VII. ABSTRACT

Case reports and limited case series of Sickle cell disease (SCD) in Sri Lanka have been reported since 1962. Yet, no attempt has been made up till now to undertake a comprehensive genotypic-phenotypic analysis of this "rare" group of patients in Sri Lanka. The national thalassaemia prevention programme in Sri Lanka is currently using Full Blood Count with (FBC) red cell indices as the technique for haemoglobionopathy screening. This approach is likely to miss sickle haemoglobin (Hb S) carriers. Present study intends to describe the clinical picture of SCD in Sri Lanka, analyze its molecular basis, including the effects of genetic modifiers on the phenotype and describe the screening utility of sickling test in identifying sickle carriers among a relatively high-risk population in Hambantota district of Sri Lanka. All accessible sickle patients, totaling 60, including, 51 Sickle β-thalassaemia (SBT) and 9 homozygous sickle patients (Hb SS) were enrolled from seven thalassaemia treatment centres. All the patients were clinically evaluated and details were recorded. β-globin haplotypes, β - thalassaemia mutations, common α+ thalassaemia gene deletions and 5 known Fetal haemoglobin (Hb F) modifiers (rs6545816, rs1427407, rs66650371, rs9402686, rs7482144) were assessed. Geographically, two prominent patient clusters were identified and the distribution of Hb S in the island contrasted with that of the other haemoglobinopathies. 3/ 9 Hb SS and 3/ 51 SBT patients were receiving regular transfusion. Joint pain was the commonest clinical presentation among all SCD patients (n=39, 65.0%). Dactylitis was significantly more common in Hb SS patients compared with the SBT group (p 0.034). Two genetic backgrounds Hb S mutation were identified and confirmed namely, Arab Indian and Benin. Among the Hb F regulators rs1427407 G>T seemed to be the most prominent modifier, with a significant association with Hb F levels (p 0.04). Sickling test demonstrated 100 % sensitivity and 100 % specificity. FBC by itself was unreliable to detect Hb S but if combined with sickling test was able to pick up Hb S in addition to most other haemoglobinopathies.

Keywords: Sickle cell, Sri Lanka, Clinical, Genetic, Sickling test