The Association of Anemia with Vitamin D Deficiency among Patients Visiting King Khalid General Hospital in Majmaah, Saudi Arabia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aims: To assess the association between vitamin D deficiency and anemia among patients visiting King Khalid General Hospital in Majmaah City, Saudi Arabia.

Methodology: We reviewed the medical records of 120 patients (median age, male 37.44 [±17.86] and female 43.22 [±16.23] years; range 1–96 years) who attended the King Khalid General Hospital laboratory in Majmaah city, Saudi Arabia, between January 2019 and January 2020. The laboratory data included the following parameters: complete blood count (Hb, MCV, MCHC, MCH, Hct, WBC, RBC, and Plt) and vitamin D (25(OH)D) levels.

Results: The chi-squared analysis showed that moderate anemia was highest among the participants who had vitamin D levels >30 ng/ml and less than 20 ng/ml, with a prevalence rate of 5% (n=6) for each category. Mild anemia was prevalent among 4.12% (n=5) of the participants with vitamin D levels <20 ng/ml. Finally, there were significant associations between parameters

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including age, RBC count, WBC count, platelet count, MCV, MCH, MCHC, hematocrit, vitamin D, and anemia. In addition, the odds ratio results indicated that mild vitamin D deficiency was associated with the degree of anemia, ranging from mild to moderate (OR=1.63 to 1.92). Moderate vitamin D deficiency was associated with the degree of anemia, ranging from mild to moderate (OR=1.76 to 1.97). The results confirmed a negative association between normal vitamin D values and the degree of anemia.

Conclusion: There is a significant association between vitamin D deficiency and anemia among patients visiting King Khalid General Hospital in Majmaah City, Saudi Arabia.

1. INTRODUCTION

Anemia is a condition characterized by a decrease in the blood's ability to perform its functions of carrying oxygen and food and other vital functions. Anemia occurs as a direct result of decreases in the quantity and efficiency of hemoglobin and erythrocytes [1]. Women and older adults are the most vulnerable to anemia. Normal hemoglobin levels should be maintained to maintain the shape of the red blood cells and avoid any disruption in blood flow. Normal hemoglobin levels vary depending on the age and gender of the person. In neonates, the normal hemoglobin level is 17–22 g/dl. In children, the normal level is 11–13 g/dl, whereas the normal levels in adult men and women are 14–18 g/dl and 12–16 g/dl, respectively. Therefore, severe anemia is indicated by levels that are less than 8 g/dl, and hemoglobin tends to be between and 8–11 g/dl in those with anemia [2]. Regardless of the methods used to estimate the amount or proportion of hemoglobin in a subject, these tend to not be sufficient to diagnose patients. Anemia can be divided into three categories based on a patient's mean cell volume (MCV). The MCV represents the average size of one's red blood cells (RBCs)[3]. Anemia is divided into subtypes, including microcytic anemia, normocytic anemia, and macrocytic anemia [4]. Microcytic anemia is defined as an MCV of less than 80 fl; 80 fl to 100 fl is considered normocytic anemia, and macrocytic anemia is defined by a MCV greater than 100 fl [5]. The causes of microcytic anemia include sideroblastic anemia, iron deficiency anemia, thalassemia, and chronic disease anemia [6].

Vitamins are nutrients that humans require in very small amounts. Vitamin D is one of four fat-soluble vitamins. It can be stored in the body because the cells of the body are surrounded by fatty layers, allowing this vitamin to easily maneuver through the body [7]. Vitamin D plays a vital role in the maintenance of the normal blood levels of phosphate and calcium, which are required for the normal mineralization of bone, nerve conduction, muscle contraction, and general cellular functions in all cells of the body [8]. In addition, adequate amounts of vitamin D during childhood and adolescence are crucial for bone health and to prevent various chronic diseases, such as autoimmune diseases, cardiovascular disorders, and cancer. It has been argued that vitamin D deficiency during infancy and childhood may increase the risk of these chronic diseases throughout life [9]. Recent reports have indicated that there might be a significant association between iron deficiency anemia and vitamin D deficiency. For example, Yoo and Cho [10] investigated the prevalence of 25-hydroxyvitamin D deficiency among Korean patients with anemia. The study included 500 patients, distributed as 200 patients with anemia and 300 patients in a control group. The results revealed that there was a high prevalence of vitamin D deficiency among anemic patients (91%). However, vitamin D deficiency was prevalent in 87.3% of the control group patients [10]. Moreover, Sim et al. [11] conducted a cross-sectional study to identify the association between vitamin D deficiency and anemia. The findings showed that vitamin D deficiency was more prevalent in anemic patients (49%) than in normal patients (36%) [11]. In another study carried out by Albar et al. [12], the researchers investigated the prevalence of vitamin D deficiency among Saudi children diagnosed with iron deficiency anemia. The findings showed that there was no significant association between vitamin D deficiency and iron deficiency anemia. However, Thomas et al. [13] examined the association between vitamin D status and iron deficiency anemia among pregnant women. There was a significant association between vitamin D status and iron deficiency anemia. Due to the variations in the reported research trials examining the association between vitamin D status and anemia, especially iron deficiency

anemia, most of the studies recommended conducting further retrospective and cross-sectional studies to assess vitamin D status among anemic patients [13].

Smith et al. [14] performed a cross-sectional cohort study to investigate whether vitamin D deficiency was associated with anemia among African-Americans in the United States. In addition, this study sought to identify whether race significantly affected this association. Serum 25-hydroxyvitamin D levels lower than 50 nmol/l are associated with anemia. The study reported that this association was not present among white Americans; however, race was found to be a significant predictor of vitamin D association with anemia. The study reported a significant association between vitamin D deficiency and anemia in African-Americans. In another study conducted by Lee et al. [15], the purpose was to determine the association between vitamin D deficiency and anemia among Korean children and adults. The study reported that the prevalence rate of vitamin D deficiency was mostly higher in female children and adults, with levels of 35.7% and 50.9%, respectively. In addition, anemia was more prevalent among female children and adults, with rates of 1.1% and 6.8%, respectively. The study results revealed a significant association between vitamin D deficiency and anemia among Korean children and adults. In a study conducted by Fialho et al. [16], the objective of the study was to assess the risk factors related to low 25-hydroxyvitamin D3 levels in patients with inflammatory bowel disease (IBD). The study adopted a $25(OH)D_3$ level <20 ng/mL as an indicator of deficiency. The results of the study showed that low levels of $25(OH)D_3$ were prevalent in 82% of the surveyed patients. The study findings revealed that vitamin D deficiency was significantly associated with low hemoglobin levels among patients with IBD. More recently, Madhu et al. [17] conducted a study that examined the association between low hemoglobin levels, vitamin deficiency, and acute lower respiratory infections among preschool children aged six months to five years. The results of the study showed that the prevalence rate of vitamin D deficiency was 70% among hospitalized patients diagnosed with acute respiratory tract infections. Among these 70%, 48% were diagnosed as having low hemoglobin levels. The study findings revealed that there is a significant association between low hemoglobin levels and vitamin D deficiency and susceptibility to acute lower respiratory tract infections. In

another cross-sectional prospective study in Saudi Arabia, Kaddam et al. [18] examined the prevalence of vitamin D deficiency and its associated factors in different regions of Saudi Arabia. The results showed that the prevalence rates of vitamin D deficiency in school students and employees were 49.5% and 44%, respectively. Logistic regression analysis revealed that a lack of supplementation was associated with vitamin D deficiency. This study assessed the association between vitamin D deficiency and anemia among patients visiting the King Khalid General Hospital in Majmaah City, Saudi Arabia.

2. METHODOLOGY

2.1 Study Subject and Data Collection

The study subjects included 120 patients (median age, men 37.44 [±17.86] years and women 43.22 [±16.23] years; range, 1–96 years) from January 2019 to January 2020. Patient data were collected from the logbook of the King Khalid General Hospital laboratory in Majmaah city, Saudi Arabia. The laboratory data included the following parameters: complete blood count (Hb, MCV, MCHC, MCH, Hct, WBC, RBC, and Plt) and vitamin D (25(OH)D). All the normal ranges for the tested parameters were specified according to the standard operating procedures of the hospital laboratory.

2.2 Definitions of Anemia and Vitamin D Deficiency

Anemia was defined according to the National Institute of Health's (NIH) (https://www.nhlbi.nih.gov/health-topics/iron-deficiency-anemia#:~:text=A%20complete%20blood%20count%20measures,women%20is%20diagnostic%20of%20anemia) criteria as those with hemoglobin levels less than 13 g/dl in men and less than 12 g/dl in women. Deficiency of 25(OH)D was defined as amounts less than 12 ng/ml, and inadequacy was defined as amounts less than 20 ng/ml based on the National Institute of Health's (NIH) (https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/) criteria.

2.3 Statistical Analysis

A Microsoft Excel spreadsheet was used to record the data. Data were analyzed using SAS for Windows. Descriptive statistics were obtained

for the personal characteristics. The data were tested for normality and homogeneity of variance to determine the appropriate statistics. The chi-squared statistic was used to compute the association between variables and baseline statistics of the participants; these data were based on sample blood parameters using Spearman's correlation coefficient. Odds ratios (ORs) were used to measure the strength of the association between the study variables. A probability level of 5% was used to indicate statistical significance.

3. RESULTS

A total of 120 participants were recruited for this study. A total of 34 male participants were recruited for the present study. The mean age of the participants was 34.8 years. The CBC analysis results showed that the mean level of vitamin D among the study participants was 21.3 ng/ml. In addition, the mean level of white blood cells was 5.5 × 103 cell/µL, whereas RBC levels had a mean score of 4.5 × 106 cells/µL. Hemoglobin (Hb) level measurements showed that the mean Hb level was 10.9 g/dl and the mean percentage of Hct was 35.8%. MCV measurements showed that the mean volume among the study participants was 67.0 fL. Moreover, the mean MCH level was 20.3 pg/cell, whereas the mean MCHC level was 23.2 g/dl. Finally, platelet count revealed that the mean platelet concentration among the study participants' blood samples was 20.0 × 103 cells/µl (Table 1).

A total of 86 female participants were recruited for this study. The mean age of the participants was 42.7 years. The CBC analysis showed that the mean vitamin D level among the study participants was 24.7 ng/ml. In addition, the mean level of white blood cells was 7.5 × 103 cell/µL, whereas RBC levels had a mean score of 4.5 × 106 cells/µL. Hemoglobin level measurements showed that the mean Hb level was 11.1 g/dl and the mean percentage of hematocrit was 36.8%. The MCV measurements showed that the mean volume of the study participants was 77.9 fL. Moreover, the mean MCH level was 23.6 pg/cell, and the mean MCHC level was 27.4 g/dl. Finally, the platelet count revealed that the mean platelet concentration among the study participants' blood samples was 256 × 103 cells/µL (Table 1).

Table 2 presents the study sample distribution based on the characteristics and degree of anemia. Based on age, mild anemia was most prevalent among participants aged 17–32 years, 33–48 years, and 49–64 years, as each category had 3.3% (n=4) of individuals with mild anemia. Moderate anemia prevalence was higher among the participants aged 33–48 years (8.3%, n=10), whereas severe anemia was prevalent among 0.8% (n=1) among those aged 17 to 32 years. Mild anemia was more prevalent among female participants (8.3%, n=10) compared to male participants (2.5%, n=3), moderate anemia was more prevalent among female participants (11.7%, n=14) than in male participants (1.7%, n=2), and severe anemia had a low prevalence rate among female participants (0.8%, n=1). Exploring the degree of anemia among different levels of RBC concentrations indicated that moderate anemia was the most prevalent degree of anemia among the participants, with 10.8% (n=13) of subjects having RBC levels less than 4.5×10^6 cells/µl. Meanwhile, mild anemia was most prevalent among those who had RBC levels less than 4.5×10^6 cells/µl (6.7%; n=8). Moreover, moderate anemia had a prevalence rate of 10.83% (n=13) among the participants who had WBC concentrations between 5 × 103 cells/µl and 11 × 103 cells/µl, whereas mild anemia had a prevalence rate of 8.3% (n=10) among the participants who had WBC concentrations between 5×10^3 cells/µL and 11×10^3 cells/µL. Exploring the prevalence of anemia among the participants with regard to platelet concentration revealed that the highest prevalence rate was for moderate anemia (13.3%, n=16) among the participants who had 400 × 103 cell/µl, as well as a prevalence rate of 10.8% (n=13) of mild anemia in participants who had 400 × 103 cells/µl.

Based on MCV measurements, mild anemia was prevalent among 10.8% (n=13) of participants who had an MCV of 80–100 fl, whereas moderate anemia had a prevalence rate of 8.3% (n=10) among the participants who had an MCV of 80–100 fl. The prevalence rate of anemia based on MCH measurements revealed that moderate anemia had a prevalence rate of 9.2% (n=11) among the participants with MCH levels less than 26 pg/cell, whereas the mild anemia prevalence rate among the same category was 5.8% (n=7). In addition, exploring the prevalence of different anemia degrees based on different MCHC levels showed that moderate anemia was prevalent among the study participants who had MCHC levels less than 31 g/dl, whereas mild anemia was prevalent among 10% (n=12) of the participants having less than 31 g/dl based on the MCHC measurements. For hematocrit

measurements, moderate anemia was prevalent among 13.3% (n=16) of participants who had hematocrits less than 40%, whereas mild anemia was prevalent among 7.5% (n=9) of the study participants who had hematocrits less than 40%. Cross-tabulating the degrees of anemia with the

Table 1. Clinical characteristics and blood parameters of the male population of the study

Characteristics Sex	Mean (SD±) (n=34) M	Mean (n=86) (SD±) F
Age (years)	34.8 (18.2)	42.7 (16.3)
Vitamin D (ng/ml)	21.3 (15.7)	24.7 (14.1)
WBC (×10^3 cell/μl)	5.1 (2.3)	7.1 (3.5)
RBC (10^6 cell/μl)	4.1 (0.6)	4.2 (0.4)
Hb (g/dl)	10.9 (1.5)	11.1 (1.5)
Hematocrit (%)	35.8 (4.5)	36.8 (3.7)
MCV (fL)	67.0 (5.0)	77.9 (6.4)
MCH (pg/cell)	20.3 (1.9)	23.6 (2.5)
MCHC (g/dl)	23.2 (1.6)	27.4 (2.0)
Platelet (×10^3 cell/μl)	200.8 (46.7)	256.0 (63.8)

Table 2. Prevalence of mild, moderate and severe anemia according to study subject characteristics, blood parameters, and vitamin D levels

Study subject		N (%)	Degree of anemia (120)		
			Mild (%) 11–12 g/dl Hb	Moderate (%) 8–11 g/dl Hb	Severe (%) <8 g/dl Hb
Age (years)	From 1 to 16	9 (7.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
	From 17 to 32	24 (20.0%)	4 (3.3%)	2 (1.7%)	1 (0.8%)
	From 33 to 48	48 (40.0%)	4 (3.3%)	10 (8.3%)	0 (0.0%)
	From 49 to 64	29 (24.2%)	4 (3.3%)	3 (2.5%)	0 (0.0%)
	From 65 to 80	8 (6.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	From 81 to 96	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sex	Male	34 (28.3%)	3 (2.5%)	2 (1.7%)	0 (0.0%)
	Female	86 (71.7%)	10 (8.3%)	14 (11.7%)	1 (0.8%)
RBC (10^6 cells/ μl)	<4.5	34 (28.3%)	8 (6.7%)	13 (10.8%)	1 (0.8%)
	≥4.5–5	43 (35.8%)	4 (3.3%)	3 (2.5%)	0 (0.0%)
	>5	43 (35.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
WBC (× 10^3/μl)	<5	18 (15.0%)	3 (2.5%)	3 (2.5%)	0 (0.0%)
	≥5–11	93 (77.5%)	10 (8.3%)	13 (10.8%)	1 (0.8%)
	>11	9 (7.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet (× 10^3/μl)	<140	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	≥140–400	117 (97.5%)	13 (10.8%)	16 (13.3%)	1 (0.8%)
	>400	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MCV (fl)	<80	15 (12.5%)	0 (0.0%)	6 (5.0%)	1 (0.8%)
	≥80–100	105 (87.5%)	13 (10.8%)	10 (8.3%)	0 (0.0%)
	>100	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MCH (pg/cell)	<26	53 (44.2%)	7 (5.8%)	11 (9.2%)	1 (0.8%)
	≥26–32	67 (55.8%)	6 (5.0%)	5 (4.2%)	0 (0.0%)
	>32	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MCHC (g/dl)	<31	80 (66.7%)	12 (10.0%)	15 (12.5%)	1 (0.8%)
	≥31–36	40 (33.3%)	1 (0.8%)	1 (0.8%)	0 (0.0%)
	>36	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hematocrit (%)	<40	38 (31.7%)	9 (7.5%)	16 (13.3%)	1 (0.8%)
	≥40–50	77 (64.2%)	4 (3.3%)	0 (0.0%)	0 (0.0%)
	>50	5 (4.17%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vitamin D (ng/ml)	Normal ≥30	46 (38.3%)	4 (3.3%)	6 (5.0%)	0 (0.0%)
	Mild ≥20–<30	27 (22.5%)	4 (3.3%)	4 (3.3%)	0 (0.0%)
	Moderate <20	44 (36.7%)	5 (4.12%)	6 (5.0%)	1 (0.8%)
	Severe <7	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3. Odds ratio (OR) values for the association between vitamin D deficiency and the degree of anemia using logistic regression analysis

Study subject		Degree of Anemia					
		Mild (%) 11–12 g/dl Hb		Moderate (%) 8–11 g/dl Hb		Severe (%) <8 g/dl Hb	
		p-value	OR	p-value	OR	p-value	OR
Vitamin D (ng/ml)	Normal ≥30	0.001	0.87	0.001	0.62	0.001	0
	Mild ≥20–<30	0.001	1.63	0.001	1.92	0.001	0
	Moderate <20	0.001	1.76	0.001	1.97	0.001	0
	Severe <7	0.001	0	0.001	0	0.001	0

level of vitamin D among the study participants showed that moderate anemia was highest among the participants who had vitamin D levels greater than 30 ng/ml and less than 20 ng/ml, with a prevalence rate of 5% (n=6) for each category. Mild anemia was prevalent among 4.12% (n=5) of the participants with vitamin D levels <20 ng/ml.

Table 3 indicates that there is a significant positive association between higher degrees of anemia and the degree of vitamin D deficiency. The odds ratio (OR) analysis shows ascending values. Mild vitamin D deficiency was associated with the degree of anemia from mild to moderate (OR=1.63 to 1.92). In addition, moderate vitamin D deficiency was associated with the degree of anemia, ranging from mild to moderate (OR=1.76 to 1.97). Moreover, the results confirmed a negative association between normal vitamin D values and the degree of anemia.

4. DISCUSSION

The present study aimed to investigate the association between vitamin D deficiency and anemia among patients visiting King Khalid General Hospital in Majmaah City, Saudi Arabia. There is accumulating evidence regarding the association between vitamin D deficiency and several physiological disorders [10,15,19-20]. However, its association with anemia remains a controversial issue that has attracted the attention of researchers [11,13,21]. The study revealed that the prevalence of anemia was 25%. Based on reports from the World Health Organization (WHO) and the Center of Disease Prevention and Control (CDC), anemia is a minor health problem. This prevalence rate of anemia was lower than the prevalence rate reported in Al-Hassan [22], which was 45% and 49% for moderate and severe anemia, respectively. The prevalence of anemia depends mainly on a combination of different factors, such as age, sex, health status, and other related factors. The

sampling procedure adopted in this study might significantly affect this prevalence rate, as there was no diversification of patients, and the patients were not specifically diagnosed with anemia. In this study, we mainly focused on investigating the prevalence of vitamin D levels among patients visiting King Khalid General Hospital in Majmaah City, Saudi Arabia, using a baseline of ≥30 ng/ml, as this is considered an adequate level of vitamin D. We demonstrated that Saudi female subjects had higher prevalence rates of vitamin D deficiency than male subjects. This might be attributed to the lack of sunlight exposure among Saudi women compared to men. Anemia might be a predisposing factor for patients with vitamin D deficiency, as anemic patients are less likely to be exposed to sunlight due to fatigue, which could prevent them from obtaining appropriate sun exposure. Moreover, the results of the current study showed that higher prevalence rates of vitamin D deficiency were observed among participants aged 33–48 years. This might be attributed to the decline in vitamin D starting from this age period, which was reflected directly in its prevalence rates.

Investigating the association between anemia and participants' clinical and demographic characteristics showed that there was a significant statistical association between anemia and vitamin D levels (Table 2). Vitamin D appears to be associated with anemia. However, the underlying mechanism is still unclear. A possible mechanism is that vitamin D modulates the levels of systemic cytokine production, which reduces the inflammatory milieu that causes the development of anemia. In addition, vitamin D stimulates erythroid precursors. Vitamin D receptors have been reported to be present in different non-renal tissues, such as bone marrow.

These results are in line with the findings of Yoo and Cho [10] and Lee et al. [15], who found that

vitamin D deficiency is significantly associated with anemia among examined study subjects. However, the findings are inconsistent with the findings reported by Albar et al. [12], who indicated that there was no significant association between vitamin D deficiency and anemia among Saudi subjects. Based on the findings of this study, further studies are needed to assess whether there is a causal relationship between vitamin D deficiency and anemia.

5. CONCLUSION AND LIMITATION

This study had several limitations. First, the sample size of the study was relatively small, with a low representation of male participants. A second limitation is the missing values of severe vitamin D deficiency, which affects the generalizability of the results in the study population. In addition, the higher representation rate of female participants in this study, which was double that of men, is considered another limitation of the study. Furthermore, the absence of a sufficient number of participants from older age groups is a limitation of this study. In conclusion, the results of the present study indicate that there is a significant association between vitamin D deficiency and anemia among patients visiting King Khalid General Hospital in Majmaah City, Saudi Arabia.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was obtained from the Saudi Ministry of Health (Central IRB log No: 20-207E).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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