INTRODUCTION

Sickle cell disease refer to a genetic blood disorder characterized by a hemoglobin variant called HbS (John et al 2010) and clinically characterized by chronic hemolysis, intermittent vaso-occlusive event and increased susceptibility to infection (Nur et al 2004).

In India, haemoglobinopathies, especially sickle hemoglobin are the commonest genetic disorders in the tribal belt of Central and Southern India. Madhya Pradesh and Chhattisgarh harbours the largest tribal population in India, which is about one fourth of the total tribal population of the country. These tribal groups are characterized by their unique socio-cultural and religious practices and follow strict endogamous practice. These tribal populations are stated to be aboriginal population of India. Sickle haemoglobin was first discovered from a tribal population of Nilgiri Hills of South India in 1952. Later, it was reported from the tribal population of Central India i.e. Madhya Pradesh and Chhattisgarh and its surrounding areas falling in the states of Rajasthan, Gujarat, Maharashtra, Andhra Pradesh and Orissa. The prevalence of sickle haemoglobin from various parts of Madhya Pradesh and Chhattisgarh varied from 15 to 30 percent. It was found that the non-tribal people of HbS belt especially Scheduled Castes and other Backward class communities have sickle haemoglobin in similar proportion as that of tribals of the area. As per census 2001, the total Scheduled tribe and
Scheduled Caste population of Madhya Pradesh is over 120 lacs and 91 lacs respectively which is about 20% and 15% of the total population of the state. Out of 45 districts of the state, 27 districts fall under the sickle cell gene belt. These districts are Jhabua, Barwani, Dindori, Mandla, Dhar, Shahdol, Umaria, Betul, Seoni, West Nimar, Chhindwara, Harda, East Nimar, Jabalpur, Ratlam, Dewas, Katni, Damoh, Hoshangabad, Sagar, Satna, Balaghat, Ujjain, Indore, Mandsaur, Neemuch and Narsimhpur. There are 12 districts in Chhattisgarh which fall in main sickle cell belt of the state. These districts are: Dantewada, Bastar, Kanker, Korba, Mahasumund, Rajnandgaon, Dhamtari, Kawardha, Bilaspur, Durg, Raipur and Jangir- Champa (Gupta 2004). Sickle cell trait a condition in which a person has one abnormal allele of the hemoglobin beta gene (heterozygous) but does not display the severe symptoms of sickle cell anemia.

Sickle cell anemia results from a point mutation in the genetic code adenine to thymine (GAG to GTG) such that glutamic acid is replaced by valine at 6th position of β-globin chain of hemoglobin (Hb). This substitution transforms normal adult hemoglobin (HbA) into sickle hemoglobin (HbS), change the net charge of hemoglobin, oxygen affinity and three dimensional structure of hemoglobin thus rendering it as unstable hemoglobin. In a low oxygen tension environment, Hb S in Sickle erythrocyte polymerizes (or aggregates) reversibly in to paracrystalline polymer (also called gels, liquid
crystal, or tactoids) inside the cell, the replaced valine can bind to a complementary hydrophobic site on beta subunit of another hemoglobin tetramer in a polymerization process that leads to the sickling of the red blood cells (RBCs). Polymerization of deoxygenated sickle hemoglobin (HbS) tetramers is central to the process of vasoocclusion (Bandeira et al 2004, Cançado et al 2002). The polymers make the erythrocyte rigid, distort its shape, and cause structural damage in the red-cell membrane, all of which alter the rheologic properties of cell, impair blood flow through the microvasculature and leads to hemolysis. It is the presence of polymer that causes the reversible, oxygen-linked changes in the rheological properties of the sickle erythrocyte that characterize the disease and vasoocclusive episodes (Cançado et al 2007). The main clinical manifestations of SCA are infections, acute chest syndrome (ACS), splenic sequestration, pain crises, renal disorders, cardiac disorders (heart failure), osteoarticular disorders (such as dactylitis or hand-foot syndrome), neurological disorders (stroke), ocular disorders, sores on the lower limbs and priapism (Florentino et al 2011). Chronic activation and damage of endothelial cells by sickle red blood cells, heme, polymorphonuclear neutrophils (PMNs) and inflammatory mediators contributes to progressive microvesicular damage in all organs (Frenette et al 2002, Van Beers et al 2008, Hebbel et al 2009). Sickle cell spontaneously generates approximately two times more amount of reactive
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oxygen species. A high production rate of reactive oxygen species in Sickle cell disease caused by several factors such as chronic inflammation, intravascular hemolysis, ischemia reperfusion injury and decreased level of antioxidants (Fasola et al. 2007).

In Sickle cell disease oxidative stress is increased and might play a significant role in the pathophysiology of SCD related microvesicular dysfunction, vaso-occlusion and development of organ damage (Nur et al. 2004). Reactive oxygen species are produced as the result of intracellular catabolism that requires oxygen as a terminal acceptor (oxidants), under normal condition there is a balance between the ROS and the defense system of antioxidants (superoxide dismutase, Catalase, glutathione peroxides, ascorbate, flavonoid, carotonoid,) thereby preventing or limiting oxidative damage (Hundekar, et al. 2010).

Hence oxidative stress is a result of imbalance between oxidants and antioxidants in favor of the former. Increased production of oxidants and decrease availability of antioxidants trigger a cascade of oxidative reactions damaging lipids, proteins, and DNA ultimately leading to cell death.

Recently, the pro-oxidants and anti-oxidant status in patients with sickle cell anemia were assessed. The available reports suggested that sickle cell erythrocytes are susceptible to endogenous free radical mediated oxidant damage, there remains some discrepancy in the status of antioxidant enzymes
and antioxidant vitamins in these patients. In sickle cell disorder the Hemoglobin stabilizing capacity is also impaired making the RBC even more vulnerable to oxidative stress. This may overwhelm the antioxidant defense system (Nagababu et al 2008). Therefore, SCD is characterized by lifelong continuous oxidative stress (Nur et al 2004).

Antioxidants can be broadly classified by their mechanism of action as primary antioxidants, which break the chain reaction of oxidation by hydrogen donation and generation of more stable radicals. The endogenous antioxidant like uric acid, bilirubin, albumin, Glutathione, xanthine oxidase, SOD, GPx, GR, Catalase, which protect the formation of TBARS. Secondary antioxidants, which slow the oxidation rate by several mechanisms, including chelation of metals, regeneration of primary antioxidants, decomposition of hydroperoxides, and scavenging of oxygen, among others. These substances may occur naturally in foods, such as tocopherols and ascorbic acid. The exogenous antioxidants are mainly vitamins which play an essential role in antioxidant defense system (Nagababu et al 2008, Akohoue et al 2007). Vitamin E & C have protective role against membrane attack and are chain breaking antioxidants, while carotenoids act at a low oxygen tension. Hematological profile of SCD is also extremely variable.

Since the various membrane abnormalities of sickle erythrocytes might result from excessive accumulation of oxidant damage and decrease activity
of antioxidant defense in sickle cell patients, hence we planned our study to know the status of endogenous and exogenous antioxidants in Sickle cell disorder (Heterozygous HbAS and Homozygous HbSS).