Original Article

Association of serum vitamin-D level with renal function in a rural population of Bangladesh

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Abstract

Background: *Vitamin D deficiency is an emerging global health problem. Recent studies have indicated that the prevalence of vitamin D deficiency even in tropical countries is as high as that observed in Western populations. Vitamin D deficiency has high impact on renal disorders which are leading causes of death in humans.*

Methods: *This was a cross sectional analytical study. According to inclusion criteria of the study total 259 participants were recruited from a rural area, Baidyerbazar union of Narayanganj district. After taking history and clinical examination, relevant investigations were done. Serum 25(OH)D was measured using chemiluminescent immunoassay (CLIA) technology (DiaSorin Inc, Stillwater, MN). Renal functions of the study population were assessed by e-GFR (calculated by CKD-EPI equation), urinary ACR and urine microscopy.*

Results: *In this study out of 259 study subjects on vitamin-D status 6.2%, 33.6% and 60.2% had vitamin-D sufficiency, insufficiency and deficiency respectively. Among participated female (133) 78.2% had vitamin-D deficiency and among participated male (126) 41.3% had vitamin-D deficiency. Among vitamin-D sufficiency, insufficiency and deficiency group the mean eGFR was 102.94, 104.87 and 109.33 ml/min/1.73 m^2 respectively. The mean uACR level was 6.97, 22.89 and 37.29 mg/gm respectively.*

Conclusion: *The findings of the study suggest that 93.8% of study population had either vitamin-D insufficiency or deficiency. Vitamin-D deficiency was more prevalent in females than males. Serum 25- hydroxyvitamin D level was negatively associated with urinary ACR level.*

Keywords: *25-hydroxyvitamin D, eGFR, uACR*

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INTRODUCTION

The American guideline for evaluation, prevention, and treatment of vitamin D deficiency establishes that vitamin D should be determined by measurement of serum 25(OH)D with the following cutoff points: (i) deficiency when <20 ng/mL (<50 nmol/L), (ii) insufficiency when between 20 to 30 ng/mL (50 to 75 nmol/L) and (iii) sufficiency when >30 ng/mL (>75 nmol/L)[1]. Based on these cutoffs, it has been estimated that about one billion people, worldwide, have 25(OH)D deficiency or insufficiency. The prevalence of serum 25(OH)D deficiency and insufficiency reportedly varies between 30% and 93%. The highest prevalence of hypovitaminosis D has been reported in temperate climate regions that receive limited sunlight, especially during winter[2]. It is our general belief that vitamin D deficiency is prevalent only in western countries, but actual condition is reverse. It is surprising that in South Asia, 80% of the apparently healthy population is deficient in vitamin D (<20 ng/mL) and up to 40% of the population is severely deficient (<5 ng/mL)[3]. In the adult population, 35% of adults in the United States are vitamin D deficient

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whereas over 80% of adults in Pakistan, India, and Bangladesh are Vitamin D deficient[4].

Some of the associated risk factors of vitamin D deficiency are age, sex, race, body mass index, use of medications known to affect vitamin D metabolism, inadequate amount of vitamin D in food, low sun exposure, use of sunscreens, distance from the Equator, black skin, smoking, poor food absorption, and kidney and liver disease[2]. By cross-sectional analysis of the NHANES III (1988–1994) and NHANES 2001–2004 databases that are representative of the US adult population, a number of studies consistently demonstrated an association of low serum 25(OH) D levels with increased prevalence of renal risk factors. It showed a correlation between low serum 25(OH) D and the risk of all-cause mortality in the general population[5,6].

Vitamin D levels significantly decrease with increasing age. This is expected, because the skin thickness decreases with age and thus, the production of 7-dehydrocholesterol is also compromised. The decreased level could be due to the fact that, a more sedentary and indoor lifestyle is easily adopted with advancing age[2].

Vitamin D deficiency is more common in female than male. This is due to many women stay at home and perform indoor activity. There are little exposure to sunlight. The other conditions: Covering the entire body with clothing as customary in women in some religions, use of sunscreen may significantly reduce the production of vitamin D3 in the skin[7].

The color of skin of South Asian populations varies from light brown to almost dark. Dark color skin has been found to decrease skin synthesis of vitamin D because UV light cannot reach the appropriate layer of the skin due to presence of melanin[3]. Melanin acts as an effective natural sunscreen and, therefore, increased skin pigment can greatly reduce the solar UVB mediated cutaneous synthesis of vitamin D3[7]. Vitamin D binding protein (DBP) levels in blacks are significantly lower compared to whites to compensate for lower total serum 25(OH)D in blacks[6].

Impaired GFR is a cardinal manifestation of kidney disease. Lower GFR, even within its normal range, is associated with markedly increased risk of cardiovascular death[8]. The relationship between eGFR and vitamin-D is debated. Some studies have shown that eGFR increased as vitamin-D level increased, some have shown that eGFR increased as vitamin-D level decreased and others found no association. The exact reason for these discrepancies is not clear, however the findings differed depending on whether the subjects were patients with CKD or individuals with normal or mildly decreased eGFR[9].

Vitamin-D is known to suppress the renin gene transcription. In vitamin-D deficiency renin is synthesized which activate RAAS. Angiotensin- II is a key mediator to raise efferent glomerular arteriole resistance which raises the glomerular filtration pressure and leads to increased GFR[10]. However in CKD patients there is positive association between eGFR and vitamin-D level. It occurs as CKD patients are lack of outdoor activities and dietary sources. Besides this, in the circulation 25(OH)D complexes with vitamin D binding protein (DBP). Following glomerular filtration the 25(OH)D-DBP complex is reabsorbed via megalin-mediated endocytosis in the proximal tubules, where 25(OH)D is converted to 1,25(OH)2D3 by renal 1α- hydroxylase (CYP27B1). In renal insufficiency, the decline in megalin-mediated endocytotic activity and renal 1α-hydroxylase activity and the loss of 25(OH)D-DBP into the urine because of proteinuria contribute to the development of 25(OH)D and 1,25(OH)2D3 deficiency[5].

Albuminuria is a major risk factor for renal disease progression. A cross-sectional analysis of the NHANES III data showed that the prevalence of albuminuria increased in a progressive fashion with decreasing vitamin D level. It suggest that vitamin D has an intrinsic anti-proteinuric activity[5]. Hypovitaminosis D causes albuminuria through a number of mechanisms. First, lower circulating vitamin D level causes activation of the renin-angiotensin- aldosterone system and lead to albuminuria through both hemodynamic and nonhemodynamic mechanisms. Second, vitamin D deficiency reduces pancreatic beta cell function and is associated with reduced peripheral insulin sensitivity. Diabetes and insulin resistance are established risk factors for albuminuria. Third, vitamin D has direct effects on cell proliferation, differentiation, and apoptosis of podocytes. Insufficient vitamin D may contribute to albuminuria by podocyte loss and glomerulosclerosis through

direct cellular effects[8]. It is also possible that albuminuria leads to low levels of vitamin D. In the kidney, vitamin D is filtered at the glomerulus and actively reabsorbed in the proximal tubule by a process facilitated by the luminal receptors megalin and cubulin. It is possible that increased filtration of albumin into the urinary space interferes with vitamin D reabsorption, leading to greater losses of vitamin D in urine[11].

METHODS

This was a cross sectional analytical study. The study was conducted for six months from July to December of 2019. According to inclusion and exclusion criteria of the study total 259 participants were recruited from a rural area, Baidyerbazar union of Narayanganj district, where CKD screening program is going on. After taking history and clinical examination, relevant investigations were done. Serum 25(OH)D was measured using chemilumin-escent immunoassay (CLIA) technology (DiaSorin Inc, Stillwater, MN). Renal functions of the study population were assessed by e-GFR (calculated by CKD-EPI equation), urinary ACR and urine microscopy.

Selection criteria: At first people with age ≥18 years living in rural area were included in this study. Then pregnant women; patient with cognitive impairment; patient who are on medication known to affect vitamin D absorption or metabolism such as anticonvulsant, glucocorticoids, calcium, vitamin D supplements were excluded from this study.

RESULTS

Table I. shows the distribution of the total 259 study populations according to different catagories. Maximum study populations were in age group 31 – 40 years (31.3%). Females (51.4%) were slightly predominant than males (48.6%). Maximum study populations had vitamin-D deficiency (60.2%) followed by vitamin-D insufficiency (33.6%), vitamin-D sufficiency (6.2%). The eGFR value ≥90 ml/min/m^2 was maximum in 87.3% and uACR value <30 mg/gm was maximum in 91.9% of the study populations.

Table I: *Distribution of the study population (N=259)*

	Frequency(n)	Percentage(%)
Age		
≤30	65	25.1
31 – 40	81	31.3
41 – 50	49	18.9
51 – 60	27	10.4
>60	37	14.3
Gender		
Male	126	48.6
Female	133	51.4
Vitamin-D status		
Sufficiency	16	6.2
Insufficiency	87	33.6
Deficiency	156	60.2
eGFR (ml/min/m^2)		
≥90	226	87.3
60 – 89	31	11.9
<60	2	0.8
uACR (mg/gm)		
<30	237	91.9
≥30	21	8.1

Table II shows the association of vitamin-D status with gender and renal risk factors. Females (78.2%) were significantly more affected than males (41.3%) in case of vitamin-D deficiency group. High uACR value were found in vitamin- D deficiency group (90.5%) and the results were statistically significant. Table III shows the comparison of renal risk factors in relation to vitamin-D status. Fasting blood glucose, HbA1c, BMI levels were significantly increased in case of vitamin-D deficiency group.

Table II: *Association of vitamin-D status with gender and renal risk factors*

	Total (n=259)	Vitamin-D Sufficiency	Vitamin-D Insufficiency	Vitamin-D Deficiency	P value
Gender					0.0001
Male	126	14 (11.1%)	60 (47.6%)	52 (41.3%)	
Female	133	2 (1.5%)	27 (20.3%)	104 (78.2%)	
uACR (mg/gm)					0.012
<30	238	16 (6.7%)	85 (35.7%)	137 (57.6%)	
≥30	21	0 (0.0%)	2 (9.5%)	19 (90.5%)	

Chi square test was done.

Table III: *Comparison of Renal factors in relation to vitamin-D status*

	Total (n=259)	Vitamin-D Sufficiency (n=16)	Vitamin-D Insufficiency (n=87)	Vitamin-D Deficiency (n=156)	P value
BP (mm of Hg)					
SBP	129.85 ± 19.62	125.50 ± 18.87	130.17 ± 15.91	130.12 ± 21.53	0.648
DBP	79.43 ± 11.01	74.88 ± 6.32	78.48 ± 10.72	80.43 ± 11.43	0.149
FBG (mmol/l)	5.96 ± 2.27	5.18 ± 0.63	5.59 ± 1.27	6.24 ± 2.73	0.036
HbA1c (%)	6.06 ± 1.53	5.43 ± 0.24	5.87 ± 1.16	6.23 ± 1.75	0.049
BMI (kg/m2)	25.20 ± 4.34	21.51 ± 3.49	24.44 ± 4.13	25.99 ± 4.27	0.034
eGFR(ml/min/m^2)	107.44 ± 17.44	102.94 ± 16.91	104.87 ± 16.51	109.33 ± 17.83	0.091
Creatinine (mg/dl)	0.76 ± 0.21	0.86 ± 0.16	0.80 ± 0.16	0.72 ± 0.23	0.003
uACR (mg/gm)	30.55 ± 79.18	6.97 ± 4.65	22.89 ± 50.25	37.29 ± 94.42	0.279
Calcium (mg/dl)	10.82 ± 1.73	10.07 ± 1.37	10.99 ± 1.57	10.80 ± 1.83	0.142
Phosphate (mg/dl)	4.17 ± 0.78	3.76 ± 0.54	4.22 ± 0.74	4.19 ± 0.82	0.092
ALP (u/l)	102.77 ± 36.12	84.63 ± 21.77	104.57 ± 34.26	103.62 ± 37.92	0.114

Data were expressed as mean ± SD. ANOVA test were done

DISCUSSION

Growing scientific evidence has implicated vitamin D deficiency in a multitude of chronic conditions, including diabetes mellitus, hypertension, cardiovascular disease, renal disease and among others. With the growing prevalence of vitamin D deficiency and its association with these leading causes of mortality, it has become more important than ever to delineate vitamin D's role in the pathogenesis of these diseases and use data to pinpoint established risk factors for vitamin D deficiency[12].

This study was conducted among 259 rural population. Mean age of the study subjects was 41.62 ± 14.74 years within a range of 18 to 88 years. Females (51.4%) were slightly predominant than males (48.6%).

In this study, serum 25-OH-vitamin-D was assayed by DiaSorin, Stillwater, MN. Kit which uses chemiluminescent immunoassay (CLIA) technology The internal QC test value was 13.9 ng/ml with range 9.73 to 18.1 ng/ml. In this study ivD QC result was 14.6 ng/ml. 93.8% subjects was found either vitamin-D insufficiency or deficiency. According to Mayo Clin Proc. July 2013 the vitamin-D deficiency scenario in South East Asia (78 – 98%), Middle East (90%) and Europe (57 – 64%). High prevalence of vitamin- D deficiency of this study may be due to culture of people and seasonal variation. About half of the samples were collected during winter season.

In this study vitamin-D deficiency is more common in female (98.5%) than male (88.9%). It is due to less sun exposure of female as they perform more indoor activity and in outside their whole body is covered by clothing like borkha. This finding is similar to Jeon et al, 2011; Martins et al, 2007 study[11,13].

In this study, uACR showed negative correlation with serum vitamin-D level. The uACR was 6.97 ± 4.65, 22.89 ± 50.25, 37.29 ± 94.42 in vitamin- D sufficiency, insufficiency and deficiency group respectively. This finding is similar to Boer et al, 2011; Kim et al, 2018 study[8,10]. Adjustment for hypertension and diabetes resulted in some attenuation of this association, suggesting that these factors may mediate or confound

a portion of the relationship of vitamin-D with albuminuria.

In this study, when eGFR is ≥60 ml/min/m2 it is negatively associated with serum vitamin-D level and when eGFR <60 ml/min/m2 it is positively associated with serum vitamin-D level. Several studies have investigated the association between renal function and vitamin D levels. However, the relationship between eGFR and vitamin-D is debated. Although some studies have shown that eGFR decreased as vitamin-D levels increased[9,14] and some studies have shown that eGFR increased as vitamin-D levels increased[15], others found no association between vitamin D and GFR[16,17]. The exact reason for these discrepancies is not clear; however, it may be that most studies in patients with CKD have found a positive association between eGFR and vitamin D levels, whereas those conducted in the general population typically found no association.

CONCLUSION

The prevalence of serum 25(OH) D sufficiency, insufficiency and deficiency in a rural population of Bangladesh is 6.2%, 33.6% and 60.2% respectively. Vitamin-D deficiency is more prevalent in females. Low serum level of 25(OH) D is associated with the declining eGFR and increasing urinary albumin excreation.

LIMITATION OF THE STUDY

This study carried out at a short period of time, more time is needed for such study. As this was a cross-sectional study, so it was impossible to infer causal or temporal relationship. The study did not evaluate use of medications known to affect the blood pressure and blood glucose level.

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