Introduction: Sickle cell disease (SCD) is one of the commonest genetic blood disorders caused by a point mutation in the β-globin gene which affects the hemoglobin configuration. The sickled erythrocytes predispose to occlusion of microvascular circulation resulting in painful crisis and multi-organ complications causing high morbidity and mortality rates. There is a huge variation in the phenotypic expression of SCD clinically due to the influence of multiple genetic and environmental factors. The study aims to characterize whole blood gene expression profile in Bahraini patients with SCD determining the differentially expressed genes in steady-state and during vaso-occlusive crises (VOC) compared to healthy control.

Methods: Twenty sickle cell disease patients (10 subjects in steady-state and 10 subjects in VOC) and eight healthy volunteers were enrolled. The participants underwent clinical and laboratory assessment. Microarray technology was used to assess the gene expression levels, where the result of two selected significantly dysregulated genes were further confirmed using real-time polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA).

Results: The PLSCR4 showed almost six-folds up-regulation in microarray, four-folds up-regulation in RT-PCR and an average protein concentration of 0.856 ng/ml in ELISA in SCD patients in VOC compared to SCD patient in steady-state ($p<0.01$). Whereas the RUNX3 was four-folds down-regulated in microarray, three-folds down-regulated in RT-PCR and an average protein concentration of 457.93 pg/ml in ELISA in SCD patients in VOC compared to SCD patient in steady-state ($p<0.01$). Evaluation of the differentially regulated genes in relation to the disease severity revealed two significant down-regulated genes PI3 and KCNJ15 in microarray in SCD patients with moderate severity compared to mild severity ($p<0.01$), requiring further validations.

Conclusion: PLSCR4 and RUNX3 genes were associated with hemolysis and inflammation and may serve as biomarkers for the development of VOC and targeted therapy. Future large-scale validation and proteomic analysis are recommended.