to contact with ultraviolet rays from the solar. Vitamin D is converted to its active hormonal form 1-25 HydroxyvitaminD2 with the help of kidneys. In blood the usual levels of calcium and phosphorus are maintained by Vitamin D. Bones are structured and made stronger with calcium that is retained by the help of Vitamin D [1]. Vitamin D in association with a number of other nutrients, minerals, and hormones contribute to bone mineralization. Increased incidence of Vitamin D insufficiency was found in subjects with chronic kidney diseases [2]. Risks of hyperparathyroidism in subjects with CKD (chronic kidney disease) has been related to the decreased levels of Vitamin D [1]. Vitamin D has a recognized role in the mineral equilibrium along with its other major functions. Secondary hyperparathyroidism along with other bone diseases and modified mineral metabolism are developed and advanced in subjects with CKD due to Vitamin D deficiency. Current disclosure of the wider role of Vitamin D additionally advocate that its deficiency might also make a contribution to reduced cardiac and immune function in CKD sufferers [3]. In patients with chronic kidney disease, Vitamin D deficiency occurs due the reason that inactive form of Vitamin D is not converted into active form i.e. 1-25 hydroxy Vitamin D2 by the kidney [4]. Osteomalacia as well rickets are the ailment, which result due to inadequacy of Vitamin D [4]. Skeletal abnormalities are commonly found in kids due to rickets and muscular weakness occurs in

adults due to osteomalacia, both are caused by Vitamin D inadequacy. 1-25 hydroxy Vitamin D2 synthesized by the kidneys is the active form of Vitamin D, but for diagnosis of hypovitaminosis serum levels of 25(OH)₃ hydroxy Vitamin D3 are offered superior in respect for Vitamin D position in subjects [5]. Less than 20 ng/ml of 25(OH) D3 (hydroxy Vitamin D3) is taken as deficient and its half-life is 2 weeks [6]. Calcium and phosphorus are not absorbed from the diet effectively, only 10-15% of calcium and 50-60% of phosphorus are absorbed when Vitamin D is deficient [7]. Vitamin D lack can occur at the commencement of chronic kidney disease. Bone formation and maintenance, PTH (parathyroid hormone) regulation and calcium phosphorus homeostasis are maintained by Vitamin D [8]. In a study, a large number of subjects (97%), who were on maintenance hemodialysis, have suboptimal range of Vitamin D [1]. A study has shown that there were suboptimal levels of Vitamin D in 39%, inadequacy in 33% and serious deficiency in 6% of subjects with chronic kidney disease⁹. There is lack of data regarding Vitamin D insufficiency in our population with CKD. Similar studies were not performed in Pakistan or south Asia and no references were found thru literature search. This study is being conducted to find the frequency of Vitamin D deficit among patients with CKD, so as to institute early preventive measures in the targeted population. Thus the aim of present study was to determine the frequency of Vitamin D deficiency in patients with CKD. CKD is defined as damage to kidneys or decreased GFR (Glomerular Filtration Rate) <60 ml/minute for minimum of 3 or more than 03 months regardless of the etiology.

Classification of Chronic Kidney Disease Stages as below:

| Stage of CKD | Glomerular Filtration Rate |
|--------------|--|
| 1 | Some evidence of kidney damage reflected by haematuria, microalbuminuria / proteinuria, or histological changes. Normal or increased GFR. |
| 2 | (89 – 60 ml/min/1.73m ²). Mild decrease in GFR |
| 3 | (59 – 30 ml/min/1.73m ²). Moderate decrease in GFR |
| 4 | (29 – 15 ml/min/1.73m ²). Severe decrease in GFR |
| 5 | GFR < 15 ml/min/1.73m ² (ESRD), When renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life. |

CKD= Glomerular Filtration Rate

Vitamin D Deficiency: Levels of Vitamin D less than 20ng/ml will be taken as deficient in subjects.

METHODOLOGY:

Type of our research was cross-sectional and was performed in the Nephrology Unit of Sindh Institute of Urology and Transplantation Karachi, from January 2015 to July 2016. Sample size calculation was based on 33% Vitamin D insufficiency, with margin error of 10%. We have taken 100 patients in our study. Purposive sampling technique was used. Patients of CKD with duration for ≥ 03 months (both males and females) of age 18 years and above were included in our study. Patients of CKD already taking Vitamin D treatment, patients of CKD who have either liver or biliary disease or both (liver disease also cause Vitamin D deficiency) and patients of CKD who are on maintenance hemodialysis (ESRD)

were excluded from study. Informed consent was taken before inclusion. After strong aseptic measures 5 ml of venous blood was collected and then sent to Sindh Institute of Urology and Transplantation laboratory for the analysis of 25-Hydroxy Vitamin D3 (Vitamin D) Patients with level of $< 20\text{ng/ml}$ was taken as deficient. Data was collected in the form of pro forma. For analysis of collected data, SPSS version 20.0 was used. Mean age and Standard deviation for age of subjects were estimated. Sex and Vitamin D deficiency were presented in frequency and percentage. Stratification was done with respective of age, gender, duration of & severity of CKD.

RESULTS:**TABLE I. GENDER WISE FREQUENCY AND DISTRIBUTION OF SUBJECTS**

| Gender | Volunteers with Vitamin D Deficiency. | Volunteers with normal Vitamin D Level | Total Subjects Investigated |
|---------|---------------------------------------|--|-----------------------------|
| Males | 42 | 13 | 55 |
| Females | 41 | 4 | 45 |

In our study population, there were 55 male patients and 45 females. Out of Fifty-five male patients, the Vitamin D deficiency was seen in 42 (76.4%). Whereas, 41 (91.1%) of female patients was Vitamin D deficient, while 13 male and 04 females had normal Vitamin D levels (Table: I).

TABLE II. AGE, DURATION, GENDER AND SOCIOECONOMIC STATUS WISE FREQUENCY DISTRIBUTION OF VITAMIN D DEFICIENT AND NORMAL VOLUNTEERS

| Vit: D Deficient Volunteers | Volunteers with Vit: D Def. | Volunteers without Vit: D Def. |
|---|-----------------------------|--------------------------------|
| Young (20-40 Years) | 15 | 4 |
| Middle (41-60 Years) | 54 | 11 |
| Old (>60 Years) | 14 | 0 |
| Percentage of Total Volunteers with Vit: D Def. | 83 | 17 |
| Duration of Vit: D Def. Disease (0.6-2Years) | 55 | 28 |
| Duration of Vit: D Def. Disease (>2Years) | 28 | 4 |
| Males with Vit: D Deficiency | 42 | 41 |
| Females with Vit: D Deficiency | 13 | 4 |
| Males with Vit: D Deficiency | 42 | 41 |
| Females with Vit: D Deficiency | 13 | 4 |
| Volunteers with poor socioeconomic status | 47 | 9 |
| Volunteers with middle socioeconomic status | 34 | 4 |
| Volunteers with rich socioeconomic status | 0 | 4 |

Vit:=Vitamin, Def.=Deficiency

Out of 100 patients 19 patients were of young age (20 – 40 years), among them 15 (78.9 %) were Vitamin D deficient. Sixty-five were of middle age (41 – 60 years), and among these 54 (83.1 %) shows Vitamin D deficiency. Sixteen were more than 60 years of age, from this group 14 (87.5 %) showed Vitamin D deficiency. This difference was statistically insignificant. Six patients belong to rich family out of them 02 (33.3%) were found to have Vitamin D deficiency. Thirty-eight patients belong to middle class out of them 34 (89.5%) were Vitamin D deficient. This was also statistically insignificant (Table II).

Vitamin D deficient. While 56 patients were from poor socio economic background, out of them 47 (83.9%) had Vitamin D deficiency. This difference was not significant statistically. Sixty-eight patients presented between 6 months to two years of developing of symptoms, of these, 55 patients (80.9%) had Vitamin D deficiency. Thirty-two patients presented after more than 02 years of developing symptoms, out of them 28 patients (87.5 %) had Vitamin D deficiency.

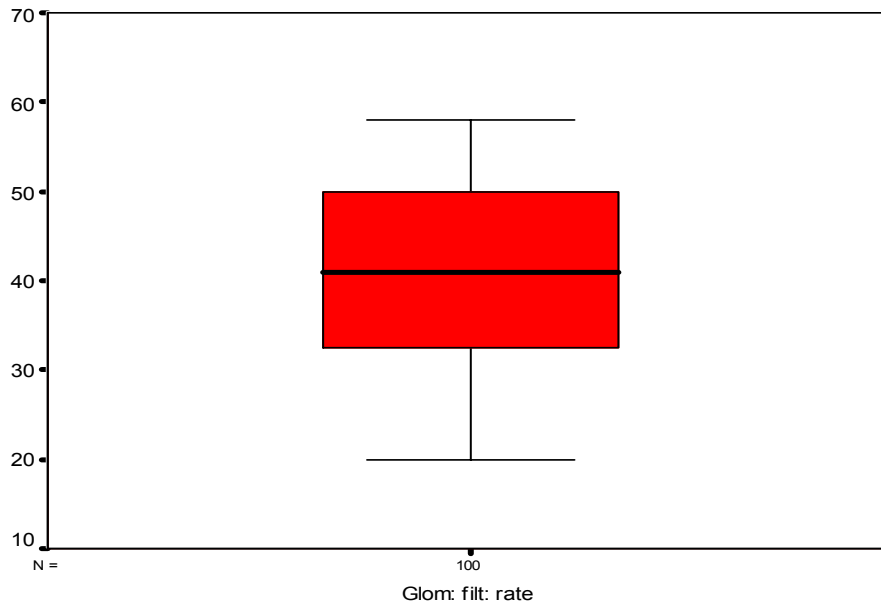


FIGURE I: MEAN OF GLOMERULAR FILTRATION RATE (GFR)

Mean GFR was 40.7 ± 10.49 ml/min/1.73 m² (Figure I).

TABLE III. CHRONIC KIDNEY DISEASE STAGE WISE FREQUENCY DISTRIBUTION OF VITAMIN D DEFICIENT SUBJECTS

| Chronic Kidney Disease | No. of subjects | No. of Sub. with Vit: D Def. in CKD | No. of Sub. without Vit: D Def. in CKD |
|------------------------|-----------------|-------------------------------------|--|
| Stage 1 | 0 | 0 | 0 |
| Stage 2 | 0 | 0 | 0 |
| Stage 3 | 82 | 70 | 12 |
| Stage 4 | 18 | 13 | 5 |
| Stage 5 | 0 | 0 | 0 |

Eighty-two out of total 100 patients were in CKD stage 03, of these 70 (85.4 %) had Vitamin D deficiency. Eighteen were in stage 04, out of them 13 (72.2%) showed Vitamin D deficiency. This parameter also found statistically insignificant (Table III).

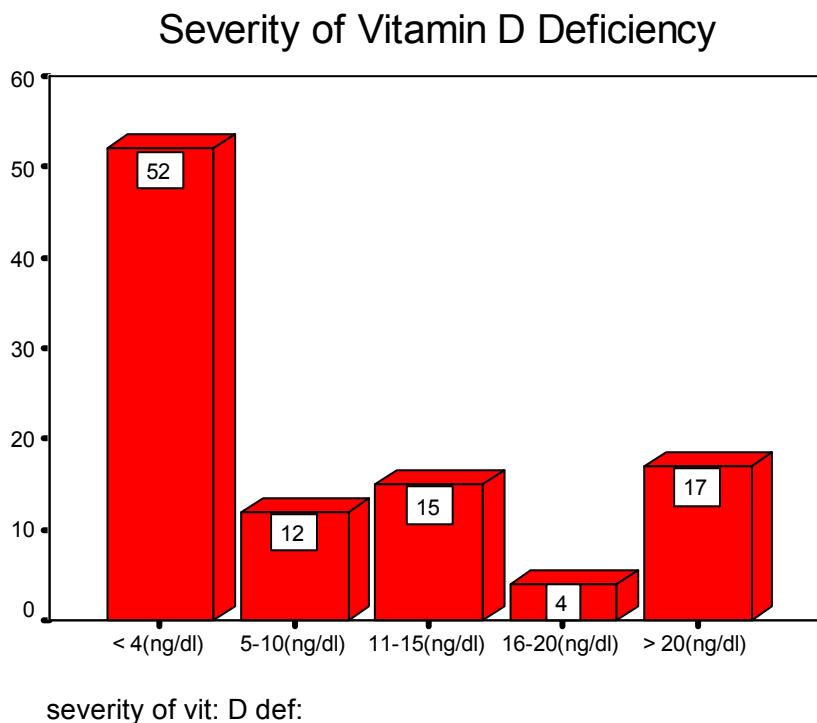


FIGURE II. PERCENTAGE OF VITAMIN D DEFICIENCY CONCENTRATIONS

Regarding the severity of Vitamin D deficiency in chronic renal failure (CKD) 52 patients had less than 4ng/ml, 12 had 05-10ng/ml, 15 had 11-15ng/ml, 04 had 16-20ng/ml and 17 patients had more than 20 ng/ml respectively (Figure II).

Final Outcome:

As a whole, 83% of studied population has shown Calciferol (Vitamin D) insufficiency. Decreased concentrations of Calciferol (Vitamin D) were found in female gender, old age, middle socio economic class, CKD stage 3 and patients presenting after prolonged period of illness (Table I-III).

DISCUSSION:

Vitamin D insufficiency is a frequent medical condition¹⁰. There is increased occurrence of 25-hydroxy Vitamin D insufficiency in subjects with CKD¹¹. In both developed and developing countries, Vitamin D insufficiency is widely seen in CKD subjects. Lack of Vitamin D is profoundly wide spread in north Indians, and in CKD patients, it is more fluent. A study have shown that patients with CKD have insufficiency of Vitamin D up to (77%) [12]. A researcher found that among patients with CKD, Vitamin D insufficiency was found 39%, 33% found to be Vitamin D deficient and 6% found with severe Vitamin D deficiency [9]. A study found that the pervasiveness of Vitamin D inadequacy in our sound Pakistani populace was high. 76.2% subjects of research populace had inadequacy of Vitamin D (20 – 30 ng) [13]. In view of this study, in our Chronic Kidney Disease population we found that 83% patients were Vitamin D deficient (less than 20ng) (Figure II). A previous study showed that a large

number of subjects (97%), who were on maintenance hemodialysis have suboptimal range of Vitamin D¹. 1-25 OH D₂ (1-25 hydroxy Vitamin D₂) synthesized by the kidneys is the active form of Vitamin D, but for diagnosis of hypo-vitaminosis serum levels of 25 (OH) 3hydroxy Vitamin D₃ are offered superior in respect for Vitamin D status in subjects [5]. A level less than 20 ng/ml of hydroxyl Vitamin D₃ is considered Vitamin D deficiency [6]. Our study shows that 83% of the CKD population had Vitamin D deficiency (Figure II). Our country has a lot of sun exposure all the year; despite of that surprisingly our CKD population has elevated occurrence of Vitamin D insufficiency. Reason being foods containing Vitamin D are not available to majority of population in our country where 85% population lies below poverty line. Subsequent to decreased flowing levels of 25 hydroxy Vitamin D in CKD subjects the eagerness for the nutritious recognition of Vitamin D of these subjects has been re-established, not only the active form of 1,25 dihydroxy Vitamin D can assist

the progress of the hyperparathyroidism. For the maintenance and restoration of Vitamin D insufficiency in chronic kidney disease subjects add on therapy with Cholecalciferol has been suggested [14]. It is well established that the diet taken is insufficient to fulfill the requirement of Vitamin D levels to carry on its functions in younger as well as older especially females. As per recommendation by medicine institute US, in nutrition supply of Vitamin D it is essential for both more youthful and older women who have below normal levels.

Present study also shows that, female subjects are more prone to develop Vitamin D insufficiency as in comparison to male gender (Table 1). Reason behind that are, mostly our females remain inside their houses with inadequate exposure to sun light. Burka (a head to toe covering, which only has small openings for the eyes) & hijab, that is very common in our female population, also a major factor regarding decreased sun exposure. There is wide verbal confrontation on the need to direct Vitamin D supplements deliberately due to the pleiotropic impacts of this hormone and which are disconnected to improvement of renal bone sickness. The information proposes that over half of more youthful and older women are not devouring prescribed measures of Vitamin D. Their information additionally indicates women of America or Africa of low socioeconomic class are especially inclined to expending low measures of Vitamin D in their eating regimen [15]. Our study also showed that low poverty status is also a major contributing factor in Vitamin D deficiency. Although patients belonging to middle class families had slightly increased ratio for Vitamin D deficiency than patients of poor class group, which was not statistically significant (Table II). In a research it was shown that 39.6% of subjects have Vitamin D levels between 16 to 30 ng/ml, that were insufficient this was more common in females¹⁶. It can be assumed that the dwellers of the South Asia may not have insufficiency of this vitamin as day light exposure is sufficient round the year. Sadly, increased occurrence of Vitamin D inadequacy had been observed, because of absence of appropriate eating routine, poor calcium consumption, social traditions and staying bound to the four dividers of primitive lodging that denies the elderly, kids and female populace of the advantage of the daylight [17]. In the past study, on account of these questions, there is no consensus on routine organization, in spite of the fact that there is accord on the need to determine 1, 25-dihydroxyVitamin D and 25-hydroxyVitamin D esteems and to sit tight for the aftereffect of various investigations that are being completed on the effect of Vitamin D on association

of cardiovascular hazard factors in CKD and the conceivable outcomes [18].

In secondary hyperparathyroidism Vitamin D levels are usually decreased [19,20], in CKD subjects hyperparathyroidism can be aggravated due to augmented turnover of bones. Usually, if not across the world in CKD subject's hyperphosphatemia, low cortisol levels and secondary hyperparathyroidism are connected with abnormalities of bone and mineral metabolism [21].

Nationwide campaigns should be arranged to give the awareness about the hazards of Vitamin D insufficiency predominantly amongst vulnerable inhabitants as to eradicate the risk of rickets related ailments. Active tuberculosis is also a risk seen in patients with decreased levels of Vitamin D²²⁻²⁴. This danger is likewise increased in our population as we are living in endemic vicinity for tuberculosis. Myocardial dysfunction, sudden cardiac death and death in cardiac failure has also detected in subjects who have decreased levels of Vitamin D [25].

Notwithstanding its established part in calcium-phosphate homeostasis, Vitamin D has calming impacts that may influence vascular problem. A study showed that total of 92% of their studied population had Vitamin D deficiency²⁶. The lowermost level (< 17.8 ng/ml) of 25(OH) D has been declared as unrestricted combined agent with all cause death in general populace [27].

There is increased risk of incident hypertension that is unbiased of age, body mass index, bodily activity, race, menopausal condition, and different covariates affiliated in subjects with insufficiency of Vitamin D as discovered by Forman JP *et al*. They additionally found an unbiased inverse affiliation among expected 25(OH) D levels and danger of incident hypertension [28]. In a study it was reported that levels in serum for 25(OH) D much less than 30 ng/mL (<75nmol/L) were more in older people and women [29]. Present findings show that Vitamin D insufficiency is more frequent in female subjects and older people among the ages of 61–80 years (Table I,II). The reason in female patients, we already discussed, the reason in elderly male patients is their poor diet and sedentary habits. To avoid the secondary hyper-parathyroidism in the earlier stages of CKD, the Vitamin D supplements must be given due to the fact that once parathyroid hyperplasia and osteodystrophy has developed; they cannot be absolutely reversed, so it is the responsibility of us as primary health care personals to give adequate Vitamin D supplements in early stage of CKD. Wellbeing is dependably a

critical thought while detailing suggestions for supplement consumption. In elder adults as compared with young adults, Vitamin D insufficiency is more common. Dietary requirements in older adults for Vitamin D restricted facts is established [30,31].

A board of Food and Nutrition assessed the possibility for the Vitamin D violent intakes to exhibit unfavorable consequence and using similar methodology a secure considerable upper intake level determination, A scientific committee of European commission on food also recognized a vitamin D3 upper intake level of 50µg/ml. Vitamin D3 upper intake level of 25µg/ml was set by experts through a less quantitative utility of identical method [32]. Admission of normal dosages of Vitamin D supplements by all accounts is related with diminishes in absolute death ratio. The correlation amongst baseline Vitamin D status, dosage of Vitamin D dietary supplements, and entire mortality rates are to be investigated [33].

CONCLUSION:

Chronic kidney disease is a major contributing cause of Vitamin D insufficiency (83%); low socioeconomic status (63%) composes a significant number of cases. Current disclosure of CKD may increase severe Vitamin D deficiency; additionally advocate that it may also make a contribution to various health risk factors and disease complications.

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