Prevalence of Vitamin D & Renal Dysfunction in Metabolic Syndrome

Tabassum Yasmin¹, Mohd Shafat Imam Siddiqui²

ABSTRACT

Background: Chronic kidney disease (CKD) is characterized by a progressive loss of renal function that often leads to end-stage renal disease (ESRD), high risk for cardiovascular disease, and high mortality.[1,2] CKD is a growing global health problem due to increased prevalence worldwide. In the United States, the prevalence of CKD was estimated to be 11% based on data from the Third National Health and Nutrition Examination Survey (NHANES III).

Methods: The case control study was carried out in the Departments of Biochemistry and Medicine of Heritage institute of Medical Sciences, Varanasi. Duration of this study was six months.

Results: Twenty five patients each of hypovitaminosis & have chronic kidney disease in age group 31-60 years were included as cases. The prevalence of vitamin D status was low in control group as well as case group.

Conclusion: Treatment with active vitamin D or its analogues shows Renoprotective effects by preventing fibrosis, apoptosis, and inflammation in various experimental models. Furthermore, vitamin D deficiency or insufficiency is a common condition in predialysis or dialysis patients with CKD, and serum levels of vitamin D appear to be inversely correlated with kidney function.

Key words: Chronic kidney disease, Hypovitaminosis, Deficiency, Insufficiency

INTRODUCTION

Chronic kidney disease (CKD) is characterized by a progressive loss of renal function that often leads to end-stage renal disease (ESRD), high risk for cardiovascular disease, and high mortality.[1,2] CKD is a growing global health problem due to increased prevalence worldwide. In the United States, the prevalence of CKD was estimated to be 11% based on data from the Third National Health and Nutrition Examination Survey (NHANES III).[3] In Korea, the prevalence of CKD stage 3 to 5 was 7.7% in 2007 based on data from the Korean National Health and Nutrition Examination Survey.[4] Under current guidelines, the therapeutic strategies for patients with CKD include aggressive blood pressure control, and medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and statins. However, despite these treatment options, individuals with CKD still have high rates of morbidity and mortality.[5] Over the years, studies have improved the understanding of the biological and clinical consequences of the interaction between disordered vitamin D metabolism and CKD. Vitamin D (e.g., 25-hydroxyvitamin D [25(OH)D₃] and 1,25-dihydroxyvitamin D [1,25(OH)₂D₃]) deficiencies are now becoming a global epidemic problem in both the general population and patients with CKD.[6,7] Several observational studies have demonstrated an

Access this article online
Website: www.iabcr.org
DOI: 10.21276/iabcr.2018.4.2.51

How to cite this article: Yasmin T and Siddiqui MSI. Prevalence of Vitamin D & Renal Dysfunction in Metabolic Syndrome. Int Arch BioMed Clin Res. 2018;4(2):179-183.

Source of Support: Nil, Conflict of Interest: None
important link between vitamin D deficiency, impaired glomerular filtration rate (GFR), and increased mortality in patients with CKD. Moreover, activated vitamin D treatment reduces all-cause and cardiovascular mortality rates in patients with CKD and those undergoing hemodialysis.

Vitamin D has been recognized for decades as a key player in the control of bone metabolism through regulating calcium and phosphate homeostasis. Vitamin D is hydroxylated to 25-hydroxyvitamin D (25(OH)D) in the liver and converted into its active form, 1,25-dihydroxyvitamin D (1,25(OH)2D), by the enzyme 1α-hydroxylase. The fact that 1α-hydroxylase is predominantly, although not exclusively, found in renal tubular epithelial cells has suggested renal involvement in the process of vitamin D metabolism. Indeed, the kidney plays a central role in vitamin D metabolism and in regulating its circulating levels, and thus any form or severity of renal disease may affect vitamin D metabolism through reduced 1α-hydroxylase activity, subsequent loss of renal capacity to generate 1,25(OH)2D and resultant decreases in serum 1,25(OH)2D, tissue vitamin D receptor (VDR) content and their actions. On the contrary, given that a number of experimental studies suggest that vitamin D axis has a Reno protective role, prosurvival vitamin D activity such as inhibiting the renin-angiotensin system (RAS), attenuating intestinal inflammation and reducing proteinuria help to maintain kidney health. Thus, impaired vitamin D metabolism may contribute to the development and progression of kidney disease. It is known that vitamin D-deficient individuals with normal renal function have low serum 25(OH)D levels in spite of normal glomerular filtration rates (GFRs). These low serum 25(OH)D levels result in marked reduction of the levels of 25(OH)D filtered and available for uptake by proximal kidney tubular cells, thereby compromising the activation of 25(OH)D to 1,25(OH)2D and the VDR induction of renal medullar for urinary reabsorption. These findings may lay the foundation for pursuing serum vitamin D levels as potential markers of renal injury. Currently, both serum 25(OH)D and 1,25(OH)2D can be measured to evaluate vitamin D status. Because the 25-hydroxylation of vitamin D is mainly substrate dependent and 25(OH)D has a longer half-life than 1,25(OH)2D, circulating levels of 25(OH)D are used to determine vitamin D status and the biological effects of vitamin D in clinical practice. Some epidemiological studies have placed emphasis on monitoring serum 25(OH)D levels, because serum 25(OH)D has been thought to correlate well with clinical parameters including bone mineral density and immune system function. However, some data have shown no definite association between serum 25(OH)D and kidney function after adjustment for confounders. Rather, the level of 1,25(OH)2D has been reported to decline even in the early stage of chronic kidney disease (CKD), and this finding indicates that serum 1,25(OH)2D levels are closely associated with renal dysfunction.

**METHODS**

**Study population:** Twenty five patients each of hypovitaminosis D and have chronic kidney disease in age group 31-60 years were included as cases.

**Study Area:** The case control study was carried out in the Departments of Biochemistry and Medicine of Heritage institute of Medical Sciences Varanasi.

**Study duration:** Duration of this study was six month.

**Sampling technique & Data collection:** 10 ml of fasting venous blood was collected for measurement of 25-hydroxyvitamin D (25(OH)D), intact parathyroid hormone (iPTH) and other routine blood tests. Urine was collected for urine dipstick, microscopy and urine protein creatinine index.

**Inclusion Criteria:** The inclusion criteria for groups were based detailed clinical history and examination. We included CKD stages 2-4 and aged 18 to 65 years old. Twenty Five healthy age matched people were recruited for the study as controls. Controls consisted of healthy volunteers without any prior history of medical disorders. Fasting sample was taken for the controls also.

**Exclusion Criteria:** Exclusion criteria for this study include: acute renal failure, end stage renal disease, chronic liver disease, malabsorption syndromes, granulomatous disease and patients who were on medications known to affect vitamin D absorption or metabolism such as anticonvulsants, isoniazid, rifampicin, theophylline, glucocorticoids, calcium and vitamin D supplements.

**Data Analysis:** Data were analyzed by using Microsoft excel & SPSS.

**RESULTS**

In our study, two groups one control and another one case group were included. Both groups had twenty five patients. Among the twenty five, 76% female and 24% male in control group as well as in case group 56% male and 44% female. In the control group 44% patient belong to 50-60 age group followed by 32% (40-50) & 24% (31-40). But in case study group 50-60 age group patients were slightly higher than control group. The prevalence of vitamin D status was low in control group as well as case group.

**Table 1. Gender-wise distribution**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Control</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6(24%)</td>
<td>14(56%)</td>
</tr>
<tr>
<td>Female</td>
<td>19(76%)</td>
<td>11(44%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25(100%)</td>
<td>25(100%)</td>
</tr>
</tbody>
</table>

**Fig: 1 Distribution of patients according to gender in both group**

**DISCUSSION**

In our study, every patient has hypovitaminosis D in both groups. In our study, two groups one control and another one case group were included. Both groups had twenty-five patients. Among the twenty-five, 76% female and 24% male in control group as well as in case group 56% male and 44% female. In the control group 44% patient belong to 50-60 age group followed by 32% (40-50) & 24% (31-40). But in case study group 50-60 age group patients were slightly higher.
than control group. In the present study, 48% vitamin D insufficiency and 52% vitamin D deficiency were found as contrast to 60 % with vitamin D insufficiency and 40 % with vitamin D deficiency found in the CKD group.

Table 2:- Age wise distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Control</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>6(24%)</td>
<td>4(16%)</td>
</tr>
<tr>
<td>40-50</td>
<td>8(32%)</td>
<td>9(36%)</td>
</tr>
<tr>
<td>50-60</td>
<td>11(44%)</td>
<td>12(48%)</td>
</tr>
<tr>
<td>Total</td>
<td>25(100%)</td>
<td>25(100%)</td>
</tr>
</tbody>
</table>

The incidence of hypovitaminosis D has been constantly and unpredictably high in mostly all populations calculated worldwide and transversely the age spectrum. In the previous studies in primary school children aged 7-12 years old (n = 402) founded the incidence of hypovitaminosis D(< 30 ng/ml) to be 73%.\(^{[23]}\)

Whereas, in another studies found that in the women after-menopausal aged 50 to 65 years the level of 25(OH) D to be expressively lower in the postmenopausal Malay women compared to Chinese women (p < 0.05).\(^{[24]}\)

Though the vitamin D level in true serum that showed hypovitaminosis D remains objectionable. Mostly studies used a serum 25(OH) D level of less than 30 ng/ml to express hypovitaminosis D. However, a current United States guideline on dietary requirements for calcium and vitamin D suggested a serum 25(OH) D levels of at least 20 ng/ml should be considered as an adequate vitamin D level which meets the requirements of at least 97.5 % of the population.\(^{[25]}\)

Hypovitaminosis D has been shown to be related with increased risk of cardiovascular disease and its risk factors such as obesity, hypertension and diabetes.\(^{[26]}\)

Though at present the exact mechanism between increased risk is not clear with some studies told less than 20 mg/mL and also varies with different races.\(^{[27]}\)

As to what the optimal level we required to target to discuss aids is not clear although levels > 37 mg/mL has been recommended by one study.\(^{[26]}\)

Subsequently the incidence of hypovitaminosis D in both of our groups was high, it raised the question of what were the common similar factors in both groups. What could be the trigger factors? Could it be genetuc? Could it be dietary? The two main determinants of vitamin D levels are sunlight exposure and dietary intake.

In spite of this method is prone to recall bias and may not signify an individual’s general dietary intake and habits. The Sunlight exposure between studies is also non-consistent and often there is no objective measurement of sun exposure.\(^{[28]}\)

The validated measures of sun exposure have only been published very recently.\(^{[29]}\)

Hypovitaminosis D of both normal and CKD subjects due to the lack of sun exposure is undeniably important as Malaysia is a tropical country with a hot and humid climate. Surprisingly, many other countries with a lot of sun exposure such as in the Middle East also showed a similar prevalence of hypovitaminosis D.\(^{[30]}\)

In Muslim countries women may be fully covered excluding for the hands and face thus falling their exposure to sunlight. This finding has been supported by studies in European countries where the incidence of hypovitaminosis D is high in immigrants who are covered and veiled.\(^{[31]}\)

In our study also consists of predominantly Muslim women (76 % in control group and 42 % in CKD group) who had similar clothes as their counterparts worldwide, this is play a major role in contributing to the decrease serum vitamin D levels from sun exposure.

South Asian women had significantly higher serum PTH and lower serum 25(OH)D concentrations than Caucasian women in the UK. However, this was not associated with higher levels of markers of bone resumption or reduced bone quality in the South Asian women.\(^{[31]}\)

In the present study, female gender and diabetes mellitus were found to be independently related with lower levels of...
25(OH)D. Female gender was originate to have an inverse association with serum 25(OH)D levels in earlier study. [32] This might explain the high incidence of hypovitaminosis D in our population whereas in diabetes, there is developing data showed Vitamin D deficiency to be a associated factor for the growth of both type 1 and 2 diabetes. The β cells of pancreas not only secrets insulin but also contains vitamin D receptor (VDRs) as well as 1-α hydroxylase enzymes. It has been proven that treatment with vitamin D improves glucose tolerance and insulin resistance. [33]

Obesity and BMI have also been concerned with hypovitaminosis D. Obesity decreases the availability of vitamin D due to sequestration of vitamin D in body fat. [34] These findings highlight the need for suitable interferences to address the problem of obesity in our younger population to reduce the risk of the metabolic syndrome later in life. In our study, the control group was found to be overweight whereas in the CKD group were noted to be obese. In CKD, the loss of the renal 1α-hydroxylase is largely responsible for the hypovitaminosis D. Several epidemiological studies have reported patients with CKD stages 3 to 5 to have lower 25(OH)D concentrations than the general population. [35] These in keeping with our findings, the documentation of extra renal 1α-hydroxylase suggests that 25(OH)D status is an significant consideration in patients with CKD. [36] Preferably, the serum levels of 1,25 (OH)2D3 which is the physically active form of Vitamin D should be measured.

Though, low levels of the 25(OH)D itself may contribute to reduced levels of 1,25(OH)2D3 production, particularly in CKD patients with nephrotic range proteinuria. There is an association between lower serum 25(OH)D levels and poorer kidney function, higher BMI and higher albuminuria, lower serum calcium and higher serum phosphorus, intact parathyroid hormone (iPTH) and alkaline phosphatase (ALP). Nutritional factors associated with higher 25(OH)D levels were stable weight, higher albumin and HDL cholesterol. [37]

In our CKD group, the albumin in serum levels, haemoglobin, calcium and high-density lipoprotein cholesterol (HDL) reduced consistently with advancing CKD stage. While, levels of serum phosphorus, ALP and iPTH design significantly. Once eGFR drops to less than 30 ml/min/1.73m² (CKD stage 4), the 1α-hydroxylase activity develops reduced.

This in turn will cause an important decrease in intestinal calcium absorption leading to a reduction serum calcium in circulation. As a result, secondary hyperparathyroidism develops which results into osteopenia, osteoporosis and increasing fracture risk. Parathyroid hormone also causes increased phosphaturia, resulting in low-normal serum phosphorus. Without an adequate calcium phosphorus product, mineralization of the collagen matrix is diminished hence aggravating the renal bone disease in CKD. In view of such a high prevalence of hypovitaminosis D in CKD and its possible complications, we have proceeded with a further study to see the effects of vitamin D replacement in this group of patient.

CONCLUSION

This study concludes that, there is so many proof to treat patients with hypovitaminosis D and chronic kidney disease. Though, the role of vitamin D replacement in the general healthy population remains debatable. Thus, a larger study with longer follow up is required.

REFERENCES