

Diverse Clinical manifestations in Sickle Cell Anemia: study in District Amravati, MS India.

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Abstract

Background of Study: Sickle cell anemic patients show diverse clinical symptoms with varied complications influenced by genetic, environmental and socioeconomic factors. Sickle cell anemia is prevalent in district Amravati, MS, India.

In the present study, some symptomatic presentation of sickle cell anemic patients district Amravati, MS were studied in order to know pathophysiological complications going on in sickle cell anemia. In total, 67 sickle cell anemic patients were investigated. Information regarding some clinical symptoms was gathered from the patients and filled in the data sheets. It was observed that 77.77% patients frequently suffer from fever, 85.18% patients suffers from joint and chest pain, 81.48% experience recurrent tiredness, 85.18% experience shortness of breath, swelling of abdomen was found in 29.62% patients, 48.14% experience unusual headache. From the study of data sheet it was found that 29.62% sickle cell patients suffer from jaundice. In 51.85% patients, growth was delayed. Recurrent occurrence of pain episodes was observed in 55.55% patients. Thus sickle cell anemia in district Amravati shows variable clinical manifestations in variable percentage. Thus it is proposed to manage the disease properly as soon as it is detected.

Keywords: Sickle cell anemia; Clinical features; Amravati; Symptoms

Introduction

Sickle cell anemia is a genetic disorder, caused by mutation in the hemoglobin coding gene. Sickle cell anemia is caused due to substitution of valine for glutamic acid at sixth position of beta globin of hemoglobin [1,2]. This mutated and defective hemoglobin is less soluble and after deoxygenation undergo polymerization causing distortion of shape of (RBCs) Red Blood Cells [3]. The pattern of inheritance of this disorder is recessive. Sickle cell anemia is distributed widely in Africa, Asia and Middle East, the parts of the world where malaria is endemic. Sickle cell anemia carrier (trait) are asymptomatic and generally are not aware of the diseased gene they carry [4].

Sickle cell anemia, or homozygous sickle cell disease, affects about 250,000 children worldwide every year; most of them die before they attain age of two years due to multiple strokes [5,6]. Life expectancy of sickle cell patients is less. Sickle cell anemic patients die due to complications like pain, acute chest syndrome and stroke, pulmonary hypertension, renal failure, infections and unknown etiology [7].

Sickled RBCs cause severe vaso-occlusive phenomena. The severity of the complications of this disease varies from patient to patient such as severe obstruction of blood vessels which prevents supply of oxygen to downstream tissues, hemolytic anemia [8]. In sickle cell anemia children and adults experience painful vaso-occlusive events which are generally dealt with aggressive hydration, anti-inflammatory and narcotic analgesics. Patients are treated with drugs like hydroxyurea to manage the complications. This drug is able to modify pathogenesis of the disorder. In the developed countries, the mortality rate of sickle cell anemic children is 0.5 to 1.0 per 100,000 but this rate is high in developing countries which are recorded to be 15.5 per 1000 children [9]. Sickle cell anemic (SCA) patients need to have regular blood transfusions and may have high risk for infections of hepatitis and others. Recurrent blood transfusions lead to cause high level of iron in serum. There could be damage to the organ such as endocrine organs, hepatic parenchyma cardiac myocytes by ROS-mediated lipid peroxidation due to accumulation of iron [10,11].

Sickle cell anemic patients present heterogeneous clinical symptoms with acute and chronic complications which could be modified by genetic, environmental and socioeconomic factors [1,2]. Sickle cell anemia affects many organ systems [12-14]. In the present study symptomatic features in sickle cell anemic patients are tried to be explored out in order to observe pathophysiology and complications in such patients.

Materials and Methods

Study area and population

The study population consisted of 67 randomized subjects with Sickle cell anemia from district Amravati, Maharashtra, India. The mean age of the selected patients was 20.48. This study was approved by Institutional Human Ethics Committee. Written consent from each participant was taken.

Study of some clinical parameters

Patient's health history was taken to understand the various complications going on in the body of the patients. Data sheet was filled on the basis of questionnaire answered by patients. Socioeconomic status of the patients was noted. Pedigree was developed on the basis of family history given by the participants. For few parameters such as pulse rate, delayed growth, fever etc patients were examined.

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Result and Discussion

Study of clinical parameters

Clinical parameters like recurrent fever, joint and chest pain, recurrent tiredness, shortness of breath, swelling of abdomen, unusual headache, jaundice, delayed growth, recurrent occurrence of pain episodes, yellow eyes etc., were observed in sickle cell anemia. It was observed that 77.77% patients suffer from fever, 85.18% patients suffers from joint and chest pain, 81.48% experience recurrent tiredness, 85.18% experience shortness of breath, swelling of abdomen was found in 29.62% patients, 48.14% patients experienced unusual headache. In 51.85% patients, growth was delayed. Recurrent occurrence of pain episodes was observed in 55.55 patients. Some clinical parameters of sickle cell anemic patients are shown in figure 1. These complications may be due to hypoxic condition of SCA.

Clinical manifestation in Sickle cell disease varied and it is not well understood and explained by single mutation. Variability regarding symptoms is observed in the frequency and intensity of painful vaso-occlusive crises and also in the degree of organ dysfunction. Pathophysiology appears because of combined effects of hemolysis and vaso-occlusion. Hemoglobin picks up and releases oxygen repeatedly and undergoes polymerization and depolymerization leading to hemolysis. As a result free hemoglobin uses significant amount of nitric oxide (NO) [15] that results in abnormal regulation in the vascular homeostasis [15-17].

In SCA, important cause of morbidity and mortality is ACS (Acute Chest Syndrome) which found to occur in 45% of patients and recurred in 80% afflicted patients [18-20]. The chief pathologic incidence in ACS is vaso-occlusion, the etiology of which is perhaps multifactorial. Abnormal adherence of sickle RBCs, WBCs and/or platelets to the vascular endothelium is one of the phenomena causing vaso-occlusion. The factors leading to cellular adhesion and vascular damage are not completely understood. Areas of ischemia/reperfusion build up during local vaso-occlusion. Oxidizing molecules for example O_2^- , H_2O_2 , $\bullet OH$ radical and ONOO- are produced in large number during periods of reperfusion [21]. These compounds have ability to activate second messengers that causes up regulation of endothelial adhesion molecules. Molecules such as vascular cell adhesion molecule (VCAM)-1 and intercellular adhesion molecule (ICAM)-1, facilitate binding of sickle RBCs and WBCs to the vascular endothelium and thus may be responsible for vaso-occlusion [22-25]. Further, oxygen-related species directly can damage endothelium by per-oxidation of the lipid membrane and/or DNA fragmentation, causing cellular

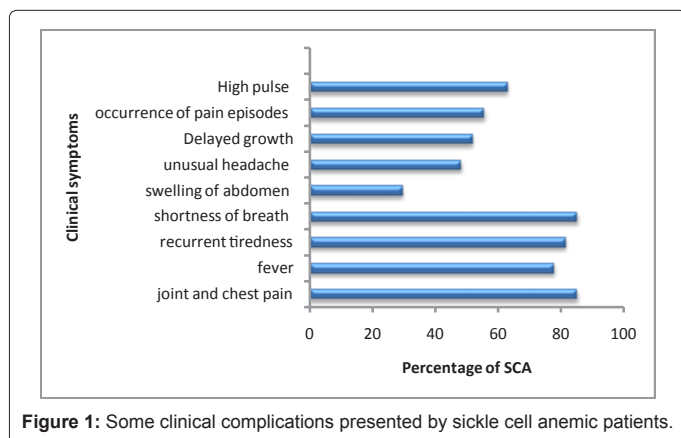


Figure 1: Some clinical complications presented by sickle cell anemic patients.

apoptosis. SCD patients are subjected to great oxidative stress, mainly during vaso-occlusive crises (VOCs) and ACS [26]. It was stated that transgenic sickle cell mice had higher levels of oxidative stress markers, like ethane excretion and $\bullet OH$ radical generation. During hypoxia, sickle cell mouse showed evidences of ischemia/reperfusion injury. This is represented by increased levels of oxygen radical and leukocyte adherence and emigration [23,26]. Within the renal tubular epithelium ONOO- are formed with associated cellular apoptosis [27]. Risk of stroke to sickle cell anemic child is 221-fold higher than a healthy child [28]. Abnormal imaging is observed in sickle cell anemic patients. 46% sickle cell patients suffered from brain injury visible by MRI [29]. Niebanck et al. [30] reported cases of headache in sickle cell anemic patients. Many factors may involve in the symptoms of headache in sickle cell anemia and linked to migraine, VOE, bone marrow hyperplasia, OSA, or cerebral vessel stenosis [30].

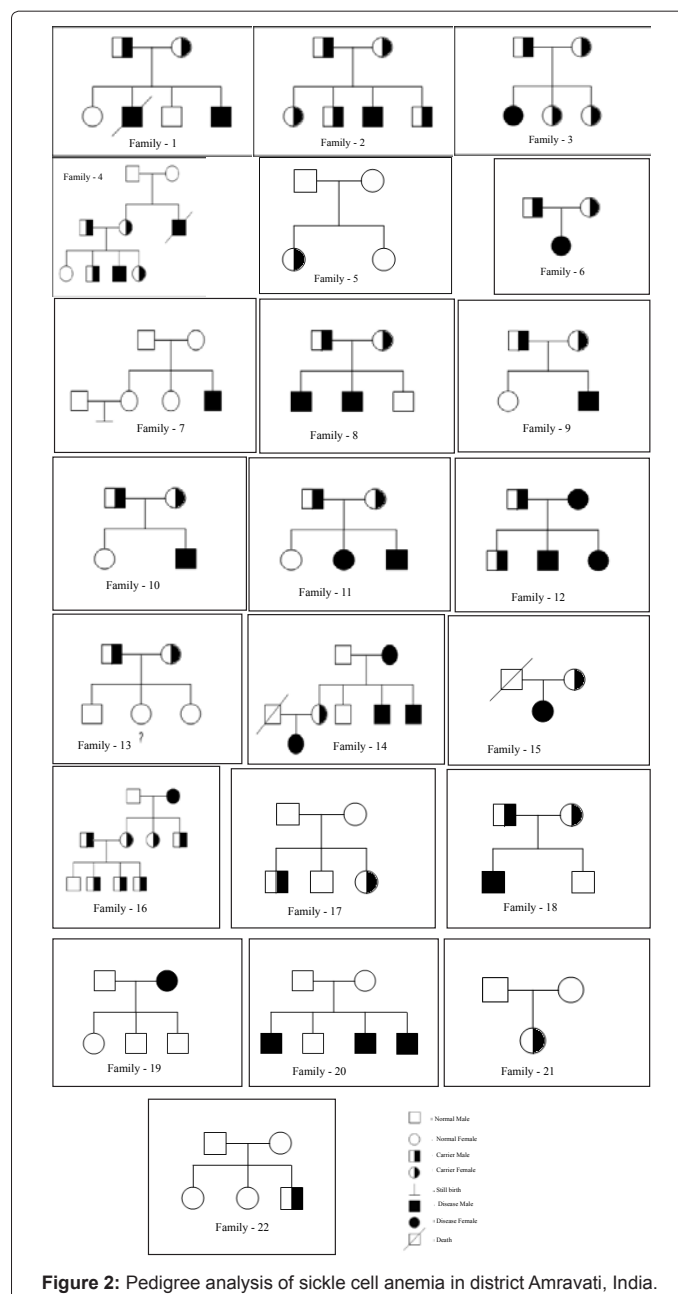


Figure 2: Pedigree analysis of sickle cell anemia in district Amravati, India.

In sickle cell anemia, tissue ischemia resulting in acute and multi-organ dysfunction is caused by intermittent episodes of vascular occlusion [31] which is characterized by chronic inflammation and ischemia-reperfusion injury [23,26,32]. Neutrophils have significant function in tissue damage [33]. Adhesion of lymphocytes and monocytes to the endothelium sickled induced by red blood cells may add to the pathogenesis of vascular occlusion [34]. The observations in the present study are in support of above mentioned studies.

Pedigree analysis of sickle cell anemia in district Amravati

It was found that in 12 families both the parents were carrier of the sickle cell gene. In 2 families death occurred due to sickle cell disorder. In 9 families sickle cell was absent in parents but appear in children due to mutation. In some families sickle cell anemia exist from many generations. In some families death of the family members had occurred due to unknown diseases. In most of the families both the parents are carrier of sickle cell anemia. This may be due to marriages in close relatives. Pedigree of some sickle cell anemic patients are expressed in the figure 2.

Conclusion and Recommendations

Thus it could be concluded that the sickle cell anemic patients of district Amravati are under the great stress of the disease and should be treated and educated to manage the disease. Thus it is proposed to provide proper and immediate facilities to sickle cell patients to manage the complications.

Counseling and support can act as a potential factor to spread awareness in affected population. Health care workers who provide counseling should be properly educated to increase awareness about the disorders and, hopefully, help reduce the stigma attached to the disorders. There is a need to carry out more meticulous and larger-scale study regarding all aspects of sickle cell anemia.

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