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Prevalence of Vitamin-D Deficiency in Transfusion-Dependent Sickle Cell Anaemia Patients in Al-Qunfudah Region

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Abstract **Background:** Vitamin D deficiency (VDD) is a significant public health concern, particularly in Saudi Arabia, where limited sunlight exposure, cultural clothing practices and dietary patterns contribute to high prevalence rates. Individuals with chronic haematological disorders specifically those with transfusion-dependent sickle cell anaemia (SCA) face heightened risk owing to increased metabolic demands, chronic haemolysis and restricted mobility. This study aimed to assess and compare serum vitamin D [25(OH)D] levels between transfusion-dependent SCA patients and age- and sex-matched healthy controls in the Al-Qunfudah region, southwestern Saudi Arabia. **Methods:** A cross-sectional case-control study was conducted between November 2024 and March 2025 at Al-Mudilif General Hospital, Al-Qunfudah. One hundred participants were enrolled: 50 transfusion-dependent SCA patients and 50 healthy controls. Serum 25(OH)D levels were measured by electrochemiluminescence immunoassay. Between-group comparisons were performed using the independent samples t-test, with statistical significance set at $p<0.05$. **Results:** The mean serum 25(OH)D level was 11.7±4.66 ng/mL in patients versus 31.16±5.89 ng/mL in controls (95% CI for difference: 17.18-21.74 ng/mL; $p<0.001$). Patients also exhibited significantly lower haemoglobin (8.17±1.60 vs. 13.79±1.10 g/dL), haematocrit (24.12±5.66 vs. 40.74±4.91%) and red blood cell counts (3.09±0.93 vs. 4.59±0.76 $\times 10^6$/µL) compared with controls (all $p<0.001$). **Conclusion:** Serum vitamin D levels are markedly lower in transfusion-dependent SCA patients in Al-Qunfudah than in healthy individuals. VDD represents a prevalent and potentially modifiable comorbidity in this population. Routine vitamin D screening and targeted supplementation should be integrated into standard clinical care for high-risk SCA patients.

Key Words Vitamin-D Deficiency, Transfusion-Dependent Sickle Cell Anaemia, 25-Hydroxyvitamin D, Case-Control Study, Al-Qunfudah, Saudi Arabia

INTRODUCTION

Sickle cell anaemia (SCA) is a chronic autosomal-recessive haemoglobinopathy characterised by significant morbidity, including vaso-occlusive crises, chronic haemolysis and multi-organ complications. It is particularly prevalent in regions with a high carrier frequency of haemoglobin S, including western Saudi Arabia [1].

Vitamin D deficiency (VDD) is highly prevalent in Saudi Arabia due to limited sun exposure, cultural clothing practices and dietary insufficiency. Individuals with SCA are especially vulnerable to VDD because of chronic haemolysis, impaired vitamin D metabolism, reduced physical activity and frequent hospitalisations [2,3]. Saudi Arabia has reported some of the world's highest rates of VDD, a burden that extends to patients with haematological disorders [4].

VDD in SCA patients has been linked to adverse outcomes including bone fragility, increased frequency of vaso-occlusive pain crises and heightened susceptibility to infections [5,6]. Despite growing evidence for the clinical relevance of vitamin D status in SCA, population-specific data from Al-Qunfudah a region in southwestern Saudi

Arabia with a documented high prevalence of SCA remain scarce. This study was therefore conducted to provide region-specific evidence to guide clinical screening and supplementation practice.

Objectives

The objectives of this study were:

- To measure and compare serum 25(OH)D levels between transfusion-dependent SCA patients and healthy controls in Al-Qunfudah
- To compare key haematological parameters (haemoglobin, haematocrit, red blood cell count) between the two groups
- To establish regional baseline data on VDD prevalence in SCA to inform clinical practice and public health interventions in Al-Qunfudah and comparable Saudi regions

METHODS

Study Design and Setting

This cross-sectional case-control study was conducted at Al-Mudilif General Hospital, a tertiary care centre in Al-Qunfudah, Saudi Arabia, between November 2024 and March 2025.

Study Population

A total of 100 participants were recruited and assigned to two groups:

- Patient group (n = 50): Adults with a confirmed diagnosis of transfusion-dependent SCA receiving regular blood transfusions (at least once every 6-8 weeks for the preceding 12 months), managed at Al-Mudilif General Hospital
- Control group (n = 50): Age- and sex-matched healthy adults without any chronic illness or known haematological or metabolic disorder, recruited from adult blood donors at the hospital blood bank

Inclusion and Exclusion Criteria

Inclusion criteria:

- Aged 18 years or older
- Patient group: confirmed diagnosis of transfusion-dependent SCA with regular transfusion history
- Control group: no history of chronic disease and not taking vitamin D supplements

Exclusion criteria:

- Current use of vitamin D supplements or medications known to affect bone metabolism (e.g. corticosteroids, anticonvulsants)
- Known hepatic, renal or endocrine disorders
- Recent acute illness or hospitalisation within the past month
- Pregnancy or lactation

Data Collection and Sample Handling

Demographic data, medical history and transfusion frequency were collected through structured patient interviews and review of medical records. Blood samples were collected under sterile conditions: EDTA-anticoagulated tubes for complete blood count (CBC) analysis and plain clot-activator tubes for serum vitamin D assay. Serum samples were obtained by centrifugation at 3,000 rpm for 10 minutes at room temperature and stored at −20 °C until analysis. For control participants, samples were collected at the time of blood donation.

No participant data were missing; all 100 enrolled participants provided complete haematological and biochemical data.

Laboratory Analysis

CBC analysis was performed on a Sysmex XN-550 automated haematology analyser. Serum 25(OH)D was measured on a Roche Cobas e411 immunochemistry analyser using electrochemiluminescence immunoassay (ECLIA). Both analysers underwent routine calibration and quality-control verification prior to sample testing. Vitamin D status was classified according to Endocrine Society guidelines [7]:

- Deficient:<20 ng/mL
- Insufficient: 20-29 ng/mL
- Sufficient: 30-100 ng/mL
- Toxicity risk: >100 ng/mL

Statistical Analysis

Data were analysed using IBM SPSS Statistics, version 26. Continuous variables are reported as mean±standard deviation (SD). Normality was assessed using the Shapiro-Wilk test; all variables were normally distributed. The independent samples t-test was therefore selected as the appropriate parametric method for between-group comparisons of two independent samples. Results are reported with 95% confidence intervals (95% CI) and p-values. A p-value<0.05 was considered statistically significant.

Selection Bias Considerations

Control participants were recruited from blood donors, who are routinely screened and may represent a healthier subset of the general population. This may have introduced selection bias, potentially leading to an overestimation of the difference in vitamin D levels between groups. Readers should interpret between-group comparisons with this limitation in mind.

RESULTS

All 100 enrolled participants (50 patients, 50 controls) provided complete data; no missing values were recorded. Key trends are highlighted below.

Table 1: CBC results for the patient group (transfusion-dependent SCA; n = 50)

Parameter	Normal Range	Mean	Std. Deviation	Minimum	Maximum
HB (g/dL)	F: 12.3-15.7 | M: 13.5-17.0	8.17	1.60	4.2	10.9
HCT (%)	F: 37-46 | M: 42-52	24.12	5.66	11.6	36.6
RBC ($\times 10^6$/µL)	4.0-5.2	3.09	0.93	1.28	5.00

F: Female, M: Male, HB: Haemoglobin, HCT: Haematocrit, RBC: Red blood cells

Table 2: CBC results for the control group (healthy adults; n = 50)

Parameter	Normal Range	Mean	Std. Deviation	Minimum	Maximum
HB (g/dL)	F: 12.3-15.7 | M: 13.5-17.0	13.79	1.10	12.3	17.1
HCT (%)	F: 37-46 | M: 42-52	40.74	4.91	30.0	54.0
RBC ($\times 10^6$/µL)	4.0-5.2	4.59	0.76	4.0	6.0

F: Female, M: Male, HB: Haemoglobin, HCT: Haematocrit, RBC: Red blood cells

Table 3: Between-group comparison of CBC parameters (patients vs. controls)

Parameter	Reference Range	Group	N	Mean	Std. Deviation	P value
HB (g/dL)	F: 12.3-15.7 M: 13.5-17.0	Patient	50	8.17	1.60	<0.001
		Control	50	13.79	1.10	
HCT (%)	F: 37-46 M: 42-52	Patient	50	24.12	5.66	<0.001
		Control	50	40.74	4.91	
RBC ($\times 10^6$/µL)	4.0-5.2	Patient	50	3.09	0.93	<0.001
		Control	50	4.59	0.76	

Independent samples t-test, p<0.001 for all parameters

Table 4: Serum 25(OH)D results for the patient group (transfusion-dependent SCA; n = 50)

Parameter	Reference Range	Mean (ng/mL)	Std. Deviation	Minimum	Maximum
25(OH)D (ng/mL)	30-100 ng/mL (Sufficient)	11.74	4.66	4.0	23.0

25(OH)D: 25-hydroxyvitamin D, deficiency threshold: <20 ng/mL

Table 5: Serum 25(OH)D results for the control group (healthy adults; n = 50)

Parameter	Reference Range	Mean (ng/mL)	Std. Deviation	Minimum	Maximum
25(OH)D (ng/mL)	30-100 ng/mL (Sufficient)	31.16	5.89	25.0	50.0

25(OH)D: 25-hydroxyvitamin D, sufficiency range: 30-100 ng/mL

Table 6: Between-group comparison of serum 25(OH)D levels (patients vs. controls)

Parameter	Reference Range	Group	N	Mean (ng/mL)	Std. Deviation	p-value
25(OH)D (ng/mL)	30-100 ng/mL	Patients	50	11.74	4.66	<0.001
		Controls	50	31.16	5.89	

Independent samples t-test, 95% CI for mean difference: 17.18-21.74 ng/mL, p<0.001

Haematological Parameters Patient Group

Table 1 presents CBC parameters for the patient group. All haematological indices were below normal reference ranges, consistent with the chronic haemolytic anaemia of SCA. Mean haemoglobin was 8.17±1.60 g/dL, mean haematocrit was 24.12±5.66% and mean RBC count was 3.09±0.93 $\times 10^6$/µL.

Haematological Parameters Control Group

Table 2 presents CBC parameters for the control group. All values fell within normal reference ranges, confirming the health status of enrolled controls.

Between-Group Comparison of Haematological Parameters

Table 3 shows between-group comparisons. Patients had significantly lower haemoglobin, haematocrit and RBC counts than controls (all p<0.001), reflecting the expected haematological burden of transfusion-dependent SCA.

Serum Vitamin-D Patient Group

Table 4 presents 25(OH)D results for the patient group. The mean level of 11.74±4.66 ng/mL falls within the deficient category (<20 ng/mL) according to Endocrine Society criteria [7].

Serum Vitamin D Control Group

Table 5 presents 25(OH)D results for the control group. The mean level of 31.16±5.89 ng/mL falls within the sufficient range (30-100 ng/mL).

Between-Group Comparison of Serum Vitamin D

Table 6 demonstrates a statistically significant difference in 25(OH)D between groups (p<0.001). Patients had a mean level 19.42 ng/mL lower than controls (95% CI: 17.18-21.74 ng/mL), confirming a markedly higher prevalence of VDD in the patient group.

DISCUSSION

This study evaluated serum 25(OH)D levels and haematological parameters in transfusion-dependent SCA patients at Al-Mudilif General Hospital, Al-Qunfudah and compared them with healthy controls. The principal finding was that patients exhibited markedly lower vitamin D levels (mean 11.74 ng/mL, deficient range) compared with controls (mean 31.16 ng/mL, sufficient range), with a statistically significant between-group difference (p<0.001). This difference is clinically meaningful: all patient-group values fell below the deficiency threshold of 20 ng/mL.

Globally, VDD is well-documented in SCA. Chronic haemolysis, increased metabolic demands, reduced sunlight exposure secondary to pain-related immobility and prolonged hospitalisations are the primary contributing mechanisms [2,8]. A meta-analysis by Osunkwo *et al.* reported that 63.8% of SCD patients were vitamin D deficient, with significantly lower 25(OH)D concentrations than healthy controls [9]. Our findings are consistent with this global picture and with earlier Saudi Arabian data: Al-Jama *et al.* similarly identified high VDD rates among SCA patients in the Eastern Province [1] and Al-Saqladi *et al.* reported low 25(OH)D levels associated with bone pain and avascular necrosis in SCD patients [10]. The current study extends these observations to the Al-Qunfudah region, where no comparable data previously existed.

The clinical implications are substantial. Low vitamin D levels in SCA have been associated with increased vaso-occlusive pain crises, higher hospitalisation rates and reduced bone mineral density [12]. Randomised evidence supports the clinical benefit of high-dose vitamin D supplementation in reducing pain frequency in SCD [13]. Routine vitamin D screening and targeted supplementation should therefore be considered a standard component of care for transfusion-dependent SCA patients particularly given the feasibility and low cost of both assessment and intervention.

Genetic and disease heterogeneity may modulate vitamin D metabolism in Saudi SCD patients. The Arab-Indian haplotype, common in this population, is associated with milder disease expression and may affect vitamin D kinetics [11]. Future studies should explore haplotype-specific vitamin D metabolism to personalise supplementation strategies.

CONCLUSIONS

Vitamin D deficiency is highly prevalent among transfusion-dependent SCA patients in the Al-Qunfudah region, with mean 25(OH)D levels (11.74±4.66 ng/mL) substantially lower than those in healthy controls (31.16±5.89 ng/mL; $p<0.001$). VDD represents a prevalent and clinically important comorbidity in this population. Key recommendations for clinical practice are:

- Routine vitamin D [25(OH)D] screening for all transfusion-dependent SCA patients
- Targeted vitamin D supplementation for patients with deficient or insufficient levels, in line with Endocrine Society guidelines
- Monitoring of skeletal health parameters (bone mineral density, calcium, PTH) in high-risk patients

These findings are relevant beyond Al-Qunfudah: given the high background prevalence of VDD across Saudi Arabia, similar screening programmes are warranted in other regions managing SCA populations.

Strengths

This study provides the first vitamin D data from a transfusion-dependent SCA cohort in Al-Qunfudah, filling an important regional evidence gap. The inclusion of age- and sex-matched healthy controls, measurement of multiple haematological and biochemical parameters and use of validated laboratory platforms strengthen the validity of the findings.

Limitations

The following limitations should be considered when interpreting the findings:

- Small sample size (n = 50 per group): the study may have been underpowered to detect smaller between-group differences and results should be replicated in larger cohorts
- Single-centre, single-region design: findings may not be generalisable to SCA populations in other Saudi regions or settings
- Cross-sectional design: no causal inferences can be drawn and temporal relationships between VDD and clinical outcomes cannot be established
- Vitamin D assessment only: related bone metabolism markers (parathyroid hormone, serum calcium, bone mineral density) were not measured, limiting the characterisation of skeletal risk
- Selection bias: control participants were blood donors, who may represent a healthier subgroup of the general population, potentially inflating the apparent between-group difference in vitamin D levels

No long-term follow-up: the clinical impact of VDD on pain frequency, hospitalisation rates and bone health outcomes over time could not be assessed.

Innovation and Contribution

To our knowledge, this is the first study to assess vitamin D status specifically in a transfusion-dependent SCA population in the Al-Qunfudah region of Saudi Arabia. The findings provide regional baseline data of immediate clinical relevance and support the case for integrating vitamin D screening into routine SCA management protocols across southwestern Saudi Arabia.

Implications for Practice

The high prevalence of VDD demonstrated in this study supports the implementation of routine vitamin D screening and supplementation programmes for transfusion-dependent SCA patients. Although the study was conducted in Al-Qunfudah, the findings are likely applicable to other Saudi Arabian regions given the nationally documented high background rates of VDD [4,8]. Healthcare providers managing SCA populations elsewhere in Saudi Arabia are encouraged to consider similar screening protocols adapted to their patient demographics.

Recommendations for Future Research

Future studies should:

- Employ larger, multi-centre designs across diverse Saudi regions to improve generalisability

- Incorporate bone metabolism markers, including serum calcium, parathyroid hormone and bone mineral density, to fully characterise skeletal risk
- Conduct longitudinal follow-up to evaluate the effect of vitamin D supplementation on clinical outcomes such as pain crisis frequency, hospitalisation rates and bone health

Explore genotype-vitamin D interactions, particularly the influence of haemoglobin S haplotypes on 25(OH)D metabolism in Saudi SCA patients.

Ethical Statement

Ethical approval was granted by the Institutional Review Board of the Ministry of Health, Makkah Region, Saudi Arabia (IRB-Makkah; IRB No. H-02-K-076-1124-1201) on 06 November 2024. Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the Declaration of Helsinki.

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