Sickle cell disease (SCD) is a chronic inflammatory disease in which vaso-occlusive crisis and endothelial dysfunction are present (1). Sickling and hemolysis disturb microcirculation with resultant oxidative and inflammatory stress in SCD (2). The aims of the study were to investigate the serum and salivary total antioxidant and oxidant status and oxidative stress index levels in children with SCD and to compare them with their healthy counterparts. Forty-three children with SCD and 43 healthy children were included in the study. The blood and saliva samples were collected. Total oxidant status (TOS) and total antioxidant status (TAOC) levels in serum and saliva were measured by an automatic colorimetric method. The oxidative stress index (OSI) a novel biomarker for oxidative stress was calculated as \[ \text{TOS} / (\text{TAOC} \times 100) \]. The serum TOS and OSI level was increased in children with SCD whereas serum TAOC levels significantly decreased in comparison with the controls \((p<0.05)\). While the serum OSI values of the SCD patients were significantly higher, there was no statistically significant difference between the groups regarding salivary OSI values. Besides, serum TAOC level positively correlated with salivary TAOC level and negatively correlated with serum and salivary OSI levels. In conclusion, sickle cell disease increases oxidative stress in blood but it has no effect on oxidative stress in saliva. The antioxidant systems in saliva may be effective on elimination of oxidative stress in the mouth.