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Role of Vitamin D in Female Sickle Cell Anemia Patients in Saudi Arabia

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ABSTRACT

Background & Objectives: *Sickle-Cell Disease (SCD) patients make up around 20% of Saudi Arabia population. Several studies showed an association between vitamin D deficiency (VDD) and chronic pain crisis as well as reports of improved pain symptoms and decreased analgesic use with vitamin D supplementation. The current study was aimed to improve quality of life in patients with Sickle-Cell Anemia (SCA), determining the role of vitamin D in improve VDD symptoms among SCA patients in Saudi Arabia.*

Methods: *Seventy-five female SCA respondents vary aged between (16 and more than 30 years). Thirty-six respondents were SCT and thirty-nine respondents were SCA and positive and negative for VDD were enrolled to interviewing and self-administered close-format questionnaire.*

Results: *The level of daily life activities with patients who taking VD supplements are various. In young SCA female group (16-20 years old) was low (% of patients who are taking VD 50%~ % of patients who felt in low daily life activity 50%), in group (21-25 years old) was also low (35.71%~50%), in group (26-30 years old) was significant low (75%~100%), and in group (more than 30 years old) was low too (57.14%~57.14%).*

Conclusion: *Patients with Sickle Cell Anemia have increased risk of VDD. In this study, VDD is related to decrease daily life activity and increase the chronic pain of SCD female patients. More physicians' awareness needed to realize the role of VD in long-term relieving rather than temporary relief.*

Keywords: *Adult female, Vitamin D deficiency VDD, Sickle Cell Disease SCD, Sickle Cell Trait SCT, Chronic pain.*

1. INTRODUCTION

Sickle cell anemia is the most common form of sickle cell disease (SCD), which is refers to serious hereditary disorder in which the body makes sickle-shaped red blood cells, due to mutation of Hemoglobin genes[1]. SCD patients make up around 20% of Saudi Arabia population[2]. Recent studies report a high prevalence of vitamin D deficiency (VDD) among patients with SCD, with rates as high as 65–100% depending on the season. Despite this evidence, VDD remains both under-recognized and under-treated in patients with SCD. There appears to be substantial overlap between the symptoms of chronic pain seen in SCD and VDD. In both conditions, pain is commonly localized to the lower spine, pelvis and extremity bones and described as a dull, aching pain exacerbated by activity and weight

bearing. Both conditions are associated with an increased risk of low bone mineral density (BMD) [3], which may leads to Osteoporosis.

Thus it is worthwhile to understand the role of prescribed Vitamin D to resolve VDD in SCA patients, role of importance of annual bone tests in SCA and physicians education about this importance. Hence we can improve symptoms, outcomes, and quality of life in SCD patients.

2. OBJECTIVES

- ✓ The primary objective of this study to improve quality of life in patients with SCA.
- ✓ Determined the role of VD in altering daily activities of SCA patients.
- ✓ Understood the importance of early bone test in all SCA patients
- ✓ Spread the awareness between SCA patients, about importance of early bone test for them.
- ✓ Compared taking prophylactic Vitamin D among SCA patients.

3. REVIEW OF LITERATURES

Bone involvement is the commonest clinical manifestation of sickle cell disease both in the acute or chronic setting[4]. Adults with sickle cell disease have a high prevalence of low bone density and chronic pain with poorly defined etiologies[5].

Vitamin D is essential for strong bones because it helps the body use calcium from the diet[6]. Generally, Women have lower vitamin D levels than men for a few possible reasons: Women tend to have more body fat than men, they spend a bit more time indoors, and tend to wear hats and sunscreen more often than men[7]. Beside these reasons, SCA women have RBC abnormality with low oxygen level in, which blocks oxygen to the bone and contributes in bone loss and pain[8]. Several studies showed an association between VDD and chronic pain syndromes as well as reports of improved pain symptoms and decreased analgesic use with vitamin D supplementation. The mechanisms by which vitamin D modulates pain remain unclear and may be a result of direct nervous system effects or indirectly from improved bone health[9].

Vitamin D deficiency is a common finding among children and adults with SCD. Although one study suggested no correlation between low bone mineral density and vitamin D levels, another found a correlation between lower levels of plasma vitamin D and more frequent and severe bone disease in adults. Treatment with vitamin D and calcium supplementation can improve bone mineral density, but does not affect markers of bone resorption[10].

In evidence, Research suggests that vitamin D could play a role in the prevention and treatment of a number of different conditions, including type1 and type 2 diabetes, hypertension, glucose intolerance, and multiple sclerosis[11]. Endocrine organ dysfunctions are commonly encountered in children and adolescents with SCD, and vitamin D deficiency is the most commonly encountered endocrine disorder. Regular follow-ups of patients for endocrine complications starting at early ages and initiation of appropriate treatments will elongate expectancy and quality of life[12]. There is possibility that such risk can be minimized through treatment of vitamin D deficiency[13].

The use of prophylactic vitamin D in SCD resulted in delayed post-operative analgesic request and less total analgesic consumption. Administration of vitamin D was also associated with noticeable less post-operative SCD complications. This work focused on the significance of vitamin D in management of SCD patients. Prophylactic vitamin D has proved a modifiable effect on the anesthetic outcome in male SC children[14].

4. METHODOLOGY

We conducted close-format questionnaire based study. The study was approved by Almaarefa College for Science and Technology. Questionnaires were interview based and self-administered, involved Saudi citizen randomly. Interviewing-administered done in Alqatif city mall in Alqatif, Eastern region of Saudi Arabia on Friday 18/04/2014 by distributing the questionnaires to visitors and shoppers. Self-administered was on Google Drive survey from 24/03/2014 to 23/04/2014, Almaarefa College's Facebook page on 7/04/2014, and Werathah forum website for hereditary diseases on 28/03/2014. One hundred and seven were total respondents. Seventy-five female SCA respondents varies between (16-more than 30 years) and positive and negative for VDD were enrolled. Most of them were students. Thirty-six respondents were SCT and thirty-nine respondents were SCA. Eighteen male respondents were excluded because of the few number responding and fourteen respondents, who didn't know if they had SCA, were excluded too.

5. RESULTS

We found 60% of SCT female in age 16-20 years old; never experience any pain attacks lifelong, compared to 78.57% of SCD female respondents in same age, who often experience SCA pain attack. In SCT, visiting hospitals will definitely decreased by 40%, therefore, hospitalization decreased by 80%, compared to SCD, who increased visiting hospitals monthly by 50% and annually by 35.71%, therefore, hospitalization increased more than one time for every single respondents by 64.28% and one time by 14.28% of respondents. Also, we found 40% of SCT respondents are negative for VDD and 40% of them do not know if they have VDD, while; only 20% are positive for VDD. On the other hand, 28.57% of SCD respondents are positive for VDD, but, 42.85% of them are negative and 28.57% of them do not know if they have VDD. 100% of SCT respondents do not take any VD supplements, while, 50% of SCD respondents do and 42.85% of them do not. It was observed in our study that 40% of SCT respondents asked for giving blood sample by SCA's physician to check VD level and same percentage for whose did not, compared to 85.71% of SCD respondents asked for the blood sample and only 14.28% did not. Fortunately, all of SCT respondents felt that SCA doesn't decrease their daily life activity, while, the major numbers of SCD respondents felt that SCA decrease their daily life activity by 50% and only 21.42% of them did not.

We found 56.25% of SCT female in age 21-25 years old, never experience any pain attacks lifelong, compared to 50% of SCD female respondents in same age, who often experience SCA pain attack and 42.85% of them are always suffer. In SCT, visiting hospitals will definitely decreased by 87.5%, therefore, hospitalization decreased by 93.75%, compared to SCD, who increased visiting hospitals monthly by 35.71% and annually by 42.85%, therefore, hospitalization increased more than one time for every single respondents by 64.28% and one time by 14.28% of respondents. Also, we found

equal percentages for SCT respondents who are negative and positive for VDD with 31.25% and 37.5% of them do not know if they have VDD, also, we reported equal percentages for SCD respondents who are negative and positive for VDD with 35.71% and 28.57% of them don't know if they have VDD. 75% of SCT respondents do not take any VD supplements and 64.28% of SCD respondents do not too. It was observed in our study that 37.5% of SCT respondents asked for giving blood sample by SCA's physician to check VD level and 62.5% did not, compared to 100% of SCD respondents asked for the blood sample. Fortunately, 68.75% of SCT respondents felt that SCA doesn't decrease their daily life activity, while, half numbers of SCD respondents felt that SCA decrease their daily life activity and the others did not.

We found 57.14% of SCT female in age 26-30 years old, never experience any pain attacks lifelong, compared to 75% of SCD female respondents in same age, who often experience SCA pain attack. In SCT, visiting hospitals will definitely decreased by 85.71%, therefore, hospitalization decreased by 100% of the same respondents, compared to SCD, who increased visiting hospitals monthly by 50% and annually by 50%, therefore, hospitalization increased more than one time for every single respondents by 75% and one time by 25% of respondents. Also, we found only 14.25% of SCT respondents are negative for VDD and 42.85% are positive, while, 42.85%of them do not know if they have VDD. On the other hand, 50% of SCD respondents are negative, only 25% are positive for VDD and 25% of them do not know if they have VDD. 42.85% of SCT respondents are taking VD supplements and equal percentages are not, while, 75% of SCD respondents do and only 25% of them do not. It was observed in our study that 42.85% of SCT respondents asked for giving blood sample by SCA's physician to check VD level and the major numbers by 57.14% did not, compared to SCD respondents, all of them asked for the blood sample. 42.85% of SCT respondents felt that SCA doesn't decrease their daily life activity and equal percentage for does, while, all respondents of SCD respondents felt that SCA decrease their daily life activity.

We found 50% of SCT female in age more than 30 years old, never experience any pain attacks lifelong and 50% of them are rarely do, compared to 71.42% of SCD female respondents in same age, who often experience SCA pain attack. In SCT, visiting hospitals will definitely decreased by 87.5%, therefore, hospitalization decreased by 87.5%, compared to SCD, who increased visiting hospitals monthly by 28.57% and annually by 57.14%, therefore, hospitalization increased more than one time for every single respondents by 71.42%. Also, we found 50% of SCT respondents are negative for VDD and 12.5% of them do not know if they have VDD, while, only 37.5% are positive for VDD. On the other hand, 42.85% of SCD respondents are negative for VDD and 14.28% do not know if they have VDD, while, only 42.85% of them are positive. 75% of SCT respondents do not take any VD supplements, while, 57.14% of SCD respondents do and the rest do not. It was observed in our study that 50% of SCT respondents asked for giving blood sample by SCA's physician to check VD level and same percentage for whose did not, compared to 85.71% of SCD respondents asked for the blood sample and only 14.28% did not. Fortunately, 50% of SCT respondents felt that SCA doesn't decrease their daily life activity, while, high numbers of SCD respondents felt that SCA decrease their daily life activity by 57.14% and the rest of them did not.

TABLE 1. Role of SCT and SCD in altering daily activities of patients in age group 16-20 years

Questions	(A)		(B)		(C)		(D)		(E)	
	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD
How often do you have sickle cell anemia pain attack?	Always		Sometimes		Rarely		Never			
	0	2 **14.28%**	1 **20%**	11 **78.57%**	1 **20%**	1 **7.14%**	3 **60%**	0		
How often do you visit hospital because of sickle cell anemia pain attack?	Weekly		Monthly		Annually		Never		I don't know	
	0	0	0	7 **50%**	0	5 **35.71%**	2 **40%**	0	3 **60%**	2 **14.28%**
Did you ever hospitalized because of Sickle cell anemia pain attack?	Yes, many times		Yes, once		No, I did not		I don't remember			
	0	9 **64.28%**	0	2 **14.28%**	4 **80%**	3 **21.42%**	1 **20%**	0		
Did your physician diagnose you with Vitamin D deficiency?	Yes		No		I don't know					
	1 **20%**	4 **28.57%**	2 **40%**	6 **42.85%**	2 **40%**	4 **28.57%**				
Are you taking Vitamin D supplement (pills, injection, ...etc)?	Yes		No		I don't know					
	0	7 **50%**	5 **100%**	6 **42.85%**	0	1 **7.14%**				
Have you ever asked to give blood sample by your physician whom treating your Sickle cell anemia symptoms?	Yes		No		I don't know					
	2 **40%**	12 **85.71%**	2 **40%**	2 **14.28%**	1 **20%**	0				
Are you taking any other medications for sickle cell anemia treating?	Yes		No		I don't know					
	0	9 **64.28%**	5 **100%**	4 **28.57%**	0	1 **7.14%**				
Do you feel that Sickle cell anemia decrease your daily life activity, even with medications?	Yes		No		I don't know					
	0	7 **50%**	5 **100%**	3 **21.42%**	0	4 **28.57%**				

No of respondents in SCT: 05; No of respondents in SCD: 14; data is expressed as 'no of responses (percentage of response); SCT: Sickle cell trait; SCD: Sickle cell Disease.

TABLE 2. Role of SCT and SCD in altering daily activities of patients in age group 21-25 years

No of respondents in SCT: 16; No of respondents in SCD: 14; data is expressed as 'no of responses (percentage of response); SCT:

Questions	(A)		(B)		(C)		(D)		(E)	
	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD
How often do you have sickle cell anemia pain attack?	Always		Sometimes		Rarely		Never			
	0	6 **42.85 %**	4 **25%**	7 **50%**	3 **18.75%**	1 **7.14 %**	9 **56.25 %**	0		
How often do you visit hospital because of sickle cell anemia pain attack?	Weekly		Monthly		Annually		Never		I don't know	
	0	0	1 **6.25 %**	5 **35.71 %**	1 **6.25%**	6 **42.85 %**	14 **87.5 %**	1 **7.14 %**	0	2 **14.28%**
Did you ever hospitalized because of Sickle cell anemia pain attack?	Yes, many times		Yes, once		No, I did not		I don't remember			
	0	9 **64.28 %**	1 **6.25 %**	2 **14.28 %**	15 **93.75%**	2 **14.28 %**	0	1 **7.14 %**		
Did your physician diagnose you with Vitamin D deficiency?	Yes		No		I don't know					
	5 **31.25%**	5 **35.71 %**	5 **31.25 %**	5 **35.71 %**	6 **37.5%**	4 **28.57 %**				
Are you taking Vitamin D supplement (pills, injection, ...etc)?	Yes		No		I don't know					
	4 **25%**	5 **35.71 %**	12 **75%**	9 **64.28 %**	0	0				
Have you ever asked to give blood sample by your physician whom treating your Sickle cell anemia symptoms?	Yes		No		I don't know					
	6 **37.5%**	14 **100%**	10 **62.5 %**	0	0	0				
Are you taking any other medications for sickle cell anemia treating?	Yes		No		I don't know					
	3 **18.75%**	9 **64.28 %**	13 **81.25 %**	4 **28.57 %**	0	1 **7.14 %**				
Do you feel that Sickle cell anemia decrease your daily life activity, even with medications?	Yes		No		I don't know					
	3 **18.75%**	7 **50%**	11 **68.75 %**	7 **50%**	2 **12.5%**	0				

Sickle cell trait; SCD: Sickle cell Disease

TABLE 3. Role of SCT and SCD in altering daily activities of patients in age group 26-30 years

Questions	(A)		(B)		(C)		(D)		(E)	
	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD
How often do you have sickle cell anemia pain attack?	Always		Sometimes		Rarely		Never			
	1 **14.28%**	0	0	3 **75%**	2 **28.57%**	1 **25%**	4 **57.14 %**	0		
How often do you visit hospital because of sickle cell anemia pain attack?	Weekly		Monthly		Annually		Never		I don't know	
	0	0	0	2 **50%**	0	2 **50%**	6 **85.71 %**	0	1 **14.28 %**	0
Did you ever hospitalized because of Sickle cell anemia pain attack?	Yes, many times		Yes, once		No, I did not		I don't remember			
	0	3 **75%**	0	1 **25%**	7 **100%**	0	0	0		
Did your physician diagnose you with Vitamin D deficiency?	Yes		No		I don't know					
	3 **42.85%**	1 **25%**	1 **14.28%**	2 **50%**	3 **42.85%**	1 25%				
Are you taking Vitamin D supplement (pills, injection, ...etc)?	Yes		No		I don't know					
	3 **42.85%**	3 **75%**	3 **42.85%**	1 **25%**	1 **14.28%**	0				
Have you ever asked to give blood sample by your physician whom treating your Sickle cell anemia symptoms?	Yes		No		I don't know					
	3 **42.85%**	4 **100%**	4 **57.14%**	0	0	0				
Are you taking any other medications for sickle cell anemia treating?	Yes		No		I don't know					
	0	2 **50%**	7 **100%**	2 **50%**	0	0				
Do you feel that Sickle cell anemia decrease your daily life activity, even with medications?	Yes		No		I don't know					
	3 **42.85%**	4 **100%**	3 **42.85%**	0	1 **14.28%**	0				

No of respondents in SCT: 07; No of respondents in SCD: 04; data is expressed as 'no of responses (percentage of response); SCT: Sickle cell trait; SCD: Sickle cell Disease

TABLE 4: Role of SCT and SCD in altering daily activities of patients in age group more than 30 years

Questions	(A)		(B)		(C)		(D)		(E)	
	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD	SCT	SCD
How often do you have sickle cell anemia pain attack?	Always		Sometimes		Rarely		Never			
	0	1 **14.28 %**	0	5 **71.42 %**	4 **50%**	1 **14.28 %**	4 **50%**	0		
How often do you visit hospital because of sickle cell anemia pain attack?	Weekly		Monthly		Annually		Never		I don't know	
	0	0	0	2 **28.57 %**	1 **12.5%**	4 **57.14 %**	7 **87.5%**	1 **14.28 %**	0	0
Did you ever hospitalized because of Sickle cell anemia pain attack?	Yes, many times		Yes, once		No, I did not		I don't remember			
	0	5 **71.42 %**	1 **12.5 %**	0	7 **87.5%**	2 **28.57 %**	0	0		
Did your physician diagnose you with Vitamin D deficiency?	Yes		No		I don't know					
	3 **37.5 %**	3 **42.85 %**	4 **50%**	3 **42.85 %**	1 **12.5%**	1 **14.28 %**				
Are you taking Vitamin D supplement (pills, injection, ...etc)?	Yes		No		I don't know					
	2 **25%**	4 **57.14 %**	6 **75%**	3 **42.85 %**	0	0				
Have you ever asked to give blood sample by your physician whom treating your Sickle cell anemia symptoms?	Yes		No		I don't know					
	4 **50%**	6 **85.71 %**	4 **50%**	1 **14.28 %**	0	0				
Are you taking any other medications for sickle cell anemia treating?	Yes		No		I don't know					
	2 **25%**	3 **42.85 %**	6 **75%**	4 **57.14 %**	0	0				
Do you feel that Sickle cell anemia decrease your daily life activity, even with medications?	Yes		No		I don't know					
	1 **12.5 %**	4 **57.14 %**	4 **50%**	3 **42.85 %**	3 **37.5%**	0				

No of respondents in SCT: 08; No of respondents in SCD: 07; data is expressed as 'no of responses (percentage of response); SCT: Sickle cell trait; SCD: Sickle cell Disease.

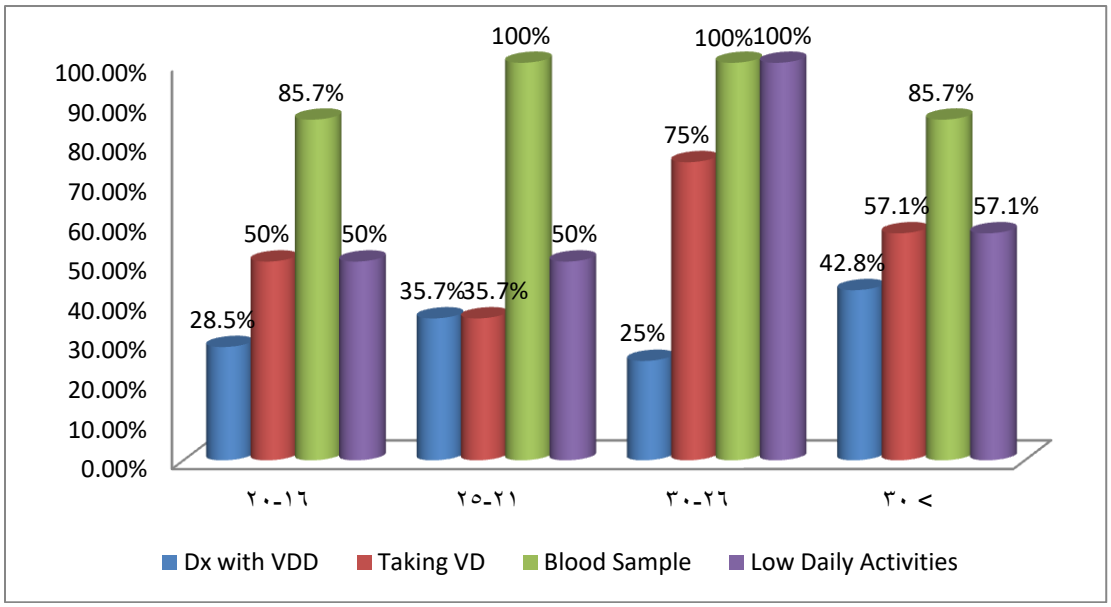

Figure 1. Percentage comparison in positive (VDD diagnosing, taking VD supplements, blood sample requesting, and decreasing daily-life activity by SCA), between all adopted ages

DISCUSSION

Pain remains the leading cause of morbidity and healthcare utilization for individuals with SCD[15]. We aimed to increasing daily life activity of SCA patients by emphasize the importance of checking VD level regularly. We found large number of patients didn't have knowledge about their condition and if they had VDD and how much VDD risk they had, which need high awareness and education. Fortunately, there is slight daily activities improvement between SCA patients, who take VD, which definitely will decrease bone pain, but it won't take away the entire pain crisis. Therefore, patients will need SCA medications and pain killer (if necessary) beside the VD. That will never eliminate the existing of VDD risk in SCA.

We tried hardly to reach Hematology physicians to find out prevalence of VDD in SCA patients and how much they considering VD in their intervention, but unfortunately, they weren't co-operative with us except few of them, so we got only nine respondents, which the major number of them believed that VDD increases pain in SCD patients and prescribing VD earlier with SCD medications was controversial, 33.33% believed that helps in relieving the pain 50% and higher, also the same percentage for those who believed that relieving the pain under 50% and who believed that not helping at all. 66.7% of them said that there are many effective alternatives in relieving the pain rather than VD such as; opioid analgesics, Hydroxyurea, and pain killers. On the other hand, they believe in the role of VD in relieving chronic pain in SCD patients.

CONCLUSION

Patients with Sickle Cell Anemia have increased risk of VDD. In this study, VDD is related to decrease daily life activity and increase the chronic pain of SCD female patients. More physicians' awareness needed to realize the role of VD in long-term relieving rather than temporary relieve of those patients. Randomized clinical trial strongly needed to know the pathway of VD effects in SCD patients.

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