



Influence of Pregnancy on Bone Mass in Sickle Cell Anemia

L'influence de Grossesse sur la Masse d'Os dans l'Anémie de Cellule de Faucille

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ABSTRACT

BACKGROUND: Sickle cell disease (SCD) causes osteopenia and osteoporosis, This osteopenia may be further influenced by pregnancy.

OBJECTIVE: To find out the effect of pregnancy on bone skeleton density in patients with SCD.

METHODS: Consecutive adult female SCA patients who were treated at the out-patients clinics of King Fahd University Hospital Al-Khobar, Saudi Arabia, between January and July 2007, were the cases of study. Patient's age, number of pregnancies and duration after pregnancy were documented. Weight and height were recorded to calculate body mass index (BMI). Blood was collected for haematology and biochemistry purposes. Bone mineral density (BMD) measurement was done using dual energy X-ray absorptiometry (DEXA) at upper femur and lumbar spine.

RESULTS: Thirty-eight patients were evaluated. There were 20(52.6%) patients who were delivered in (Group A) and 18(47.4%) who were nulliparous in Group B. The average age in group A was 27.55 ± 4.9 years while group B was 26.30 ± 2.1 years. Thirteen (65%) of the patients in group A were osteoporotic when compared to five (27.7%) in group B ($p=0.01$). Osteopenic patients in group B were seven (38.9%) versus four (20%) in group A ($p=0.2$). Osteoporosis in both groups was highest at lumbar spine compared to the hip region ($P=0.001$). BMD was lower in parous women when compared to the nulliparous women. There was no significant difference in haematological parameters which included the percentage of sickle hemoglobin, hemoglobin level between normal, osteopenic and osteoporotic patient.

CONCLUSION: This study shows that SCA female patients suffer from low bone mass in young age. Pregnancy predisposes the SCA patients to further osteopenia and osteoporosis. *WAJM* 2009; 28(3): 169–172.

Keywords: Pregnancy, Low Bone Mass, Osteoporosis, Osteopenia, Sickle Cell Anemia.

RÉSUMÉ

CONTEXTE: la cellule de Faucille (SCD) provoque(cause) osteopenia et anémie osteoporosis qui est la grossesse influencée de plus.

OBJECTIF: découvrir l'effet de grossesse sur la squelette d'os dans les patients avec.

MÉTHODES: les patients SCA femelles adultes consécutifs que l'on a traité aux cliniques de malades externes d'Hôpital de Roi Fahd University Al-Khobar, l'Arabie Saoudite, entre le janvier et le juillet de 2007, étaient les cas d'étude. L'âge de patient, le nombre de grossesses et de durée après la grossesse ont été documentés. Le poids et la hauteur ont été enregistrés pour calculer l'index de masse de corps (BMI). Le sang a été recueilli pour les buts de biochimie et haematology. La densité de minéral d'os (BMD) la mesure a été faite en utilisant des Rayons X d'énergie doubles absorbtometry (DEXA) au fémur supérieur et à la colonne vertébrale lombaire.

RÉSULTATS: Trente-huit patients ont été évalués. Il y avait 20 patients (de 52.6 %) que l'on a livré dans (le Groupe A) et 18 (47.4 %) qui étaient nulliparous dans le Groupe B. L'âge moyen dans le groupe A était 27.55 ± 4.9 ans pendant que le groupe B était 26.30 ± 2.1 ans. Treize (65 %) des patients dans le groupe A étaient osteoporotic quand comparé à cinq (27.7 %) dans le groupe B ($p=0.01$)., les patients d'Osteopenic dans le groupe B étaient sept (38.9 %) contre quatre (20 %) dans le groupe ($p=0.2$). Osteoporosis dans les deux groupes était le plus haut à la colonne vertébrale lombaire comparée à la région de hanche ($P = 0.001$). BMD était inférieur(plus bas) dans les femmes parous quand comparé aux femmes nulliparous. Il n'y avait aucune différence significative dans les paramètres haematological qui ont inclus le pourcentage d'hémoglobine de faucille, niveau d'hémoglobine entre normal, osteopenic et le patient osteoporotic.

CONCLUSION: Cette étude montre que les malades SCA souffrent de la masse d'os basse dans le jeune âge. La grossesse prédispose les patients SCA à plus loin osteopenia et osteoporosis. *WAJM* 2009; 28(3): 169–172.

Mots clé: Grossesse, La Masse d'Os Basse, Osteoporosis, Osteopenia, l'Anémie de Cellule de Faucille.

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Abbreviations: BMD, Bone Mineral Density; BMI, Body mass index; DEXA, dual energy X-ray absorbtometry; HbSS, Haemoglobin SS; SCA, Sickle cell anaemia; SCD, Sickle cell disease; WHO, World Health Organisation.

INTRODUCTION

Sickle cell gene is prevalent in 26% of the Saudi population, patients with homozygous sickle cells (HbSS) suffer the brunt of the chronic disease.¹

The skeleton is the most common site of infection due to marrow hyperplasia which destroys the trabecular pattern of the bony architecture making liable for osteopenia, osteoporosis with increased incidence of fractures. Apart from other complications which both gender suffers,²⁻⁵ it was reported that female SCA patients suffer additional complications due to their pregnancies. The disease itself was shown to have an adverse effect on the mother and child.⁶ Even in patients with normal hemoglobin, the effect of pregnancy on the maternal bony skeleton still evolves and many researchers have reported conflicting results of the immediate effect of pregnancy on bone mass.⁷⁻¹⁰

With the improved management of sickle cell disease, patients are surviving longer and many are consider bearing children. A high prevalence of osteoporosis and osteopenia has been reported in young male and female SCA patients,¹¹⁻¹³ pregnancy may further add to the bone loss resulting in increased risk of morbidity. Review of the English literature did not yield any reports of the influence of pregnancy in SCA patients, hence this study was undertaken to assess the influence of pregnancy on BMD in SCA patients.

SUBJECTS, MATERIALS, AND METHODS

This study was conducted at King Fahd University Hospital, Al-Khobar between January and July 2007. Consecutive female patients with SCA who were seen in the obstetrics and gynecology, hematology and orthopaedic clinics were studied. Patients below the age of twenty five years (as they did not reach the peak bone mass) and those who were diagnosed to have osteopenia or osteoporosis undergoing treatment was excluded from the study. After a verbal consent, detailed history was obtained to rule out any secondary cause of osteoporosis. Patients demographic data collected included age, number of children, date of last delivery, history of

blood transfusions, weight and height. A complete blood picture, renal function tests, liver function tests, calcium level, phosphorus level, hemoglobin electrophoresis, thyroid stimulating hormone, parathyroid hormone and estradiol levels. BMD was measured at lumbar spine at the upper femur using Dual Energy X-ray Absorbtiometry (DEXA) scan, Hologic Inc., Waltham, MA, USA. A T Score of -2.6 SD lower was taken as osteoporotic and those between < -1 to -2.5 SD was taken as osteopenic for analysis as defined by WHO criteria for osteoporosis and osteopenia.¹⁴ The data was entered in the data base and analyzed using SPSS (Statistical Package for the Social Test and Chi-square, as needed, with statistical significance of p value of <0.05 with confidence interval of 95%. The

study was approved by the Ethical Research Committee of the College of Medicine, King Faisal University, Dammam, Saudi Arabia.

RESULTS

Thirty-eight patients were evaluated. Group A had twenty patients who had delivered and Group B had 18 nulliparous. The average age in group A was 27.55 ± 4.9 years and group B 26.30 ± 2.1 years. Thirteen (65%) of patients in group A were osteoporotic compared to five (27.7%) in group B ($p=0.01$). In group B, osteopenic patients were seven (38.9%) while group A were four (20%) ($p=0.2$). Osteoporosis in both groups was highest at lumbar spine as compared to the hip region ($P=0.001$).

Table 2 shows the comparison

Table 1: Anthropometric and Biochemical Indices of Study Subjects

Variable	Parous (Group A)	Nulliparous (Group B)	P Value
Number of Patients	20	18	NS
Age (years)	29.55 ± 4.9	26.2 ± 2.1	NS
BMI Kg/M ²	19.87 ± 4.91	18.2 ± 2.8	NS
Hemoglobin "S"	90.2 ± 3.83	89.8 ± 3.73	NS
Hemoglobin Concentration (g/dl)	9.96 ± 0.86	9.25 ± 0.9	NS
Serum Calcium Level (mg/dl)	8.96 ± 0.67	8.47 ± 0.36	NS
Phosphorus (mg/dl)	3.75 ± 0.5	3.46 ± 0.7	NS
Alkaline Phosphatase IU	95.11 ± 27.8	113.4 ± 42.6	NS
Normal	3	6	0.1
Osteopenia	4	7	0.2
Osteoporosis	13	5	0.01

Table 2: Comparison of Bone Density of Parous and Nulliparous Patients

Variable	Parous (Group A)	Nulliparous (Group B)
Number of patients	20	18
Age in years	29.55 ± 4.9	26.2 ± 2.1
BMI kg/M ²	19.87 ± 4.91	18.2 ± 2.8
Hip BMD g/cm ²	0.729 ± 0.07 (0.434-1.1)	0.797 ± 0.01 (0.622-1.212)
Hip T-Score	-2.03 ± 0.5 (-0.8-4.2)*	0.4 ± 0.04 (-.7-3.8)*
Hip Z-Score	-1.5 ± 0.3 (-0.5- -2.6)*	-2 ± 0.6 (0.2- -3.8)*
Spine BMD g/cm ²	0.794 ± 0.09 (0.56-1.11)*	0.801 ± 0.08 (0.771-.851)*
Spine T-Score	-2.42 ± 0.9 (0.6-2.1)	-2.1 ± 0.7 (1.5- -5.4)
Spine Z-Score	-2.16 ± 0.9 (0.7- -5.1)*	-2.05 ± 0.7

* Minimum to maximum values; average values given as Mean \pm SD.

between group A and B for bone mineral density, T score and Z score. BMD was lower in parous women when compared to nulliparous women. The BMI between normal and osteoporotic patients did not reach a statistical significance as there were no differences in the BMI between normal and osteopenic patients. There were no significant differences in the studied hematological parameters which included the percentage of sickle haemoglobin, the hemoglobin level between normal, osteopenic and osteoporotic patient.

DISCUSSION

Sickle cell anemia is an inherited disorder that affects haemoglobin synthesis producing abnormal shaped red blood cells, which are easily destroyed in the capillary circulation leading to repeated blockage of the small vessels. The bone problem is involved in over 80% of patients with SCA, who suffer from acute to chronic debilitating conditions.^{2,15-18} Though, bone is so often involved, it has been overlooked resulting to patient suffering from low bone mass. This is supported by the paucity of published data in the literature low bone mass in sickle cell patients.

Bone remodeling during and after pregnancy and its effects on bone mineral density are still evolving. Reports have shown a positive correlation between parity and bone mineral density.¹⁹⁻²² Search of English language literature did not reveal any report on the effect of pregnancy on bone mass in SCA patients although, a high prevalence of osteopenia and osteoporosis up to 70-80% has been reported.^{11,12,23} Sarrai *et al* (2007)²³ believed that malnutrition, delayed growth and hormonal deficiencies could be the reason for high prevalence of low bone mass. Both groups of patients in this study had similar results indicating little or no role of the mentioned factors. The correlation of BMI to BMD is well known, and was significant in patients who were nulliparous, while patients who had borne children, the lower BMI to lower BMD did not exist. This suggests that in SCA patients high BMI may not be associated with higher BMD.

The outcome of pregnancy in SCA patients is marred with complications and

adverse effects on the mother and the baby. Serjeant *et al* (2004)⁶ reported that only 24% of pregnancies were uneventful while, post pregnancy complications were not evaluated. In normal pregnancy it has been suggested that during the first trimester there is loss of the trabecular bone which is recovered in the last trimester.²⁴⁻²⁵ But, in our patients it appears that this normal process did not occur. The patients who become pregnant continued to lose bone, increasing the prevalence of osteoporosis.

There are convincing reports which suggest that SCA patients suffer from low bone mass which occurs secondarily due to trabecular destruction. Fitzpatrick (2002)²⁶ discovered that between 30-40% of patients with sickle cell disease has a secondary cause which becomes an important factor for secondary osteoporosis. In female patients with SCA who wish to become pregnant, special attention should be given to prevent the conversion of osteopenia to osteoporosis. Necessary steps should be taken to reduce the incidence of osteopenia and osteoporosis. SCA patients, now living longer due to better health care and improved management of the disease. However, pregnant female may suffer the risk of osteoporosis with increase morbidity and high risk of fracture.

In conclusion, this study shows that there is a high prevalence of osteopenia and osteoporosis among young premenopausal SCA patients. Nulliparous patients were osteopenic, while, those who had borne children were osteoporotic. To decrease the morbidity and high risk of fractures, SCA patients of child bearing age should be investigated early, using the BMD measurements and appropriate treatment instituted for osteopenia and osteoporosis.

REFERENCES

1. el-Hazmi MA, Warsy AS, al-Swailem AR, al-Swailem AM, Bahakim HM. Sickle cell gene in the population of Saudi Arabia. *Hemoglobin* 1996; **20**: 187-98.
2. Sadat-Ali M. Sickle cell disease. Orthopaedic complications and their management. Premier Publications, India 1994.
3. Neonato MG, Guilloud-Bataille M, Beauvais P, Begue P, Belloy M,

- Benkerrou M. *et al*. Acute Clinical events in 299 homozygous sickle cell patients living in France. French Study Group on sickle cell disease. *European J Hematol* 2000; **65**: 155-64.
6. Serjeant GR, Loy LL, Crowther M, Hambleton IR, Thame M. Outcome of pregnancy in homozygous sickle cell disease. *Obstet Gynecol* 2004; **103**: 1278-85.
7. Ulrich U, Miller PB, Eyre DR, Chesnut CH, Schleich H, Soules MR. Bone remodeling and bone mineral density during pregnancy. *Arch Gynecol Obstet* 2003; **268**: 309-16.
8. Black AJ, Topping J, Durham B, Farquharson RG, Fraser WD. A detail assessment of alterations in bone turnover, calcium homeostasis, and bone density in normal pregnancy. *J Bone Miner Res* 2000; **15**: 557-63.
9. Naylor NE, Iqbal P, Fledelius C, Frazer RB, Eastell R. The effect of pregnancy on bone density and bone turnover. *J Bone Miner Res* 2000; **15**: 129-37.
10. Drinkwater BL, Chestnut CH III. Bone density during pregnancy and lactation in active women: a longitudinal study. *Bone Miner* 1991; **14**: 153-60.
11. Sadat-Ali M, Al-Elq AH. Sickle Cell Anemia: Is it a Cause for Secondary Osteoporosis? *West African J Med* 2007; **26**: 134-7.
12. Miller RG, Segal JB, Ashar BH, Leung S, Ahmed S, Siddique S *et al*. High prevalence and correlates of low bone mineral density in young adults with sickle cell disease. *Amer J Hematol* 2006; **81**: 236-41.
13. Sadat-Ali M, Al-Elq AH, Sultan O, Al-Turki H, Bukhari R, Riad Bukhari, Al-Mulhim F. Low Bone Mass Due to Sickle Cell Anemia. Is it Becoming a Real Issue. (*West Afr J Med* 2009 In Press).
14. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of WHO study group. *World Health Org Tech Rep Ser* 1994; **843**: 1-129.
15. Almeida A, Roberts I, Neumayr L. Bone involvement in sickle cell disease. *Br J Hematol* 2005; **129**: 482-90.
16. Aguilar C, Vichinsky E. Bone and joint disease in sickle cell disease. *Hematol Oncol Clin N Am* 2005; **19**: 929-41.
17. Sadat-Ali M. Avascular Necrosis of Femoral Head in Sickle Cell Disease: An Integrated Classification. *Clin Orth Rel Res*. 1993; **290**: 200-205.
18. Sadat-Ali M, Geeranavar SS and As-Suhaimi S: Orthopaedic Complications in Sickle Cell Disease. A comparative study from two regions in Saudi Arabia.

- Inter Orthop (SICOT) 1992; **16**: 307–10.
19. Sadat-Ali M, Al-Habdan I, Al-Mulhim Fatma, Yousef A. Effect of parity on Bone mineral density in Postmenopausal Saudi women. *Saudi Med J* 2005; **26**: 1588–90.
 20. Cure-Cure C, Cure-Ramirez, Teran E, Lopez-Jaramillo P. Bone-mass peak in multiparity and reduced risk of bone fractures in menopause. *Int J Gynaecol Obstet* 2002; **76**: 285–91.
 21. Forsmo S, Schei B, Langhammer A, Forsen I. How do reproductive and lifestyle factors influence bone density in distal and ultradistal radius of early postmenopausal women? The Nord-Trondelag Health Survey, Norway. *Osteoporosis Int* 2001; **12**: 222–29.
 22. Sadat-Ali M, Al-Habdan I, Marwah S. Bone Mineral Density measurements of distal radius in Saudi Arabian females. *Annals of Saudi Med* 1996; **16**: 414–16.
 23. Sarrai M, Duroseau H, D'Augustine J, Moktan S, Bellevue R. Bone mass density in adult with sickle cell disease. *British J Hematol* 2007; **136**: 666–72.
 24. Shahtaheer SM, Aaron JE, Johnston DR, Purdi DW. Changes in the trabecular bone architecture in women during pregnancy. *Br J Obstet Gynaecol* 1999; **106**: 432–38.
 25. Purdi DW, Aaron JE, Selby PL. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynaecol* 1988; **95**: 849–54.
 26. Fitzpatrick L. Secondary causes of osteoporosis. *Mayo Clinic Proc* 2002; **77**: 453–68.