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ORIGINAL RESEARCH

Association of vitamin D deficiency with greater risk of anemia

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ABSTRACT

Background: Vitamin D deficiency can be seen with high incidence rate globally. Vitamin D deficiency complications are associated with various diseases. Anemia is one of the clinical conditions which may arise in vitamin D deficient individual. It was also found that Vitamin D has an effect on erythropoiesis. Aim of this study is to investigate the association if any, in between vitamin D and anemia. **Methodology:** Total 100 subjects were enrolled in this study after proper case taking. 50 subjects were healthy controls and 50 were enrolled as cases. Subjects were investigated for the levels of 25-hydroxy-vitamin-D and hemoglobin. **Results:** Anemia was present in 48.3% in cases having (25- hydroxyl-vitamin-D <30 ng/ml) and 25 % in controls having (25-hydroxyvitamin-D >30ng/ml) and the difference was statistically significant (p=0.01). Mean of Hb in cases was (9.62±1.06) and that was (10.66±1.50) in controls and the difference was statistical significant with (p=0.001). **Conclusion:** This can be concluded that patients with vitamin D deficiency are at greater risk of Anemia.

Key words: Anaemia, Hemoglobin, 25-hydroxyvitamin-D.

INTRODUCTION

In past years an association between Vitamin D and anaemia has been recorded, indicating the vital roles of Vitamin D in homeostasis of iron and erythropoiesis. Hydroxylation of cholecalciferol in the liver and in the kidney is the basic physiology of vitamin D. The formation of 25-hydroxivitamin-D (25[OH] D) in liver and 1, 25 dihydroxyvitamin-D (1, 25(OH) $_2$ D), the hormonally active form of vitamin takes place in kidney [1]. The evaluation of total vitamin D level in serum i.e. 25(OH) D is the best indicator as this appears in main circulating form [2].

Vitamin D deficiency is associated with serious diseases including heart disease, cancer and infections etc. as this deficiency is associated with extra-skeletal health[3-5]. In past years this has been noted that vitamin D deficiency is related with anaemia [6,7].

Anaemia specially in women is consider to be the concern due to its morbidity and mortality worldwide [8,9]. Approximately 50% of all anaemia cases are diagnosed as iron deficiency anaemia (IDA) [10,11].

Anaemia is decreased concentration of Hb that leads to an insufficient oxygen transport throughout the body. Anaemia is related with chronic conditions such as chronic kidney disease and CVD [12,13]. Anaemia has various aetiology and can be classified as iron deficiency anaemia or anaemia of nutrient deficiency or anaemia of inflammation [14]. The association between vitamin D status and anaemia has been studied in children, and patients with chronic diseases or those with heart failure [6,15-17]. Past studies found the association of low vitamin D in serum and risk of anaemia in children, patients with CKD and heart failure[6,16,17,18].

Vitamin D is related with, anaemia of inflammation through its down-regulatory effects on inflammatory cytokines. The mechanism of inflammatory anaemia involves the antimicrobial peptide hepcidin, which is a a hormone involved in regulation of Fe recycling in the body by pro-inflammatory cytokines IL-6 [19-21]. Under chronic inflammatory conditions, Fe become unavailable for erythropoiesis, which may ultimately lead to anaemia [22,23]. The pathway which contributes to anaemia of inflammation is via reduced erythropoiesis and reduced life span of RBCs [24]. Vitamin D lowers the inflammatory cytokines and suppress expression of hepcidin mRNA [25,26] Thus, It

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can be noted that vitamin D may reduce the risk of anaemia through its anti-inflammatory effects.

Thus the present study is designed to evaluate the association between vitamin D status in serum and anaemia in adult population.

MATERIAL & METHODS

In this case-control study. Total 100 samples were taken, 50 were apparently healthy having age in between 25-40 years as controls and 50 having 25-Hydroxyvitamin D deficiency having age in between 25-40 years as cases. Subjects were included after proper case taking. Informed consent was taken from all enrolled subjects and subjects with autoimmune disorders, Chronic diseases, Inflammatory diseases & haematological disorders are excluded. Pregnant women are also excluded from the study.

Vitamin D levels, Total Iron levels & Total iron binding capacity were measured using commercially available kits Erba on fully automatic biochemistry auto-analyser EM200, and Transferrin saturation % was calculated using formula - ratio between serum iron and TIBC [serum iron/TIBC] × 100). Haemoglobin level < 12.0 gm/dl in non-pregnant women and < 13.0 gm/dl in men were defined to be anaemic [27]. Vitamin D deficiency was taken when the level < 30 ng/mL was recorded [28]**.** Statistical analysis was performed using (SPSS), version 20.The chi-square test was used for comparing the variables. The independent t-test was used to compare means between the variables and $p<0.05$, was considered as statistically significant.

RESULTS

The demographic criteria with vitamin D status in cases and controls are presented in **Table 1**. 72.0% of case group and 76.0% of control group were female. Prevalence of anaemia was significantly higher (62.0%) in patients with vitamin D deficiency when compared with 18% with normal vitamin D levels ($p<0.01$).

Table 1: Demographic characteristics of cases and controls.

Variable	Sex/Health status	Cases (n=50) Vitamin D=<30 ng/dL	Controls (n=50) Vitamin D=>30 ng/dL	p- value
Gender	Male	14(28%)	12(24%)	Chi square 0.205, p= 0.65
	Female	36(72%)	38(76%)	
Anaemia	Present	31(62%)	09(18%)	Chi square 19.96,p <0.01
	Absent	19(38%)	41(82%)	

The mean of age in cases (45.5±8.06) and controls (46.5±7.7) groups were statistically non-significant. The mean of haemoglobin (9.62±1.06%) is significantly low in cases with low vitamin D compared to controls (10.66±1.50%) with normal vitamin D ($p=0.001$). The mean of vitamin D in case and control groups were (12.75±0.76) and (35.40±3.34) ng/dL respectively which was statistically significant ($p=0.001$). Statistically significant difference was also observed among patients in terms of serum iron, TIBC and transferrin saturation levels shown in **Table 2.**

Table 2: Clinical Characteristics of cases and controls.

Parameters	Cases (n=50) Vitamin D=<30ng/dL (Mean±SD)	Controls (n=50) Vitamin D=>30ng/dL (Mean±SD)	p-value
Age (years)	45.5±8.06	46.5±7.7	0.53
Hb% (gm/dL)	9.62±1.06	10.66±1.50	0.001
Vitamin D (ng/dL)	12.75±0.76	35.40±3.34	0.001
Serum Iron(µg/dL)	66.12±12.60	72.71±11.60	0.007

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TIBC (µg/dL)	69.5±22.34	350.2±35.5	0.001
Transferrin Saturation (%)	19.82±5.4	22.25±5.12	0.02

When the Correlation between vitamin D levels and other biochemical parameters was analysed among cases and controls, it was found that vitamin D is correlated with Hb% and Serum total iron, shown in Table **3**.

Table 3: Correlation between vitamin D and other biochemical parameters.

Parameters	Hb% (gm/dl)	Serum Iron (µg/dL)	TIBC (µg/dL)	Transferrin Saturation (%)
(case) Vitamin D=<30ng/dL	.421	.399	-.213	.332
p value	0.001	0.002	0.002	0.009
(control) Vitamin D=<30ng/dL	.069	.214	-.129	.217
p value	.321	.291	.428	.118

DISCUSSION

Anaemia was significantly higher (48.3%) in patients with 25-hydroxyvitamin D deficiency when compared to subjects (25.0%) with normal 25-hydroxyvitamin D. The mean of serum haemoglobin was significantly lower in cases with deficiency of 25-hydroxyvitamin D when compared to controls. It has been reported in past studies that an association between vitamin D3 level and an increased risk of iron deficiency anaemia occurs among patients without any chronic kidney disease [6,16]. There could be significant influence of vitamin D deficiency and an increased risk of reticulocytosis and iron deficiency anaemia [7]. The deficiency of vitamin D has an effect on erythropoiesis including cellular proliferation and differentiation with regulation of bone and mineral metabolism [29,30]. It has also been noted that vitamin D has influence on bone marrow, with the findings that levels of calcitriol are higher in bone marrow compared to plasma [31,32]. vitamin D also regulates the level of production of systemic cytokine, which lead to anaemia of chronic disease or inflammation [7]. Vitamin D regulates cytokine release and exerts a stimulatory effect on erythroid precursors, as its receptors are also seen bone marrow [30]. 25 (OH) D deficiencies could lead to reduced calcitriol production in the bone marrow, which can limit erythropoiesis. Calcitriol has a direct proliferative action on erythroid cells forming units and also up-regulates the expression of the erythropoietin receptors [33-35].

It is evident from the previous studies that the association between vitamin D deficiency and risk for anaemia is dependent on cause behind anaemia as well as socio-economic status of the subjects [15,36,37-39].

Lee et. al., (2015) among Korean children, found the low level of 25(OH) D which was associated with increased anaemia in females [36]. Atkinson et. al., (2014) observed the relationship between 25(OH)D deficiency and anaemia in childrens, and also determined modifying factor in this association [15]. The previous studies confirm that alteration in vitamin D metabolism is related to iron deficiency, as heme-bound iron is essential in the hydroxylation process of vitamin D [40,41].

CONCLUSION

We can conclude that vitamin D deficiency is associated with the risk of anaemia in apparently healthy populations. The analysis of our study suggests that low 25(OH)D level are strongly associated with lower levels of haemoglobin. So this study suggests Iron supplementation along with Vitamin D in patients having vitamin D deficiency.

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