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Serum Bone Menirals in Patients of Sickle Cell Anemia

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Abstract **Original Research Article**

Introduction: single nucleotide substitution A by T AT 17TH nucleotide of the 6th amino-acid Glutamic acid by valine in beta subunit of Hb (HbA) results in formation of sickle hemoglobin (HbS), Sickle bone syndrome is a public health problem to sicklers (disturbed serum bone minerals and bone density sickle cell crisis pain). Because of genetic prevalence of sickle anaemia gene in Southern Sudan, sickle cell anaemia is a serious health issue and common cause of paediatrics admission at hospitals and the significance of measuring serum calcium, phosphorous and magnesium clarify the necessity to conduct this study. Which aimed to evaluate Ca, P and Mg Sudanese sicklers and correlate them to bone density and sickle cell crisis pain. ***Methods:*** A descriptive Case control study conducted in Southern Darfur Nyala-city involving Sudanese sicklers 50 and age matched control group 50,Hb electrophoresis records and clinical data for patients with sickle disease (known cases of SCD) serum Ca, P, Mg and Albumin were estimated using fully automated chemistry analyzer (Mindray BS-200) for All study groups. Data analysed using SPSS computer software v.24 ***Results:*** The results show normal magnesium levels with significant difference between serum magnesium levels among patients (2.43 (0.37) mg/dl) and controls (1.99 (0.47) mg/dl) p value 0.00, the mean serum calcium levels was significantly lower in the sickle cell disease group (8.4 (0.9 mg/dl) compared to controls (9.4 (0.6) mg/dl) p value 0.00. While the mean serum inorganic phosphorous was significantly higher in SCD group (6.6 (1.8) mg/dl) compared to control group (3.9 (0.82) mg/dl). ***Conclusion****:* Normomagnesimia hyperphosphatemia and hypocalcaemia are observed in SCD compared to controls.

Keywords: Sickle bone syndrome, sickle cell anaemia, sickle hemoglobin (HbS).

INTRODUCTION

A single nucleotide substitution A by T AT 17TH nucleotide of the 6th amino-acid Glutamic acid by valine in beta subunit of Hb (HbA) results in formation of sickle hemoglobin (HbS). Sickle cell disease results from homozygosity for this mutation, or from a compound heterozygosity for sickle hemoglobin and β-thalassemia or another β-globin variant such as HbC, HbD, HbE, or HbO Arab. The sickle mutation renders the hemoglobin molecule insoluble upon deoxygenation; thus red blood cells containing deoxy HbS polymer are rigid and have impaired rheologic properties. The downstream effects of the sickling process include: membrane changes leading to potassium loss and cellular dehydration, interaction of sickle hemoglobin with microvascular endothelium, neutrophils, and monocytes, hemolysis, nitric oxide depletion, release of inflammatory proteins and activation of coagulation. These processes lead to a hemolytic anemia, an inflammatory state, resultant shortened life expectancy (sickle crisis) [1].

Electrolyte disturbance and sickle bane syndrome is reported by many studies. O.O Oladipo et al reported hypocalcaemia, hyperphosphataemia and normomagnesimisa in Nigerian children with sickle cell disease [2], E.O Ibe results showed significant dercrease in sodium and potassium as prevalent causes of sickle cell crisis [3], Shahriar Zehbachi studied serum ionized Mg levels and Ca:Mg ratioin adults and showed Low Mg levels and high ratio [4], Adeboye H. Adewoy et al reported corrected Ca and vit D dificeint sickle bone syndrome after treatment with vit D and Ca supplement but the markers of bone resorption remains unchanged [5] , many studies reported low magnesium [6, 7]and low Calcium levels among sicklers [6, 7, 10-13]. Bone involvement is the most widespread clinical manifestation of SCD, but is perhaps the least well studied. It can present acutely as vaso-occlusive (VOC) bone and joint pain, bony infarcts, osteomyelitis, septic and aseptic arthritis, or as chronic bone deterioration, in which case it manifests as avascular necrosis (AVN), vertebral bone deformities, degenerative arthritis,

osteopenia, osteoporosis, Osteogenesis Imperfecta and pathological fractures [14-30].

Sickle bone syndrome is a public health problem to sicklers (disturbed serum bone minerals and bone density sickle cell crisis pain) because of consanguinity marriage and high genetic prevalence of sickle anaemia gene in western Sudan, sickle cell anaemia is a serious health issue and common cause of paediatrics admission at hospitals and the significance of calcium, phosphorous and magnesium clarify the necessity to conduct this study. And the bone density relationship to serum minerals in sicklers is not well studied in Sudan.

METHODS

A descriptive Case control study conducted in Southern Darfur Nyala involving Sudanese sicklers and the Sample Size according to the prevelence of sickle cell disease in Sudan is 4.8% [22-23] a 100 participents and the sample size is calculated by the following formula at the confidence level of 95% and degree of precision 0.04. $n=(t2 \times p(1-p)) / m^2$.

The Inclusion criteria were Patients with SS Hb with crisis (clinically on pain, fever, vasculitis, multi organ infections and low Hb with high TWBCs) or Non crisis sicklers (clinically stable) and Population with normal Hb AA, While Exclusion criteria were Individuals with known bone diseases and metabolic minerals disorders (renal failure – rickets, hyper-hypoparathyroidism, metabolic acidosis, beckets, multiple myeloma, cancers etc.).

Samples collected as 5ml of venous blood will be drawn by standard procedures into plain container and EDTA container and data collected using structured questionnaire. Population divided into 2 groups sicklers on crisis or sicklers not on crisis, and healthy Hb AA as control.

Techniques

We obtained Hb electrophoresis records and clinical data for patients with sickle disease (known cases of SCD). While Ca, P, Mg and Albumin were estimated using fully automated chemistry analyzer (Mindray BS-200) for All study groups.

Data analysed using PSS computer software v.24 and the Ethical consideration given by scientific research committee of faculty of medical laboratory science.

RESULT

100 participants were included in the study 50 sicklers and 50 age matched healthy control group .49 male and 51 female. The results of patients and controls are shown in table-1 and they statistical significance and manifestation of correlations is shown in figures1 and 2.

The results show normal magnesium levels with significant difference between serum magnesium levels among patients (2.43 (0.37), mg/dl (mean±sd)) and controls (1.99 (0.47) mg/dl (mean±sd)) p value 0.00, the mean serum calcium levels was significantly lower in the sickle cell disease group (8.4 (0.9 mg/dl) (mean±sd)) compared to controls (9.4 (0.6) mg/dl (mean±sd)) p value 0.00. While the mean serum inorganic phosphorous was significantly higher in SCD group (6.6 (1.8) mg/dl (mean±sd)) compared to control group (3.9 (0.82) mg/dl (mean±sd)).

In SCD group there is no correlation between cacium and phosphorous(r – 0.097 p value 0.504), calcium and magnesium (r 0.156 p value 0.280) in this study as shown in figure (1,3) spectively. While phosphorous and magnesium shown positive correlation (r 0.419 p value 0.02).

The distribution of Ca and Mg is not the same across categories of socio-economic state p value (0.043, 0.036) respectively but the same in phosphorous p value 0.705. While the distribution of Ca P Mg were not affected by gender of the participants and parental educational background.

Table-1: Case vs Control serum Ca P Mg

Group Statistics			
Parameter	**Case**	**Control**	**P. value**
Serum calcium	8.4 (0.9)	9.5 (0.59)	0.0000
Serum magnesium	2.43 (0.37)	1.99 (0.48)	0.0000
serum phosphorous	6.6 (1.8)	4.0 (0.82)	0.0000

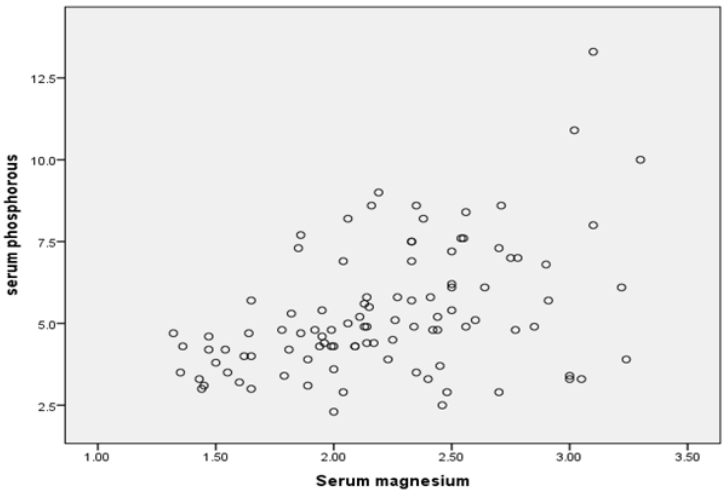

Fig-1: Relationship between phosphorus and magnesium

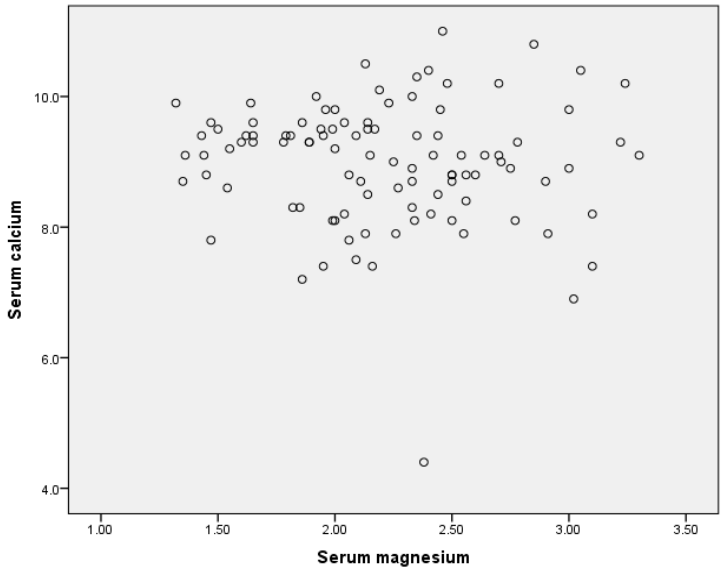

Fig-2: Relationshipbetween calcium andmagnesium

DISCUSSION

Magnesium (Mg) is a nutrient and the fourth most important and abundant cation in the body, after Sodium (Na), Pottasium (K) and Calcium (Ca). It is also the second most important and abundant intracellular cation after Pottasium. It is an essential cation that is needed for a wide variety of physiological activitie6s in the human body. It serves as a cofactor for various physiological processes in the body by activating numerous enzymes most of which are normal neurological function and release of neurotransmitters, heart and lung function and nucleic acid stability. About 1 to 2 % of the total magnesium is stored in extracellular compartment, 67% is stored in the bone whiles 31% is intracellular. Its importance in SCD has been highlighted recently because of its role in RBC dehydration, vaso-occlusion events and endothelial dysfunction red blood cell magnesium (Mg) content modulates K-Cl cotransport activity hence Mg plays a key role in sickle RBC dehydration and its subsequent pathophysiology in SCD. magnesium state in patients with SCD has variety of reports however Normomagnesima is the obtained result in this study (mean 2.4 Std dev = 0.37 mg/dl) which reported by O. O. Oladipo [2] rather than the hypomagnesimia reported by (5,6,7) and (8,9) and Akenami FOT *et al* reported high serum magnesium levels in sicklers compared to controls which can be justified by the chronic haemolytic state of sickle cell disease patients [10].

Calcium homeostasis disturbances has the lion share in the pathogenesis of sickle cell disease and hypocalcaemia has been reported by [2, 4-7, 10-13] which are the same findings of this study that can be due to many reasons, increased calcium magnesium ATPase activity [2], impaired intestinal absorption of calcium along with deficient Vit D synthesis RBCs membrane defect and membrane permeability to calcium aiding in accumulation of calcium in RBCs, all these factors combined lead to low serum calcium in sickle cell disease.

Hyperphosphotaemia has been reported by [2, 4-7, 14] it may be due to increased renal tubular reabsorption of phosphate in sickle cell disease. Positive correlation between phosphate and magnesium found in this study related to the renal management of these ions and the major reason for hyperphosphotaemia may be to the hemolytic stste and nature of sickle cell disease and release of intracellular phosphate.

While Al-harbi et al found decreases serum phosphate due to increased PTH secretion and decreased rubular renal reabsorption of phosphate [15].

The effect of socio-economic state on calcium and magnesium states may be due to nutritional habits and financial problems in handling hospitalization and supplements purchasing.

CONCLUSION

Normomagnesimia hyperphosphatemia and hypocalcaemia is the findings of this study with positive correlation between phosphate and magnesium which need further studies to elaborate this relationship and electrolytes management by physicians is crucial for these patients.

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