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Significant Reduction of Vitamin B12 Levels in Sudanese Sickle Cell Disease Patients

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Abstract

Background: Vitamin B12 (Cobalamin) one of the most important vitamins for its normal functioning to maintain the nerve system and for their role in production of DNA. **Objective:** This study was aimed to measure and assess the serum Cobalamin levels in Sudanese patients with Sickle-cell disease (SCD) and compared with those without Sickle-cell disease. **Materials and Method:** This is a case control study conducted in Sudan during March 2015. A total of 160 volunteers were enrolled in this study. 80 were known Sudanese patients professionally diagnosed with homozygous sickle cell; their age ranged from 6 months to 15 years as patients group. Further 80 normal healthy were as control group; their age and gender were similar to patient group. Serum was prepared from clotted blood samples. The Cobalamin concentrations were measured in both groups of SCD patients and in a normal healthy control group using Enzyme Linked Immune immunosorbent assay method (ELISA), Map lap Plus-Italy. For statistical analysis, the laboratory parameters were compared between the two groups and tested for statistical significance using Statistical package for social scent (SPSS) version 20. **Result:** In this study the mean of serum Cobalamin in the sickle cell patients was statistically significantly lower compared with the normal non-sickle cell disease group with p value = 0.01. **Conclusion:** 7.1% of Sudanese sickle cell disease has a deficient serum Cobalamin (hypocobalaminemia).

Subject Areas

Hematology

Keywords

Vitamin B12, Cobalamin, Sickle Cell Disease, Sudan

1. Introduction

Sickle-cell disease (SCD) is a group of genetically passed down blood disorders. The

most common type is known as sickle-cell anaemia (SCA). It results in an abnormality in the oxygen-carrying protein haemoglobin found in red blood cells. This leads to a rigid, sickle-like shape under certain circumstances. Sickle-cell disease occurs when a person inherits two abnormal copies of the hemoglobin gene, one from each parent. [1]. One of the main problems of sickle-cell disease in children is the development of cerebrovascular disease and cognitive impairment, and the role of blood transfusion and hydroxycarbamide for prevention of these complications is starting to be understood. Recurrent episodes of vaso-occlusion and inflammation result in progressive damage to most organs, including the brain, kidneys, lungs, bones, and cardiovascular system, which become apparent with increasing age [2]. Cobalamin is a water-soluble vitamin that has a key role in the normal functioning of the brain and nervous system, and the formation of red blood cells. It is involved in the metabolism of every cell of the human body, especially affecting DNA synthesis, fatty acid and amino acid metabolism [3]. Vitamin B12 deficiency, also known as hypocobalaminemia, refers to low blood levels of vitamin B12 [4]. A wide variety of signs and symptoms may occur including a decreased ability to think and change in personality such as depression, irritability. Abnormal sensations, changes in reflexes, and poor muscle function can also occur as the most inflammation of the tongue, decreased taste, low red blood cells, reduced heart function, and decreased fertility [5]. In young children symptoms include poor growth, poor development, and difficulties with movement [6]. Without early treatment some of the changes may be permanent [7]. Also manifestations of Cobalamin deficiency include megaloblastic anemia and neuropsychiatric dysfunction. The prevalence of Cobalamin deficiency in the general population is variable depending on the age, population studied and the criteria for diagnosis [8] [9] [10]. The causes of deficiency include Inadequate dietary intake of vitamin B12 [11] [12] [13], Selective impaired absorption of vitamin B12 due to intrinsic factor deficiency, Impaired absorption of vitamin B12 in the setting of a more generalized malabsorption or maldigestion syndrome. Forms of achlorhydria (including that artificially induced by drugs such as proton pump inhibitors and histamine 2 receptor antagonists) can cause B12 malabsorption from foods, since acid is needed to split B12 from food proteins and salivary binding proteins. After surgical removal of the small bowel (for example in Crohn's disease), the patient presents with short bowel syndrome and is unable to absorb vitamin B12. This can be treated with regular injections of vitamin B12 [14]. Long-term use of ranitidine hydrochloride may contribute to deficiency of vitamin B12 [15]. Celiac disease may also cause impaired absorption of this vitamin, though this is due not to loss of intrinsic factor, but rather damage to the small bowel. In case of removal of part of the stomach, procedures such as the adjustable gastric band type do not appear to affect B12 metabolism significantly. Bacterial overgrowth in parts of the small bowel is thought to be able to absorb B12. An example occurs in so-called blind loop syndrome. The diabetes medication metformin such as metformin may interfere with B12 dietary absorption [16] and nitrous oxide misuse [17]. Cobalamin deficiency has often been defined as a

serum Co-balamin concentration of less than 200 pg/mL (148 pmol/L) with limited sensitivity and specificity [18]. Subjects with sickle cell disease (SCD) may be at higher risk of Cobalamin deficiency because of increased demand, inadequate supply, coexisting folate deficiency or malabsorption [19]. Folic acid, one from treatment of sickle disease, if given particularly in large doses, can mask vitamin B12 deficiency by completely correcting haematological abnormalities. In vitamin B12 deficiency, folic acid can produce complete resolution of the characteristic megaloblastic anaemia, while allowing potentially irreversible neurological damage (from continued inactivity of methylmalonyl mutase) to progress. Thus, vitamin B12 status should be determined before folic acid is given as monotherapy [20]. More studies estimate vitamin B12 in patients with severe sickle cell anemia, some from which show significant deficiency in vitamin B12 [21] and other not [22] [23]. One study showed that there is no different of the mean of Cobalamin in patients with sickle disease and those without sickle disease [24]. In the present study, we compared serum Cobalamin concentrations between Sudanese with sickle cell disease SCD and compared with that non sickle cell disease.

2. Materials and Method

This is descriptive case control study done during March 2015 at Alneelain University, faculty of medical laboratory science, Khartoum, Sudan. A total of 160 subject were enrolled in this study 80 (50%) male and (50%) female were known Sudanese patients professionally diagnosed with homozygous sickle cell disease by hemoglobin electrophores is admitted to Jaffer ibnoof teaching hospital, Khartoum, Sudan; their age ranged from 6 month to 15 years as patients group. Further 80 normal healthy as normal control group; their age and gender were harmonized with patients group. The ethical approval was taken from the faculty of medical laboratory science; Alneelain University and the informed consent were taken before samples were collected from all participants in this study. Exclusion criteria of this study were included a previous known diagnosis of Cobalamin deficiency, current treatment with oral, intramuscular or subcutaneous Cobalamin, severe illness, or malnutrition as determined by a body mass index below 18.5. Subjects were recruited as SCD or as controls by medical history. In this study the Cobalamin concentrations were measured in both groups of SCD patients and in a normal healthy control group by using Enzyme Linked Immune immunosorbent assay (ELISA) method, Map lap Plus-Italy. For statistical analysis, the data were analyzed using SPSS version 20. T test was used to compare the serum cobalamin level between the two study group, and the level of significance was set to less than 0.05.

3. Result

The current study revealed that the mean of serum Cobalamin in the sickle cell patients was statistically significantly lower compared with the normal non sickle cell disease group (p value 0.01) (**Table 1**).

The present study showed that 7.1% of Sudanese sickle cell disease patients have low-Cobalamin but no anyone has a neurological manifestation.

Table 1. Correlation of serum Cobalamin in SCD patients and normal control group.

Parameter	Mean ± SD	P value
Cobalamin pmol/L SCD patient 80	348.9 ± 12.5	0.01
Normal control 80	629.9 ± 37.1	

Based on the gender this study showed that there is no any statistically significantly different between male and female in SCD deficient serum Cobalamin patient with (p value 0.62) (Table 2).

4. Discussion

Sickle cell anemia is an inherited blood disorder due to substitution of thyamine by adenine in glutamic acid which in turn results in the substitution of valine to glutamic acid in position number six in Beta globin chain, this will cause deoxygenated sickle haemoglobin to form polymers that ultimately destroy red blood cells [25]. In Sudan, sickle cell anaemia is the one of the major types of anaemia especially in western Sudan where the sickle cell gene is more frequent [26]. Vitamin B12 (Cobalamin) is a water-soluble vitamin that is crucial to normal neurologic function, red blood cell production, and DNA synthesis. It's very essential for three enzymatic processes: the conversion of homocysteine to methionine; the conversion of methylmalonic acid to succinyl coenzyme A; and the conversion of 5-methyltetrahydrofolate to tetrahydrofolate, a process necessary for DNA synthesis and red blood cell production [27]. The present study showed that the serum cobalamin is significantly lower in SCD patients compared with those normal non sickle cell disease groups with (p value 0.01). These findings are in agreement with Osifo BO *et al.* in 1983 and 1984 respectively [19] [28]. The interesting findings of this study were advocate the previously data cited by Al-Momen *et al.* in 1995 who concluded that in Thirty-seven of the 85 patients (43.5%) had serum vitamin B12 levels below normal values (mean 84.3 ± 28.7, range 7 - 145 pmol·L^{-1}) [21]. Our findings were consistent with Kamineni *et al.* in 2006 who conclude that 18.1% of African American with SCD had serum cobalamin defiance's [29]. The interesting finding of this study also in concordance with O. I. Ajayi *et al.* who published in 2013 that Cobalamin deficiency was present in 6.9% of SCD patients [30]. Inadequate dietary intake or increased the demand of cobalamin may be lead to the cobalamin deficiency in sickle cell patients; however others factor also might be has a role in cobalamin deficiency such as decreased cobalamin production by stomach or decreased absorption from the ileum due to the crisis of sickle cell disease [31] [32]. Based on the gender this study showed that no any statistically significantly different in SCD patient deficient serum Cobalamin (p value 0.62). This finding was in concordance with study published in 2013 by O. I. Ajayi *et al.* who reported that there is no significant difference in median of (interquartile range) cobalamin concentration for all male and female subjects [30].

In this study there are two limitations, the sample size is small and narrowing the duration of the study.

Table 2. Correlation of serum Cobalamin in SCD patients according to the gender.

Parameter	SCD patient gender	Mean ± SD	P value
Cobalamin pmol/L	Male Female	372.1 ± 32.5 327.9 ± 78.1	0.62

5. Conclusion

The present study concluded that the 7.1% of Sudanese Sickle Cell Disease patients had lower serum cobalamin concentrations in comparison with non-Sickle Cell Disease patients. Moreover, the main cause of diminished serum cobalamin concentrations in SCD remains unclear.

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