Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

Correlation between the Bone Disorder and Hemoglobinopathy in Vidarbha Region.

Dr. Pradip Jain Professor and HOD Dept. of Biochemistry Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre Nagpur-441110 (Datta Meghe Institute of Medical Sciences)

Rakesh Kumar Jha TutorDept. of Biochemistry Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre Nagpur-441110 (Datta Meghe Institute of Medical Sciences)

Dr. Neha Bhatt Assistant Professor Dept. of Pathology Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre Nagpur-441110 (Datta Meghe Institute of Medical Sciences)

Dr. Mahendra Gudhe Assistant Professor Dept. of Orthopedics Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe) Wardha-442001

Address for Correspondence
Rakesh Kumar Jha
TutorDept. of Biochemistry
Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre
Nagpur-441110 (Datta Meghe Institute of Medical Sciences)

ABSTRACT

INTRODUCTION:

In patients with thalassaemia and other haemoglobin disorders, bone disease is a significant cause of morbidity. The involvement of diabetes and hypothyroidism, parathyroid gland dysfunction, haemolytic anaemia, progressive marrow expansion, iron toxicity on osteoblasts, iron chelators, and a lack of growth hormone or insulin growth factors have all been identified as major causes of osteoporosis in thalassaemia patients. As a result, potent inhibitors of osteoclast activation, such as aminobisphosphonates, become effective drugs for the treatment of osteoporosis in patients with thalassaemia and other haemoglobin disorders.

AIM: We conducted a cross sectional study to inspect the correlation between bone disorder and hemoglobinopathy patients those came in theirregular follow up in SMHRC Nagpur.

MATERIAL AND METHODS:

Total 150 individuals of the age group between 35-80 yrs, the patients was already had hemoglobinopathy and coming for their regular check-up at Shalinitai Meghe hospital Nagpur, was choose for the research. They were split into class. One group having hemoglobinopathy with bone disorder group, another group with hemoglobinopathy not had bone disorder.In this study we include the patients those already suffered from BMD. We collected data from this patient during the research period.We assess the levels of hemoglobin, calcium, phosphorous, and Ferittin in hemoglobinopathy with had bone disorder as study group and other control group.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

RESULTS:
According to the findings of this report, osteoporosis is measured using a quantitative evaluation of BMD. There was no difference in BMD between men and women in this sample. Males had slightly higher hemoglobin and hematocrit levels. There was a statistically significant link between lumbar spine and skeletal muscle mass (SMM). Multiple regression analysis indicated that Hb has a 45.1 percent statistical impact on BMD. These results help to explain the relationship between BMD and Hb; a lower Hb level is related to a lower BMD. The highest indicator of abnormal BMD was the Hb stage.

CONCLUSION:
This study showed that a low Hb value wassignificantly correlated with low bone mass, suggesting that a low Hb value is a risk factor forchanges in bone turnover that leads to a decrease bone density.

KEYWORDS: Bone mineral density, Hemoglobin, Hemoglobinopathy, Thalassemia, Sickle cell disease.

INTRODUCTION

Since erythrocyte are created in the marrow space inside the bone, any disturbance of blood or bone homeostasis affects the entire blood-bone system.[1] Hemolytic anemia, such as thalassemia, sickle-cell anemia, and autoimmune hemolytic anemia, has been related to significant bone loss.[2] Because of the effects of bone fractures, associated morbidity and impairment, as well as social costs, a reduction in bone mass,[3] as measured by bone mineral density (BMD) loss, is a significant public health concern. [4]This is a global health concern, or several old researches have reported basic metabolic disorders as well as a number of risk factors linked to the development of osteoporosis. Adult, low Wight, a lack of body moment, a lack of schooling, and dyslipidemia are all well-known causes of bone mineral density loss (BMD). [5, 6]

The majority of bone mineral density (BMD) is acquired prior to puberty. According to previous research, the prevalence of osteoporosis in men was 1% in the United Kingdom, 4% in Japan, 3% in Canada, and 8% in France. [7] In 2013, the prevalence of osteoporosis in males aged 60–69 years and 80 years was 1,400 and 6,227 per 100,000, respectively, according to a study of Taiwan's population-based National Health Insurance claims database. [8]

Anemia is a very familiar disorder. According to the “2011 National Health Statistics,” the prevalence rates of anemia in men and women aged >10 years were 2.4 percent and 12.7 percent, respectively, and 15.3 percent and 17.8 percent, respectively, in men and women over the age of 70. BMD is caused by a number of factors, including genetics, age, sex, weight, total height, smoking, calcium supplementation, caffeine, liquor, and others.[9] Osteoporosis is a clinically silent disease in its early stages. Bone loss can strike at any time. It can lead to hip and spine breaks later in life[10]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

Sickle cell disease has a variety of side effects, one of which is skeletal damage. [11] In patients with sickle heamoglobinopathies, bone and bone marrow infarction is a frequent cause of acute morbidity [12] and can be a precursor to acute chest syndrome. [13] BMD defects in SCD patients are caused by a number of factors. Reduced BMD in adult patients with SCD has previously been linked to reduced hemoglobin levels, chronic hemolytic anemia, hyperplasia of the bone marrow, Decreased plasma zinc or sex steroid levels, increased ferritin levels, vitamin D defects, and extremely low body mass index (BMI). [15,14] Lesser physical exercise and circulating GH levels are both likely factors that contributed. [16,17]

The symptoms of thalassaemia bone disease include diffuse bone pain, scoliosis, spinal defects, nerve damage, frequent fractures, and severe osteoporosis.[18] In patients who live longer as a result of better care, however, Main causes of morbidity include osteopenia and/or osteoporosis. The prevalence of osteopenia or osteoporosis has been found to be about 40-50 percent in well-treated TM patients, suggesting that osteoporosis is a significant cause of morbidity in TM patients of both genders. [19]

Based on data from the orthopedic department at Shalinitai Meghe hospital and research centre Nagpur, the purpose of ,The aim of this study was to use different analysis methods to look at the relationship between hemoglobin, Ferittin, calcium, and phosphorous levels in BMD in men and women over the age of 20.

MATERIAL AND METHODS

Our research was carried out in the Biochemistry Department of DMMC&SMHRC Nagpur from September 2020 to March 2021. The analysis was accepted by the Institutional Ethics Committee, and informed consent was obtained prior to the report. A total of 150 people aged 35 to 80 years old were enrolled in this study. 75 subjects in the BMD study group and 75 subjects in the non-BMD control group were hemoglobinopathy patients in both groups out of 150 participants.The current research included one fifty patients aged 35 to 80 years old, of both sexes, who had hemoglobinopathy and were diagnosed according to W.H.O. criteria while visiting Shalinitai Meghe hospital in Nagpur for their daily check-up.

Inclusion criteria

- Those individuals have sickle cell anemia, Thalassemia, Bone mineral density disease are involved in this study. Informed consent was taken from all participants prior to the study.

Exclusion criteria

- The study included no underweight participants, pregnant women, individuals with malignancies/infections.

Blood sample collection and processing

With a tourniquet on the limb and fingers clenched, 5ml blood was collected in a vacutainer containing gel clot activator from the median cubital vein. To settle all the developed elements and remove serum, blood was centrifuged for 10 minutes at 10,000 rpm. The serum was immediately frozen in an autoclaved eppendorf tube before further examination. The clinical chemistry laboratory of Shalinitai Meghe Hospital Nagpur tested the samples.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

Hemoglobin, calcium, phosphorous, and Ferittin levels were calculated after aliquots of the samples were frozen at-70^0C.

Biochemical analysis

The 24-hour recall approach was used to assess calcium and iron intakes. BMI was determined based on height and body weight measurements. Blood tests were used to assess Hb and serum ferritin levels during the study period. According to WHO diagnostic criteria, anemia was identified as Hb levels of 13 g/dl for men and 12 g/dl for women. [20] For both men and women, the baseline iron deficiency status was set at15 ng/mL, and the standard upper limit of serum ferritin levels was set at 200 ng/mL for men and 150 ng/mL for women. [21]

Statistical Analysis

The general characteristics of the topic were viewed as mean± standard deviation in this analysis, or the following analyses were carried out: SPSS 20.0 for Windows was used to conduct all of the analyses. All of the findings below had bilateral P-values, and the significance level was set at P<0.05.

RESULT

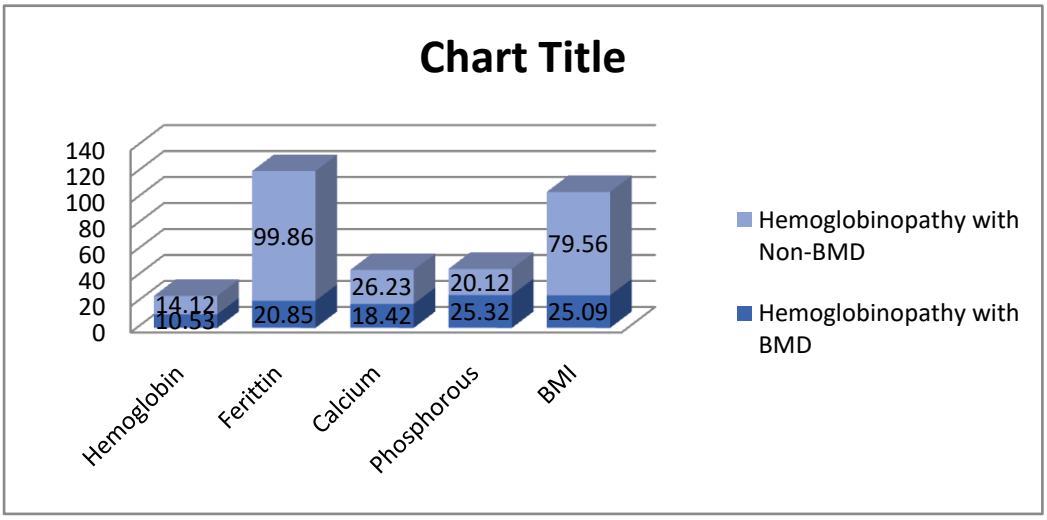
Table 1: shows comparisons the biochemical parameters in hemoglobinopathy with BMD and Non-BMD cases**.**

Parameters	Hemoglobinopathy with BMD N= 75 Age- 35-80yrs	Hemoglobinopathy with Non-BMD N= 75 Age- 35-80yrs	significance
Hemoglobin	10.53±2.55	14.12±1.23	<0.001
Ferittin	20.85±15.11	99.86±37.02	<0.001
Calcium	18.42±9.53	26.23±12.30	<0.001
Phosphorous	25.32±6.21	20.12±4.61	<0.001
BMI	25.09±7.08	79.56±15.10	<0.001

According to table 1, the research group's levels of hemoglobin, ferritin, calcium, phosphorus, and BMI are substantially lower than the control groups. This parameter is substantially higher in hemoglobinopathy patients who do not have a bone disorder than those who have a bone disorder but not a hemoglobin disorder.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

Graph-1: Comparisons the biochemical parameters in hemoglobinopathy with BMD and Non-BMD cases



Graph 1 shows the significantly increased Hemoglobin, Calcium, Phosphorous, and BMI in hemoglobinopathy patients with non-BMD as compared to the BMD patients.

DISCUSSION

We looked at the relationship between changes in bone density and hematopoietic disorders parameters like hemoglobin, calcium, phosphorous, In this observational analysis, researchers looked at ferritin, as well as bone marrow hematopoietic cellularity.

Laudisio, Marzetti, Pagano, Bernabei, & Zuccalà, 2009[22] found that haemoglobin levels were independently and significantly associated with ultrasound-derived T-score in 358 Italian adults aged 75 years or older, based on regression models that accounted for age, sex, protein intake, BMI, and physical activity.

In a cross-sectional study using data from the Korea National Health and Nutrition Evaluation Survey, **Oh, Moon, and Cho (2017)**[23] discovered that haemoglobin level was significantly associated with femoral neck and lumbar spine BMD in men. Another hypothesis suggested that diseases that continuously affect hematopoietic function, such as sickle cell anaemia (**Sarrai, Duroseau, D'Augustine, Moktan, & Bellevue, 2007)**[24] and thalassemia **(Voskaridou & Terpos, 2008)**,[25] may cause an increase in the number of hematopoietic cells. Cells such as hematopoietic growth factors and osteoclasts can help with bone resorption**.**

Sarrai M, 2007[24]these results indicated that hemoglobin has a statistically important effect on BMD. Through the communication of osteoclast-osteoblasts interaction, EPO activates osteoblastic phenotypes both directly and indirectly by encouraging osteoblastic differentiation. Since there is a connection between reduced Hb levels and lower BMD, these

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 6927 – 6934
Received 05 March 2021; Accepted 01 April 2021.

findings are crucial for explaining the relation between BMD and Hb. Haemoglobin level was the best predictor of irregular BMD.

Hemochromatosis and other forms of iron overload are often linked to osteoporosis., according to **Zarjou A, Jeney V, Arosio P, et al.2010**[26]The effect of iron on bone homeostasis has been due to a variety of mechanisms, including direct inhibition of osteoblasts activity or bone mineralization by iron, direct stimulation of osteoclast formation by iron, Reactive oxygen species (ROS) or ferroxidase activity of ferritin have indirect effects.
A number of studies related to different hemoglobin disorders were reported [27-29]. Noman et. al. reported about fetal haemoglobin as a novel prognostic determinant in sickle cell anaemia [30]. Sain et. al. studied discriminant indices for distinguishing beta thalassemia trait from iron deficiency anaemia[31]. Vanlalsawmi et. al. reported on thalassemia in children[32]. Chandak et. al. assessed haematological profile in patient of sickle cell anaemia in Vidarbha Region[33]. Ehtesham et. al. reported on Lactate Dehydrogenase as Predictor for Severity in Sickle Cell Disease[34]. Other studies related to liver problems and lifestyle risks affecting hemoglobinopathies were reviewed [35,36].

Future research on the Hb levels and BMD have a relationship will use bone formation and resorption markers in subjects for research designs that can test hypotheses based on specific hematological etiologies, as well as long-term follow-up studies of the mechanism, to understand the connection between Hb levels and BMD.

CONCLUSION

Serum hemoglobin levels may be used to identify early signs of bone mineral depletion and alert clinicians to the possibility of osteoporotic fractures in adults. In patients being treated for hemoglobinopathy, BMD should be closely controlled. Preventive treatment to reduce the risk of osteoporosis should be provided whenever possible.

REFERENCES:

1. Teti A. Osteoclasts and hematopoiesis. Bonekey 2012;1.
2. Middlemiss JH, Raper AB. Skeletal changes in the haemoglobinopathies. J Bone Joint Surg Br. 1966;48(4):693–702.
3. Compston JE. Bone marrow and bone: a functional unit. J Endocrinol. 2002;173(3):387–94.
4. Boskey AL, Coleman R. Aging and bone. J Dent Res. 2010; 89(12):1333–1348.
5. New SA. Exercise, bone and nutrition. Proc Nutr Soc 2001; 60:265-74.
6. Varenna M, Binelli L, Zucchi F, et al. Prevalence of osteoporosis by educational level in a cohort of postmenopausal women. Osteoporos Int 1999;9:236-41.
7. Wade, S. W., Strader, C., Fitzpatrick, L. A., Anthony, M. S., & O'Malley, C. D. Estimating prevalence ofosteoporosis: Examples from industrialized countries. Archives of Osteoporosis, 2014; 9,182.
8. Wang, C. Y., Fu, S. H., Yang, R. S., Shen, L. J., Wu, F. L. L., & Hsiao, F. Y. Age-and gender-specific epidemiology, treatment patterns, and economic burden of

osteoporosisand associated fracture in Taiwan between 2009 and 2013. Archives of Osteoporosis, 2017;12(1), 92.
9. Kim YR, Lee TY, Park YS, Cheon HK. The effect of lifestyle habits and nutrient intake conditions of female shift workers at general hospitals on bone mineral density values. J Radiol Sci Technol. 2012;35(1):9-15.
10. Ghobadi M, Hoseini R. Investigating the effects of physical activity levels, dairy products and calcium intakes on risk factors of osteoporosis prevention in female students of Islamic Azad University of Damavand, Iran. Medical-biological Problems of Physical Training and Sports. 2014;11:79-82.
11. Smith JA. Bone disorders in sickle cell disease. Hematol Oncol Clin North Am. 1996;10:1345–1356.
12. Milner PF, Clarence J, Burke GJ. Bone and joint disease. In: Embury SH, Hebbel RP, Mohandas N, Steinberg MH, eds. Sickle Cell Disease: Basic Principles and Clinical Practice. New York, NY: Raven Press; 1994:645–661.
13. Sisyan R, Elgazzar AH, Webner PJ, et al. Impact of bone scintigraphy on the clinical management of a patient with sickle cell anemia and recent chest pain. Clin Nucl Med. 1996;21:523–526.
14. Baldanzi G, Traina F, Marques Neto JF, et al. Low bone mass density is associated with hemolysis in brazilian patients with sickle cell disease. Clinics (Sao Paulo)2011; 66: 801-805.
15. Al-Elq AH, Al-Turki HA, Sultan OA, et al. Influence of androgens on bone mass in young women with sickle cell anemia. Saudi Med. J 2010; 29:980-983
16. Adewoye AH, Chen TC, Ma Q, et al. Sickle cell bone disease: response to vitamin D and calcium. Am J Hematol. 2008;83:271-274.
17. Fung BE,, Kawchak AD, Zemel BS, et al. Markers of bone turnover are associated with growth and development in young subjects with sickle cell anemia. Pediatr Blood Cancer. 2008;50: 620-623.
18. Cooley TB, Lee P. Series of cases of Splenomegaly in children with anaemia and peculiar bone changes. Trans Am Pediatr Soc.1925; 37:29
19. Voskaridou E, Terpos E. (2004) New insights into the Pathophysiology and management of osteoporosis in patients with beta thalassaemia. Br J Haematol. 127: 127-139.
20. WHO Scientific Group. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser 1968;405:5-37.
21. World Health Organization. Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations. 2011
22. Laudisio, A., Marzetti, E., Pagano, F., Bernabei, R., & Zuccalà, G. Haemoglobin levels are associated with bone mineral density in the elderly: A population-based study. *Clinical Rheumatology*, 2009;*28*(2), 145–151.
23. Oh, Y. H., Moon, J. H., & Cho, B. Association betweenhemoglobin level and bone mineral density in Koreanadults. *Journal of Bone Metabolism*, 2017;*24*(3), 161–173.
24. Sarrai, M., Duroseau, H., D'Augustine, J., Moktan, S., & Bellevue, R. Bone mass density in adults with sickle cell disease. *British Journal of Haematology*, 2007;*136*(4),666–672.
25. Voskaridou, E., & Terpos, E. (2008). Pathogenesis and management of osteoporosis in thalassemia. *PediatricEndocrinology Reviews*, 2008;*6*(1), 86–93.
26. Zarjou A, Jeney V, Arosio P, et al. Ferritin ferroxidase activity: a potent inhibitor of osteogenesis. J Bone Miner Res. 2010;25(1):164–72.
27. Gupta, S., A. Mohabey, V. Gawande, K. Saoji, A. Chauhan, A. Parate, and A. Sharma. "A Rare Case Report on Primary Aneurysmal Bone Cyst of the Patella."

International Journal of Current Research and Review 12, no. 16 (2020): 76–78. https://doi.org/10.31782/IJCRR.2020.121625.

28. Varma, A.D., S.V. Phatak, S. Jain, and G.V. Mishra. "Musculoskeletal Manifestation of Hemarthrosis as Presentation of Coagulopathy Disorder in a Child." Journal of Datta Meghe Institute of Medical Sciences University 15, no. 2 (2020): 306–7. https://doi.org/10.4103/jdmimsu.jdmimsu_13_20.
29. Gokhale, M., P. Agarwal, and A. Ramdas Patil. "Correlation of Body Fat Distribution with Iron Profile and Haemoglobin Level in Young Overweight Females." International Journal of Pharmaceutical Research 11, no. 1 (2019): 1153–56. https://doi.org/10.31838/ijpr/2019.11.01.203.
30. Noman, O., A. Bhake, S. Bahadure, and N. Gupta. "Fetal Haemoglobin: A Novel Prognostic Determinant in Sickle Cell Anaemia." European Journal of Molecular and Clinical Medicine 7, no. 2 (2020): 2003–8.
31. Sain, A., A. Agrawal, A. Bhake, S. Vagha, and J.M. Kumbhare. "Discriminant Indices for Distinguishing Beta Thalassemia Trait from Iron Deficiency Anaemia: Work up at Microcytic Hypochromic Anaemia." International Journal of Pharmaceutical Research 11, no. 2 (2019): 1829–33. https://doi.org/10.31838/ijpr/2019.11.02.206.
32. Vanlalsawmi, J., D. Mendhe, and M. Patil. "Thalassemia in Children: A Case Report." Indian Journal of Forensic Medicine and Toxicology 14, no. 4 (2020): 6615–17. https://doi.org/10.37506/ijfmt.v14i4.12648.
33. Chandak, P., A. Vagga, and G.A. Chaudhary. "Haematological Profile in Patient of Sickle Cell Anaemia in Vidarbha Region." International Journal of Pharmaceutical Research 11, no. 1 (2019): 1161–64. https://doi.org/10.31838/ijpr/2019.11.01.205.
34. Ehtesham, M.A., B. Lakhkar, and R. Adkane. "Lactate Dehydrogenase as Predictor for Severity in Sickle Cell Disease." International Journal of Current Research and Review 12, no. 22 Special Issue (2020): 3–5. https://doi.org/10.31782/IJCRR.2020.SP84.
35. Bawankule, S., S. Kumar, A. Gaidhane, M. Quazi, and A. Singh. "Clinical Profile of Patients with Hepatic Encephalopathy in Cirrhosis of Liver." Journal of Datta Meghe Institute of Medical Sciences University 14, no. 3 (2019): 130–36. https://doi.org/10.4103/jdmimsu.jdmimsu_88_18.
36. Gaidhane, A., A. Sinha, M. Khatib, P. Simkhada, P. Behere, D. Saxena, B. Unnikrishnan, M. Khatib, M. Ahmed, and Q.S. Zahiruddin. "A Systematic Review on Effect of Electronic Media on Diet, Exercise, and Sexual Activity among Adolescents." Indian Journal of Community Medicine 43, no. 5 (2018): S56–65. https://doi.org/10.4103/ijcm.IJCM_143_18.