WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 8, 137-146. Research Article ISSN 2277– 7105

ASSESSMENT OF VITAMIN D LEVEL IN CHILDREN AND ADOLESCENTS WITH SICKLE CELL DISEASE, JAZAN, KSA

Eman Merghani Ali*[1], Nuha M E Agabna[2], Yahya Ali Mohamad Mashragi[3], Mohamed Ali Ibrahim Ageel[3], Shahad Hassan Essa Alsabel[4], Sania A. I. Shaddad[5]

[1]PhD Student, Lecturer Clinical Phamacy, College of Pharmacy Jazan University, KSA.

[2]Depratment of Pharmacology, Faculty of Dentistry, University of Khartoum Sudan.

[3]Senior pharmacist, Pharmacy Department King Fahad Hospital, Jazan KSA

[4]Pharm D intern, College of Pharmacy Jazan University, KSA.

[5]Prof. of Pharmacology, Supervisor. Department of pharmacology Faculty of Medicine, University of Khartoum Sudan.

Article Received on
12 May 2021,

Revised on 1 June 2021,
Accepted on 20 June 2021

DOI: 10.20959/wjpr20218-20843

***Corresponding Author**
Eman Merghani Ali
PhD Student, Lecturer Clinical Phamacy, College of Pharmacy Jazan University, KSA.

ABSTRACT

Background: Sickle cell anaemia is a common condition among children and adolescents that can have deleterious complications, affecting the quality of life and reducing morbidity of this population. There is some evidence that vitamin D deficiency may have an influence on the incidence of complications with the disease. **Objective:** This study aims to assess the correlation between vitamin D levels and sickle cell anemia, including its complications among patients with sickle cell anemia in Saudi Arabia. **Design and Setting:** This is a cross-sectional, retrospective study that was carried out in a tertiary center in Jazan city, Saudi Arabia between may 2019 to February 2020. The study included data collection from Patients records who had sickle cell anemia. Collected data involved the type of Sickle cell disease, laboratory investigations, demographics of patients and complications due to sickle cell disease **Results:** 108 patient records were included. 51.9 % of the patients aged between 11 to 20 years old. Also, 61.1% were females. Mean weight of the included cohort was 34.5±12.8 Kg, while mean height was 131.6±19.2 cm. The most common type of sickle cell anemia was HbSS occurring among 91.7%, while 34.3% of the patients were on hydroxyurea treatment. As for vitamin D levels, 52.8% of the patients had severe deficiency. Complications were reported among 39.8% who had one to two pain episodes over the last

two years, while 85.2% did not have any acute chest syndromes and only 16.7% were on medications that alter vitamin D levels. Number of pain episodes was significantly and positively correlated to increasing deficiency levels of vitamin D (p-value<0.001). **Conclusion**: Vitamin D deficiency should be investigated and corrected as early as sickle cell disease diagnosis is made to reduce the incidence of complications, particularly pain episodes.

KEYWORDS: Vitamin D, deficiency, sickle cell disease, complications, children, Saudi Arabia.

INTRODUCTION

Sickle cell disease is considered one of the most common genetic hematological conditions in the world.[1] In the united states, estimates have shown a prevalence of the disease approaching 100000 patients. Sickle cell disease is usually accompanied with some complications due to multiple factors.[2] One of these common complications is pain, which leads to significant reduction of the quality of life, particularly for young children at school age.[3] It has been shown that increasing number of pain attacks in sickle cell anemia was significantly correlated to increased mortality.[4]

Vitamin D has been under the spot over the past twenty years and being linked to multiple disorders.[5] For sickle cell anemia, correcting low vitamin D levels can reduce number of pain episodes. Unfortunately, vitamin D deficiency has been found to be common among patients with sickle cell disease at different age groups.[6] Serum levels of 25-hydroxy-vitamin D $\leq$ 20 ng/mL are considered low. For non-sickle cell anemia individuals, the incidence of vitamin D deficiency is less than 20%.[7] However, this prevalence can reach up to 50% in sickle cell anemia patients, particularly some racial groups, such as non-Hispanic blacks.[8]

Furthermore, pediatric patients with sickle cell anemia are five times at higher risk of vitamin D deficiency compared to the rest of the population.[9] This significant deficiency of vitamin D puts them at high risk of sickle cell anemia, particularly pain. In this case, pain can be attributed to multiple factors, such as vaso-occlusion, and tissue injury.[10] Other complications that can be linked to vitamin D deficiency in sickle cell anemia patients are increased risk of infections, muscular weakness and increased risk of falls.[11]

Accordingly, understanding the correlations between vitamin D levels and sickle cell anemia complications can open the gates for better management, as well as prevention of these complications.[12] Hence, the present study aims to assess the relationship between vitamin D levels in both children and adolescents who have sickle cell anemia, through a patient cohort included from Saudi Arabia.

MATERIALS AND METHODS

Study design

This is a cross sectional retrospective study which involved collection of data from patients records in a tertiary hospital in Jazan city, Saudi Arabia between May 2019 to February 2020. The study included children aging between 5 to 12 years old and adults above 12 years who had sickle cell anemia and visited the hospital during the past year. Children less than 5 years, patients on calcium and Vit D in previous one year, pregnant women and patients with renal dysfunction were excluded.

Data collection

Data was collected using a data collection sheet including demographics of the patients, data about sickle cell disease (type of the disease and treatment use), laboratory investigations (vitamin D level, calcium level, phosphorous level, alkaline phosphatase level and hemoglobin). Additionally, information about sickle cell anemia complications was also collected, including number of pain episodes, acute chest pain and use of medications that alter vitamin D levels.

Statistical analyses

Descriptive analysis was carried out for numerical data in the form of means and standard deviations and for categorical data in the form of counts and precents. Comparative analysis was done using Chi square testing at level of significance p-value<0.05. SPSS version 26 was used for data analysis purposes.

Ethical considerations

Ethics committee approval and consent of participants were obtained before commencing the study**.**

RESULTS

One hundred and eight patient records were included in this study. All collected data were analyzed and described below.

Demographics of patients

Out of 108 patients, age group was classified into three groups (between 5 to 10 years, 11 to 20 years, and more than 20 years). 51.9 % of the patients were in the age group between 11 to 20 years old. As for gender, 61.1% were females, as described in table 1.

Table 1: Demographics of patients.

		Count	Percent
Age group	5 to 10 years	22	20.4
	11 to 20 years	56	51.9
	More than 20 years	30	27.8
Gender	Male	42	38.9
	Female	66	61.1

Additionally, weight and height of patients were also recorded. Mean weight of the included was 34.5±12.8 Kg, while mean height was 131.6±19.2 cm, as described in table 2.

Table 2: description of weight and height for included patients.

	Mean	SD	Min	Max
Weight	34.5	12.8	10	61
Height	131.6	19.2	62	157

Information about sickle cell disease

As for sickle cell disease, four types were reported including (HbSS, HbSC, SB^0 Thalassemia and SB±Thalassemia). The most common type was HbSS occurring among 91.7% of patients. Turning to treatment with hydroxyurea, only 34.3% of the patients were on treatment, as described in table 3.

Table 3: Information about sickle cell disease.

		Count	Percent
Type of sickle cell	HbSS	99	91.7
	HbSC	7	6.5
	SB^0 Thalassemia	1	0.9
	SB±Thalassemia	1	0.9
Patient on Hydroxyurea	Yes	37	34.3
	No	71	65.7

Laboratory investigations

Different laboratory investigations were reported in patients' records, including vitamin D, calcium, phosphorous, alkaline phosphatase and hemoglobin level. As for vitamin D levels, they were classified into four groups including: ≥30 ng/ml (Sufficient), 20 to < 30 ng/ml (Insufficient), less than 20 ng/ml (Deficiency) and <10 (Severe deficiency). It has been shown that 52.8% of the patients had severe deficiency, as described in table 4.

Table 4: Vitamin D levels among the included patients.

		Count	Percent
Vitamin D level	≥30 ng/ml (Sufficient)	1	0.9
	20 to < 30 ng/ml (Insufficient)	12	11.1
	less than 20 ng/ml (Deficiency)	38	35.2
	<10 (Severe deficiency)	57	52.8

Table 5: Other laboratory investigations.

	Mean	SD	Min	Max
Calcium level MMOL/L	4.1	18.3	2.2	193
Phosphorous level MMOL/L	1.5	0.5	1.4	7
Alkaline phosphatase U/L	176.3	25.8	16	233
Hemoglobin g/L	7.5	0.9	6	10.4

Sickle cell anemia complications

Different types of complications were also reported. It has been revealed that 39.8% of the patients had one to two pain episodes over the last two years, while 85.2% did not have any acute chest syndromes and only 16.7% were on medications that alter vitamin D levels, as described in table 6.

Table 6: Sickle cell anemia complications.

		Count	Percent
Number of pain episodes in the last 2 years	None	28	25.9
	1 to 2 episodes	43	39.8
	2-3 episodes	37	34.3
Number of acute chest syndrome in the last 2 years	None	92	85.2
	1 to 2 episodes	15	13.9
	2-3 episodes	1	0.9
Does patient on medications that alter vitamin D level	Yes	18	16.7
	No	90	83.3

Association of vitamin D deficiency with pain crisis and other complications

Different levels of vitamin D were compared over different types of complications using Chi-square testing at level of significance p-value<0.05. It has been shown that number of pain episodes was significantly correlated to increasing deficiency levels of vitamin D (p-value<0.001), as described in table 7.

Table 7: Association between vitamin D deficiency and complications.

		Sufficient	Insufficiency	Deficiency	Severe deficiency	P-Value
Number of pain episodes in the last 2 years	None	0.0%	35.7%	35.7%	28.6%	<0.001*
	1 to 2 episodes	2.3%	4.7%	46.5%	46.5%	
	2-3 episodes	0.0%	0.0%	21.6%	78.4%	
Number of acute chest syndrome in the last 2 years	None	1.1%	9.8%	37.0%	52.2%	0.849
	1 to 2 episodes	0.0%	20.0%	26.7%	53.3%	
	2-3 episodes	0.0%	0.0%	0.0%	100.0%	
Does patient on medications that alter vitamin D level	Yes	0.0%	11.1%	27.8%	61.1%	0.844
	No	1.1%	11.1%	36.7%	51.1%	

DISCUSSION

Sickle disease has been linked to multiple complications that represent a significant burden on the life of children as well as their parents.[13] In adulthood, sickle cell anemia can negatively affect the productivity and quality of life of patients. The most commonly limiting complication is recurrent pain episodes.[14] Vitamin D levels have been examined among patients with sickle cell disease among some racial groups. However, vitamin D levels among sickle cell disease patients in Saudi Arabia are still controversial.[15]

The present study aimed to evaluate vitamin D levels among both children and adolescents who had sickle cell anemia in Jazan, Saudi Arabia through a retrospective study. The findings of the present study demonstrated that females were more prevalent than males, while different types of sickle cell anemia have been identified. However, HbSS type was the most frequent among all of them. Additionally, different types of complications have been reported, with pain episodes identified as the most commonly occurring complication among patients.

An important finding was vitamin D level among the included cohort which showed alarming deficiency that should be further investigated in future studies. It has been demonstrated that 88% of the patients suffered from vitamin D deficiency, with 52.8% having severe deficiency. Moreover, these severe deficiencies in vitamin D level have been significantly correlated to the frequency of pain episodes.

Vitamin D levels have been investigated in various settings. Hood et al.[16] recently investigated the effect of vitamin D supplementation on emergency department visits for children with sickle cell anemia due to pain episodes. Through a retrospective cohort of 110 patients aging below 16 years old, Hood et al.[16] demonstrated that 45% of the patients had vitamin D deficiency. Furthermore, Hood et al.[16] showed a significant correlation between administering vitamin D supplementation and reduced emergency department admission due to pain in sickle cell anemia patients (p-value=0.03).

This finding from Hood et al.[16] supports the findings of the present study. Although the present study did not include information about vitamin D supplementation, it evaluated vitamin D levels at different categories, where higher proportion of patients had vitamin D deficiency compared to Hood et al.[16] Moreover, the present study demonstrated a significant correlation between increasing deficiency of vitamin D levels and increasing number of pain episodes (p-value<0.001).

Another study by Hamdy et al.[17] examined the complications associated with vitamin D level deficiency among a cohort of sickle cell anemia in Egypt. Hamdy et al.[17] included 80 patients aging below 16 years old and had sickle cell anemia. He demonstrated that patients with vitamin D deficiency had a significantly higher incidence of hospitalization, recurring infections, need for blood transfusion, and thrombosis.

The present study did not examine the complications examined by Hamdy et al.[17] due to the retrospective nature of the study, where information about these complications was missing. Instead, the present study examined the correlation between vitamin D deficiency and one of the most common complications, which is a pain episode. It is obvious from both Hamdy et al.[17] and Hood et al.[16] that the present study has included patients from a broader range of age groups compared to other studies.

Moreover, a study from Saudi Arabia by Aljama et al.[18] examined vitamin D deficiency level among patients with sickle cell anemia in Eastern province. Aljama et al.[18] included 640 patients with sickle cell disease who were older than 11 years old over five years. He demonstrated that 67% of the patients had vitamin D deficiency level. This percentage is closely related to the percentage of vitamin D deficiency reported in the present study in Jazan. Additionally, Aljama et al.[18] showed a significant correlation between sickle cell disease crisis and vitamin D deficiency, which is also compliant to the results from the present study.

The present study also suffered from some important limitations that should be considered. Due to the retrospective nature of the study, some laboratory investigations were missing or not available which affected the number of laboratory investigations included in the present study. Additionally, the sample size of the included cohort was relatively small which may have results in failure to achieve statistical significance for some complications of sickle cell disease.

CONCLUSION

Vitamin D deficiency has shown to play a significant role in the occurrence of sickle cell anemia complications, especially pain episodes. Accordingly, vitamin D levels should be investigated as early as a diagnosis with sickle cell anemia is made and corrected if necessary. Furthermore, awareness among parents with children having sickle cell anemia should improve about the importance of vitamin D supplementation for their children Phosphatase U/L.

REFERENCES

1. Han J, Zhang X, Saraf SL, Gowhari M, Molokie RE, Hassan J, Jain S, Shah BN, Abbasi T, Machado RF, Gordeuk VR. Risk factors for vitamin D deficiency in sickle cell disease. British journal of haematology, 2018 Jun; 181(6): 828-35.
2. Adegoke SA, Smith OS, Adeniyi AT, Adekile AD. Thrombospondin-1 and vitamin D in children with sickle cell anemia. Journal of pediatric hematology/oncology, 2019 Nov 1; 41(8): e525-9.
3. Mandese V, Bigi E, Bruzzi P, Palazzi G, Predieri B, Lucaccioni L, Cellini M, Iughetti L. Endocrine and metabolic complications in children and adolescents with Sickle Cell Disease: an Italian cohort study. BMC pediatrics, 2019 Dec; 19(1): 1-9.

4. Brown B, Long K, Agdere L, Kulpa J, Zarzoso-Fernandez S, Choudhary D, Sundarum R. The association between vitamin D deficiency and hospitalization outcomes in pediatric patients with sickle cell disease. Blood Cells, Molecules, and Diseases, 2020 May 1; 82: 102415.
5. Adegoke SA, Smith OS, Adekile AD, Figueiredo MS. Relationship between serum 25-hydroxyvitamin D and inflammatory cytokines in paediatric sickle cell disease. Cytokine, 2017 Aug 1; 96: 87-93.
6. Hama AH, Shakiba E, Rahimi Z, Karimi M, Mozafari H, Abdulkarim OA. Vitamin D level, lipid profile, and vitamin D receptor and transporter gene variants in sickle cell disease patients from Kurdistan of Iraq.
7. Adly A, Ebeid F, Sallam S, Gohar A. PB2316 EFFECT OF VITAMIN D SUPPLEMENTATION ON CLINICAL OUTC OMES OF SICKLE CELL DISEASE. HemaSphere, 2019 Jun 1; 3(S1): 1032-3.
8. Badr MA, Abdel-Latef AM, Abdel Fattah NR, Attia AH. Assessment of Vitamin D Level and Osteoporosis in Children with Sickle Cell Anemia. The Egyptian Journal of Hospital Medicine, 2020 Oct 1; 81(3): 1583-9.
9. McCaskill ML, Ogunsakin O, Hottor T, Harville EW, Kruse-Jarres R. Serum 25-hydroxyvitamin D and diet mediates vaso-occlusive related hospitalizations in sickle-cell disease patients. Nutrients, 2018 Oct; 10(10): 1384.
10. Adegoke SA, Oyelami OA, Adekile A, Figueiredo MS. Influence of serum 25-hydroxyvitamin D on the rate of pain episodes in Nigerian children with sickle cell anaemia. Paediatrics and international child health, 2017 Jul 3; 37(3): 217-21.
11. Jain D, Jaiswal S, Bakshi N, Krishnamurti L. Frequency of Vasocclusive Crises and the Relationship of Vitamin D Deficiency to the Frequency of Pain Crises in Children with Sickle Cell Disease in an Aboriginal Tribal Region in Gadchiroli, India. Blood, 2017 Dec 7; 130(Supplement 1): 3551.
12. Bordbar MR, Haghpanah S, Zarei T, Dabbaghmanesh MH, Omrani GR, Saki F. Evaluation of bone mineral density in children with sickle-cell anemia and its associated factors in the south of Iran: a case-control study. Archives of osteoporosis, 2017 Dec; 12(1): 1-9.
13. Adegoke SA, Braga JA, Adekile AD, Figueiredo MS. The association of serum 25-hydroxyvitamin D with biomarkers of hemolysis in pediatric patients with sickle cell disease. Journal of pediatric hematology/oncology, 2018 Mar 1; 40(2): 159-62.

14. Zivot A, Apollonsky N, Gracely E, Raybagkar D. Body mass index and the association with vaso-occlusive crises in pediatric sickle cell disease. Journal of Pediatric hematology/oncology, 2017 May 1; 39(4): 314-7.
15. Mohamed SO, MohamedElmugadam FA, Awadalla HF, Mohamedali AO, Alawad MO, Noureddin AA, Osman AA, Mohamed EM, Ibrahim GA, Elsayed MA. A Meta-analysis on Vitamin D Deficiency in Patients with Sickle Cell Disease. Dr. Sulaiman Al Habib Medical Journal, 2020 Jul; 2(3): 95-100.
16. Hood AM, Quinn CT, King CD, Shook LM, Peugh JL, Crosby LE. Vitamin D supplementation and pain-related emergency department visits in children with sickle cell disease. Complementary therapies in medicine, 2020 Mar 1; 49: 102342.
17. Hamdy M, Salama N, Maher G, Elrefaee A. Vitamin D and nonskeletal complications among Egyptian sickle cell disease patients. Advances in hematology, 2018 Sep 16; 2018.
18. AlJama A, AlKhalifah M, Al-Dabbous IA, Alqudaihi G. Vitamin D deficiency in sickle cell disease patients in the Eastern Province of Saudi Arabia. Annals of Saudi medicine, 2018 Mar; 38(2): 130-6.