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RESEARCH ARTICLE OPEN ACCESS

Implication of serum calcium and parathyroid hormone for bone pain crisis in patients with sickle cell anaemia: A cross-sectional Study

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Abstract
Objectives: Sickle cell anaemia is very common in tropical countries, and it is associated with severe bone pain crisis, which interferes with quality of life. The role of serum calcium and parathyroid hormone levels in the development of bone pains has not been fully explained. This study is designed to measure the serum level of calcium and parathyroid hormones in patients with sickle cell anaemia and compare them with healthy participants.
Methods: A cross-sectional study was conducted in a tertiary hospital where patients with sickle cell anaemia attending the children's outpatient clinic were recruited. A questionnaire was used to obtain vital information from all participants, and blood levels of calcium and parathyroid hormone were measured. The results were compared between patients with sickle cell anaemia and the control group.
Results: A total of 66 patients with sickle cell anaemia and 66 healthy control participants were recruited. The median (IQR) age at which sickle cell was diagnosed was 3 (1.9-7.3) years, and there were 14 (21%) patients who had other siblings living with sickle cell anaemia. Patients with sickle cell anaemia had lower levels of calcium (2.19 vs 2.32 mmol/L), p< 0.01, and higher levels of parathyroid hormone (14.3 vs 13.3 pg/ml); p= 0.01 than the healthy control participants.
Conclusions: The study showed that patients with sickle cell anaemia have lower serum calcium and higher parathyroid hormone levels. This may be associated with the bone pain they regularly experience

Keywords: Sickle cell anaemia, Calcium, Parathyroid hormone, Bone pain

Plain English Summary

Patients with sickle cell anaemia usually have severe bone pains, which interfere with their daily activities. Generally, this is believed to be due to compromised blood supply to the affected bones because of the

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abnormalities in the structure and nature of their red blood cells. However, the role of calcium and parathyroid hormones, which are major regulators of activities in the bone have not been fully explained in the development of bone pains in patients with sickle cell anaemia. Thus, this study was done to measure the levels of blood calcium and parathyroid hormones in this group of patients and compare the values with those of healthy counterparts.
This study found that patients with sickle cell anaemia have lower levels of blood calcium and higher levels of parathyroid hormone compared to their healthy counterparts. This relationship is usually associated with bone pains, even in other clinical conditions and is highly suggestive of a major contribution to bone pains in sickle cell anaemia. This makes a case for the consideration of calcium supplements and phosphonates in the prevention and management of bone pain crisis in patients with sickle cell anaemia.

Background

Sickle Cell Anaemia (SCA) results from a genetic mutation involving the β-subunit of the haemoglobin chain. The resulting red blood cell becomes abnormally sickle-shaped and characteristically prevents normal blood flow, especially in small blood vessels across different parts of the body (1). Although about 5% of the global population is healthy carriers of the sickle cell gene, it is estimated that over 300000 new births across the world have the severe types of the disease annually (2). Sub-Saharan Africa carries the highest disease burden, with the western and central regions of the continent dominating the prevalence rate. In 2021, Nigeria, Togo, Benin Republic, Equatorial Guinea, Burkina Faso and Sierra Leone together contributed up to 44% of the global incidence at birth, while the total figure generated from the entire sub-Saharan Africa was as high as 79% of the global burden (1). Other regions of the world with significant disease burden are the Caribbean, the Middle East and South Asia, which are traditionally known to be associated with a high burden of malaria disease.

In Nigeria, about four to six million people are estimated to have the sickle cell gene, making Nigeria the country with the highest number of affected individuals. Furthermore, the nationwide prevalence ranges between 1-3%, with up to 150,000 newborns in Nigeria carrying the sickle cell trait, accounting for about 33% of the global disease burden (3). A population-level model estimated analysis published in 2021 showed that the national value for the under -5 mortality rate in children with sickle cell disease was 490 per 1,000 livebirths, which was four times higher than for children with haemoglobin AA (4).

Several complications are known to occur in patients with SCA. Aplastic crises usually present with a concurrent fall in the levels of both haemoglobin and reticulocyte count in affected patients (5, 6). Closely related to that is the haemolytic crises in which patients have an accelerated rate of haemolysis, and a compensatory rise in reticulocyte count (7). Vaso-occlusive crisis, usually precipitated by dehydration, malaria, acidosis, infections, and low oxygen states, is one of the most common reasons patients with SCA present in the hospital (8). Sometimes the sickling occurs within organs, leading to the pooling of blood in those organs, thus interfering with their function and causing severe symptoms emanating from the affected organ. This is often referred to as a sequestration crisis occurring most commonly in the spleen and possibly the liver, with worsening anaemia (9).

Bone pain is the commonest manifestation of the complications resulting from red cell sickling. The pain is usually very severe, mostly interfering with the physical activities of the sufferers (10). The pain originates from the ischaemic tissue injury that results from the occlusion of blood vessels by the sickled red blood cells (11, 12). The background necrosis following compromised blood supply is usually demonstrable on radiological films, and physical signs of inflammation, including swelling, redness, warmth and tenderness, are almost always present (13). However, most studies have been silent about the involvement of calcium and parathyroid hormone, which are primarily related to bones, in the initiation and progression of pain in patients with SCA (10, 11, 12).

While a few studies have reported that SCA is associated with hypocalcaemia, there is a scarcity of reports on concurrent levels of parathyroid hormone (14, 15). However, secondary hyperparathyroidism, which is expected to correct the calcium deficit, is associated with pain (16). Although the mechanism for the pain is not expressly clear, the process of bone resorption is believed to be contributory. Even in patients without SCA, secondary hyperparathyroidism, which initiates bone resorption, is associated with pain in different parts of the body (17). This may be a major cause of the pain generally reported in patients with SCA. Thus, this study was designed to measure the levels of calcium and parathyroid hormones in patients with SCA.

Materials and Methods

Study design and setting

This was a cross-sectional study conducted at the children's outpatient unit of the University Teaching Hospital, a tertiary hospital, between June and September 2024.

Study population

Participants in this study were patients with SCA attending the children's outpatient clinic and healthy controls who were newly admitted high school students undergoing the pre-admission laboratory screening. Individuals with bone deformities, kidney disorders, previous thyroid surgery and those on medical emergencies were exempted from the study. The Sample size was determined using the formula for a cross-sectional study with quantitative variables.

Data Collection

Demography and clinical data were obtained from the participants using a structured questionnaire following informed consent by parents.

Sample processing and laboratory analysis

Three millilitres of blood sample was collected into gel separation tubes by venipuncture; samples were left to stand for at least two hours before centrifugation at 3000 radian/minute for 10 minutes. The serum obtained was transferred into clean 1.5ml Eppendorf tubes for storage at -200 °C until laboratory analyses. Serum calcium was measured using the o-cresolphthalein method in the TECO-480 chemistry autoanalyser, while parathyroid hormone was measured using the enzyme-linked immunosorbent assay technique according to the manufacturer's instructions (Melsins Medicals, Changchun, China).

Statistical analysis

The effect of SCA on serum calcium and parathyroid hormone was determined by comparing values between patients and the healthy control group. Data were reported as median (interquartile range) and frequency (percentage), as appropriate. Comparison between the two groups was done using the Mann-Whitney U test. Serum calcium values below 2.15 mmol/L were considered as hypocalcaemia and categorised as mild to moderate if the value is between 1.9 and 2.14 mmol/L, and severe if the value is below 1.9 mmol/L (18). Logistic regression analysis was used to determine selected variables associated with hypocalcaemia, and the relationship between biochemical variables (serum Calcium and Parathyroid hormone) and the presence of bone pains; *P-values* less than .05 were considered significant, and analysis was done using Statistical Package for Social Sciences (SPSS) analytical software version 26 (IBM Corporation, Armonk, NY, USA).

Results

A total of 132 participants were recruited for this study, and 83 (63%) were females. Sixty-six (50%) had SCA, while the remaining 66 (50%) formed the healthy control group. The median age of participants with SCA was 12 (8-18) years compared to 11 (10-13) years for the control group. In the SCA group, there were 43 (65%) females compared to 40 (61%) in the control group. Other comparative variables between the two groups are presented in Table 1.

Table 1: Comparison of variables between participants with sickle cell anaemia and the healthy control group.

Variables	Sickle Cell Patients (n=66)	Healthy Control (n=66)	p-value
Females, n (%)	43 (65%)	40 (61%)	0.59
Age (years)	12 (8-18)	11 (10-13)	0.96
Weight (kg)	28 (21-43)	39 (34-52)	<.01
Height (m)	1.46 (1.31-1.62)	1.54 (1.47-1.60)	0.02
BMI (kg/m^2)	13.4 (12.1 – 17.7)	16.9 (14.9 – 20.8)	<0.01
Serum Calcium (mmol/L)	2.19 (2.12-2.31)	2.32 (2.24-2.40)	<.01
Serum PTH (pg/ml)	14.3 (13.1-16.7)	13.3 (11.1-16.8)	0.01
Serum Calcium levels groups			
< 2.15 mmol/L			
2.0 – 2.14 mmol/L)	23 (34.5%)	10 (15.1%)	<.01
<1.9 mmol/L)	19 (28.8%)	10 (15.1%)	
	4 (6.1%)	0 (0)	

N.B: Variables are reported in numbers (percentages) and median (interquartile range)

In the SCA group, the median (IQR?) age at diagnosis was 3 (1.9-7.3) years, and 54 (81%) were diagnosed at a secondary government hospital. Recurrent bone pain crisis was reported in 58 (88%) patients, and there were 14 (21%) patients who had other siblings living with SCA. The median number of hospitalisations from bone pain within a year was 2 (2-4) amongst the patients. Only one patient (1.5%) was not on routine medications, while 23 (35%) had received blood transfusions in the past during bone pain crises. There were 45 patients (68%) who reported significant restrictions in physical activities due to bone pains, and 4 (6.1%) who reported bone abnormalities. The quality of care received from families and carers was described as very good by 24 (36%), good by 23 (35%), average by 7 (11%) and poor by 12 (18%) of the patients. These and other responses are presented in Table 2.

Table 2: Patients' responses to questions about their sickle cell history

Variables	Frequency
Median age at diagnosis of Sickle Cell (yrs)	3 (1.9-7.3) years
Time from diagnosis	7 (3-14) years
Patients who were diagnosed at the government hospital	54 (82%)
Patients who have other siblings living with sickle cell anaemia	14 (21%)
Patients with recurrent bone crisis	58 (88%)
Patients who were hospitalised due to bone pains	45 (68%)
Median number of hospitalisations from painful bone pain within a year	2 (2-4)
Patients who have received blood transfusions in the past during the crisis	23 (35%)

N.B Variables are reported as numbers (percentages) and median Interquartile range),

Median (IQR) Serum calcium in the SCA group was 2.19 (2.12-2.31) mmol/L compared to 2.32 (2.24-2.40) mmol/L in the control group; p< 0.01. Median (IQR) Serum parathyroid hormone in the SCA group was 14.3 (13.1-16.7) pg/ml compared to 13.3 (11.1-16.8) pg/ml in the control group; p = 0.01. There were 23 (34.8%) participants in the SCA group who had hypocalcaemia compared to 10 (15.2%) participants in the control group; p< 0.01. In the SCA group with hypocalcaemia, 19 (28.8%) were mild to moderate, and 4 (6.1%) were severe, while all 10 (15.1%) participants in the control group had only mild to moderate hypocalcaemia (Table 1).

Logistic regression analysis showed that the age, time from diagnosis, weight, height and BMI can independently predict hypocalcaemia, while sex, age at diagnosis and receiving blood transfusion did not show a significant relationship; Table 3.

Table 3: Logistic Regression of factors associated with hypocalcaemia in patients with sickle cell anaemia

variables	Odds Ratio	95% Confidence Interval	P-value
Age (years)	1.081	1.014- 1.154	0.02
Time from diagnosis (years)	1.096	1.022- 1.175	0.01
Weight (kg)	1.060	1.020- 1.102	<.01
Height (m)	1.052	1.017- 1.088	<.01
BMI (kg/m^2)			
Age at diagnosis (years)	0.979	0.858-1.118	0.76

It also showed that having a low serum calcium level and a high PTH level are independent predictors of the presence of bone pains (Table 4).

Table 4: Logistic Regression of the relationship between the biochemical factors and the presence of bone pans in patients with sickle cell anaemia

Variables	Odds Ratio	95% Confidence Interval	P-value
Serum Calcium	0.012	0.000 -03.683	0.03
Serum Parathyroid Hormone	1.486	0.905 – 2.439)	0.01

Discussion

In this study, the patients were diagnosed with sickle cell anaemia at the median (IQR) age of 3 (2-7) years, mostly in government hospitals. About 90% of the patients experienced bone pain up to 2-4 times in one year, and 14 (21%) of them have siblings who also have sickle cell anaemia and experience similar pains. The serum calcium level was significantly lower, while parathyroid hormone was significantly higher in the patients with SCA than in the healthy control group. In addition, lower serum calcium levels and higher serum parathyroid hormone were associated with the presence of bone pains.

The median age of sickle cell diagnosis was 3 (2-7) years in the patient group. This is similar to what was reported by another study from a teaching hospital in Lagos, in this same region, where the age at diagnosis was 2 years and 3months (19). However, another study with a larger cohort, from a teaching hospital in Ibadan, within the same region, reported that the median age at diagnosis was 2.0 years (2.5 months - 14.0 years) (20). This is very important information, given the high prevalence of SCA in Nigeria, to foster early detection and management, as this study showed that the time from diagnosis can determine the development of low calcium levels. More so, many developing countries still depend on post-delivery diagnosis, due to the scarcity of technology which can make diagnosis before birth by testing a sample of amniotic fluid or tissue from the placenta. Most patients with SCA in this study experienced several episodes of bone pain within one year, and about a quarter of them have siblings who also have SCA and experience similar pains. The frequency of bone pains varies from one patient to another, depending on the presence of triggers like hypoxemia, dehydration and environmental temperature changes. However, some patients are reported to have up to 6 episodes within one year, while others may have as few as one or none in a one-year period (21). This has serious financial and social concerns for patients and other members of the family, especially in families where more than one child is affected. In a Nigerian study, more than 50% of the families of affected patients reported that there were associated drop in financial stability and quality of care for other children due to treatment costs for the affected children (22).

Lower calcium levels and more severe hypocalcaemia found in patients in this study indicate that SCA can be associated with these biochemical abnormalities. This is in agreement with the previous report of serum calcium in patients with SCA (23, 24). Hypocalcaemia may be a major contributor to the reduced lifespan of red cells in sickle cell patients, given the role calcium plays in maintaining membrane stability of red blood cells and their longevity in circulation (25, 26). The reason for the hypocalcaemia has been attributed to the high influx of calcium into sickled red cells, which have dysfunctional Ca^{2+}-Mg^{2+} ATPase and increased permeability for calcium (27). This is even more predominant during sickling crisis, apparently aggravating the hypocalcaemia and all the consequent symptoms associated with the condition (14).

The parathyroid gland theoretically responds to low circulating levels of calcium in the blood by releasing parathyroid hormone, which stimulates calcium release from bones to correct the deficiency. Thus, it is not surprising to find that patients with SCA in this study had significantly higher values of parathyroid hormone compared to the healthy controls. Several other studies have reported similar findings, indicating the appropriate response to the usual hypocalcaemia in sickle cell patients (28, 29, 30). However, other studies have identified primary hyperparathyroidism as a possible finding in patients with SCA, but this is always accompanied by hypercalcaemia in affected patients. This subtype has been associated with aetiological factors like familial hypocalciuric hypercalcaemia and parathyroid adenoma that manifest with excessive secretion of parathyroid hormone (31, 32, 33). Treatment options include surgical removal of the parathyroid gland and hormonal replacement in very sick patients.

Lower serum calcium levels and a higher parathyroid hormone level are found to be associated with the presence of bone pains in this study. The mechanism by which the parathyroid hormone restores serum calcium levels in response to a hypocalcaemic state includes the stimulation of osteoclast activity, leading to bone resorption to release calcium into the circulation (34). This action has been directly linked with the development of pathological bone and chronic bone pain, as osteoclast activities create an acidic microenvironment, which is noxious to the nociceptors in the bone, leading to pain development (35). This mechanism is similar to what occurs in the pains associated with bone cancers and other bone diseases. Evidently, reversal of osteoclastic activity by administration of bisphosphonates has led to significant pain reduction in patients with bone diseases (36). Moreover, a study reported a significant reduction in the markers of osteoclast activity following radiotherapy for patients with bone pains; this

reduction correlated with the resolution of the bone pains (37). Thus, the osteoclastic activity following parathyroid hormone stimulation in response to low calcium levels in patients with SCA may be a major cause of the bone pain crisis, and this has been explained by previous studies (30, 35).

There are a few limitations to this study. The participants are paediatric patients; the findings might not be entirely the same in adults. Secondly, most of the patients were recruited in their steady non-crisis state; the result may be different in situations of sickling crisis. In addition, the possibility of inadequate calcium consumption in meals was not considered in patients' selection; both the test and control groups were similar in age and from the same population that shares a lot of similarities in diet. Also, adjusted calcium level with albumin was not done; this applied to both the test and the control group. Some of the patients may have haemoglobin S thalassemia, but it cannot be differentiated from haemoglobin SS due to the high technical expertise required. Lastly, Vitamin D receptor polymorphism, which is known to affect calcium homeostasis and bone health, was not measured in this study; it may have possibly contributed to the hypocalcaemia seen in the patients with SCA.

Conclusion

This study showed that SCA may be associated with low levels of calcium and high levels of parathyroid hormone. This biochemical status may be associated with the occurrence of bone pains in these patients. This makes a case for the consideration of calcium supplements and phosphonates in the prevention and management of bone pain crisis in patients with SCA.

List of abbreviations

SCA: Sickle cell anaemia
SPSS: Statistical Package for Social Sciences
PTH: Parathyroid hormone

Declarations

Ethics Approval and Consent to Participate

Ethical approval was obtained from the University Research Ethics Committee. The rights of confidentiality of all participants were protected throughout the study. The benefits of the study findings were explained to all participants who voluntarily took part in the study, and no form of harm was inflicted on the subjects during this study.

Consent for publication

All the authors gave consent for the publication of this study

Availability of data and materials

The datasets used and/or analysed in this study are available from the corresponding author on reasonable request.

Competing interest

The authors have no competing interests to declare.

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This study received no external funding from any source.

Authors contributions

OOA, OA, OH and AA: Developed the protocol, enrolled patients and contributed to writing the manuscript
MIN: Did data analysis and contributed to writing the manuscript
OGN: Contributed to protocol development, data analysis, and writing of the manuscript
ANE: Contributed to protocol development and writing of the manuscript

References

1. Thomson AM, McHugh TA, Oron AP, Teply C, Lonberg N, Tella VV, Wilner LB, Fuller K, Hagins H, Aboagye RG, Aboye MB. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000–2021: a systematic analysis from the Global Burden of Disease Study 2021. The Lancet Haematology. 2023 Aug 1;10(8):e585-99. https://doi.org/10.1016/S2352-3026(23)00118-7
2. World Health Organisation. accessed 18th February 2024. https://www.afro.who.int/health-topics/sickle-cell-disease
3. Nwabuko OC, Onwuchekwa U, Iheji O. An overview of sickle cell disease from the socio-demographic triangle-a Nigerian single-institution retrospective study. Pan African Medical Journal. 2022 Feb 23;41(1). https://doi.org/10.11604/pamj.2022.41.161.27117
4. Nnodu OE, Oron AP, Sopekan A, Akaba GO, Piel FB, Chao DL. Child mortality from sickle cell disease in Nigeria: a model-estimated, population-level analysis of data from the 2018 Demographic and Health Survey. The Lancet Haematology. 2021 Oct 1;8(10):e723-31. https://doi.org/10.1016/S2352-3026(21)00216-7
5. Soltani S, Zakeri A, Tabibzadeh A, Zandi M, Ershadi E, Akhavan Rezayat S, Khaseb S,

Zakeri AM, Ashtar Nakhaei M, Afzali S, Farahani A. A literature review on the parvovirus B19 infection in sickle cell anemia and β-thalassemia patients. Tropical medicine and health. 2020 Dec 2;48(1):96. https://doi.org/10.1186/s41182-020-00284-x

6. Majumdar S, Bean CJ, De Staercke C, Bost J, Nickel R, Coates T, Campbell A, Thompson A. Parvovirus B19 infection in sickle cell disease: An analysis from the Centers for Disease Control haemoglobinopathy blood surveillance project. Transfusion Medicine. 2020 Jun;30(3):226-30. https://doi.org/10.1111/tme.12671
7. Kaushal M, Byrnes C, Khademian Z, Duncan N, Luban NL, Miller JL, Fasano RM, Meier ER. Examination of reticulocytosis among chronically transfused children with sickle cell anemia. PLoS One. 2016 Apr 26;11(4):e0153244. https://doi.org/10.1371/journal.pone.0153244
8. Jang T, Poplawska M, Cimpeanu E, Mo G, Dutta D, Lim SH. Vaso-occlusive crisis in sickle cell disease: a vicious cycle of secondary events. Journal of Translational Medicine. 2021;19(1):1-11. https://doi.org/10.1186/s12967-021-03074-z
9. Kane I, Kumar A, Atalla E, Nagalli S. Splenic Sequestration Crisis. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553164/
10. Reparaz P, Serrano I, Adan-Pedroso R, Astigarraga I, de Pedro Olabarri J, Echebarria-Barona A, Garcia-Ariza M, Lopez-Almaraz R, del Orbe-Barreto RA, Vara-Pampliega M, Gonzalez-Urdiales P. Clinical management of the acute complications of sickle cell anemia: 11 years of experience in a tertiary hospital. Anales de Pediatría (English Edition). 2022 Jul 1;97(1):4-11. https://doi.org/10.1016/j.anpede.2022.06.002
11. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. The Lancet. 2010 Dec 11;376(9757):2018-31. https://doi.org/10.1016/S0140-6736(10)61029-X
12. Darbari DS, Sheehan VA, Ballas SK. The vaso-occlusive pain crisis in sickle cell disease: definition, pathophysiology, and management. European journal of haematology. 2020 Sep;105(3):237-46. https://doi.org/10.1111/ejh.13430
13. Smith WR, Scherer M. Sickle-cell pain: advances in epidemiology and etiology. Hematology 2010, The American Society of Hematology Education Program Book. 2010 Dec 4;2010(1):409-15. https://doi.org/10.1182/asheducation-2010.1.409
14. Nlemadim AC, Okpara HC, Uzomba CI, Anah MU, Meremikwu MM. Hypocalcemia and vaso-occlusive painful crises in pediatric sickle cell anaemia. Nigerian Journal of Medicine. 2021 Jan 1;30(1):34-9. https://doi.org/10.4103/NJM.NJM_154_20
15. Batte A, Kasirye P, Baluku R, Kiguli S, Kalyesubula R, John CC, Schwaderer AL, Imel EA, Conroy AL. Mineral bone disorders and kidney disease in hospitalized children with sickle cell anemia. Frontiers in pediatrics. 2023 Feb 2;10:1078853. https://doi.org/10.3389/fped.2022.1078853
16. Zhen G, Fu Y, Zhang C, Ford NC, Wu X, Wu Q, Yan D, Chen X, Cao X, Guan Y. Mechanisms of bone pain: Progress in research from bench to bedside. Bone Research. 2022 Jun 6;10(1):44. https://doi.org/10.1038/s41413-022-00217-w
17. Yahib SM, Algarni B, Alghamdi A, Nassan S, Nassan Sr S. Primary hyperparathyroidism as a rare cause of unexplained recurrent abdominal pain: Case presentation and literature review. Cureus. 2021 Oct 31;13(10). https://doi.org/10.7759/cureus.19155
18. Duval M, Bach-Ngohou K, Masson D, Guimard C, Le Conte P, Trewick D. Is severe hypocalcemia immediately life threatening?. Endocrine connections. 2018 Oct 1;7(10):1067-74. https://doi.org/10.1530/EC-18-0267
19. Akodu SO, Diaku-Akinwumi IN, Njokanma OF. Age at diagnosis of sickle cell anaemia in Lagos, Nigeria. Mediterranean journal of hematology and infectious diseases. 2013 Jan 2;5(1):e2013001. https://doi.org/10.4084/mjhid.2013.001
20. Brown BJ, Akinkunmi BF, Fatunde OJ. Age at diagnosis of sickle cell disease in a developing country. African journal of medicine and medical sciences. 2010 Sep 1;39(3):221-5.
21. Maakaron JE. Sickle cell diseae; Practice essential. Accessed on the 14th November 2024. https://emedicine.medscape.com/article/205926-overview
22. Beli II, Ali LA, Onuoha CC, Jasseh M, Zentar M, Belakoul N, Layadi Y, Deblui JA, Fathi M, Sani AH, Adamu AG. Socio-economic burden of sickle cell disease on families attending sickle cell clinic in Kano state, northwestern Nigeria.

Global Pediatrics. 2024 Sep 1;9:100193. https://doi.org/10.1016/j.gpeds.2024.100193
23. Oladipo OO, Temiye EO, Ezeaka VC, Obomanu P. Serum magnesium, phosphate and calcium in Nigerian children with sickle cell disease. West African Journal of Medicine. 2005 Oct 25;24(2):120-3. https://doi.org/10.4314/wajm.v24i2.28180
24. Antwi-Boasiako C, Kusi-Mensah YA, Hayfron-Benjamin C, Aryee R, Dankwah GB, Kwawukume LA, Darkwa EO. Total serum magnesium levels and calcium-to-magnesium ratio in sickle cell disease. Medicina. 2019 Aug 29;55(9):547. https://doi.org/10.3390/medicina55090547
25. Lew VL, Tiffert T. On the mechanism of human red blood cell longevity: roles of calcium, the sodium pump, PIEZO1, and gardos channels. Frontiers in physiology. 2017 Dec 12;8:977. https://doi.org/10.3389/fphys.2017.00977
26. Joiner CH. Cation transport and volume regulation in sickle red blood cells. American Journal of Physiology-Cell Physiology. 1993 Feb 1;264(2):C251-70. https://doi.org/10.1152/ajpcell.1993.264.2.C251
27. Litosch I, Lee KS. Sickle red cell calcium metabolism: Studies on Ca2+-Mg2+ ATPase and ca-binding properties of sickle red cell membranes. American Journal of Hematology. 1980 Jun;8(4):377-87. https://doi.org/10.1002/ajh.2830080406
28. Mohammed S, Addae S, Suleiman S, Adzaku F, Annobil S, Kaddoumi O, Richards J. Serum calcium, parathyroid hormone, and vitamin D status in children and young adults with sickle cell disease. Annals of clinical biochemistry. 1993 Jan;30(1):45-51. https://doi.org/10.1177/000456329303000108
29. El-Masry HM, Hassan MA, Hashem AM, Shaban AA. Parathyroid Hormone Profile In Sickle Cell Disease In School Aged Children. The Egyptian Journal of Hospital Medicine. 2020 Oct 1;81(4):1732-5. https://doi.org/10.21608/ejhm.2020.120002
30. Lakkakula BV, Neral A. Parathyroid hormone abnormities in sickle cell anemia patients. Journal of Parathyroid Disease. 2018 Jul 27;7(1):1-4.
31. Khan EA, Cheddani L, Saint-Jacques C, Vargas-Poussou R, Frochot V, Chieze R, Letavernier E, Avellino V, Lionnet F, Haymann JP. Primary hyperparathyroidism in homozygous sickle cell patients: a hemolysis-mediated hypocalciuric hypercalcemia phenotype?. Journal of Clinical Medicine. 2021 Nov 5;10(21):5179. https://doi.org/10.3390/jcm10215179
32. Jridi M, Mekni S, Meriem A, Rojbi I, Nacef IB, Mchirgui N, Khiari K. Sickle cell disease and hyperparathyroidism: case report. InEndocrine Abstracts 2022 May 7 (Vol. 81). Bioscientifica. https://doi.org/10.1530/endoabs.81.EP178
33. Denoix E, Bomahou C, Clavier L, Ribeil JA, Lionnet F, Bartolucci P, Courbebaisse M, Pouchot J, Arlet JB. Primary hyperparathyroidism in sickle cell disease: an unknown complication of the disease in adulthood. Journal of Clinical Medicine. 2020 Jan 22;9(2):308. https://doi.org/10.3390/jcm9020308
34. Lofrese JJ, Basit H, Lappin SL. Physiology, parathyroid. InStatPearls [Internet]. StatPearls Publishing. 2023 Jul 17.
35. Gollamudi J, Karkoska KA, Gbotosho OT, Zou W, Hyacinth HI, Teitelbaum SL. A bone to pick-cellular and molecular mechanisms of bone pain in sickle cell disease. Frontiers in Pain Research. 2024 Jan 4;4:1302014. https://doi.org/10.3389/fpain.2023.1302014
36. Andriessen AS, Donnelly CR, Ji RR. Reciprocal interactions between osteoclasts and nociceptive sensory neurons in bone cancer pain. Pain Reports. 2021 Apr 1;6(1):e867. https://doi.org/10.1097/PR9.0000000000000867
37. Hoskin PJ, Stratford MR, Folkes LK, Regan J, Yarnold JR. Effect of local radiotherapy for bone pain on urinary markers of osteoclast activity. The Lancet. 2000 Apr 22;355(9213):1428-9. https://doi.org/10.1016/S0140-6736(00)02144-9