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ORAL ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Enhanced Expression of Heme Oxygenase-1 (HO-1) Among Children with Sickle Cell Disease: Results of the Sickle Cell Disease Genomics of Africa (SickleGenAfrica) Study

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Sickle cell disease (SCD) is characterized by intense and chronic intravascular hemolysis that generates multiple erythroid danger associated molecular pattern (eDAMP) molecules in the extracellular space. Extracellular heme is a prototypical eDAMP that causes tissue injury and is associated with multiple complications of SCD including vaso-occlusive crisis, acute kidney injury and acute chest syndrome (ACS). Heme-oxygenase-1 (HO-1) is the rate-limiting enzyme that degrades heme to neutralize its deleterious effects on organ function. Raised extracellular heme is associated with 2.5 higher odds ratio of developing ACS, while HO-1 gene promoter allelic variants that drive robust HO-1 expression are associated with lower ACS-related hospitalization rates among children. Young transgenic homozygous SCD (SS) mice have higher survival rates than adult SS mice from a heme-induced ACS model due to their ability to rapidly degrade excess extracellular heme. While these data suggest that HO-1 may be involved in the well-established higher ACS survival among children, and potentially other ameliorating features of SCD in early development, no study had previously studied HO-1 expression in this patient population. The SickleGenAfrica Network enrolled over 2,000 children and adults with SCD from three sites in Ghana from 2018 to 2021, with consent for use of samples in future studies. The SCD status of participants was confirmed using automated capillary hemoglobin electrophoresis, and serum HO-1 level measured using ELISA. Patients were grouped based on age, using five-year intervals. The median HO-1 level comparisons across groups were performed using the pairwise Wilcoxon test, with Bonferroni correction for multiple comparisons. All analyses were performed using R version 4.3.1. The study included 1,971 patients with SCD, with a median age of 13 years (range 0 - 78), of which 1,067 participants (55%) were female. The majority of patients (1149 ;58%) had HbSS, 589 (30%) had HbSC, 171 (9%) sickle-hereditary persistence of fetal hemoglobin, and 62 (3%) HbS-beta(+). We observed an approximately 3-fold drop-off in median HO-1 levels between the 11-15-year-old (73.9 ng/ml) and 16-20-year-old (25.1 ng/ml) age groups (adj. $p<0.001$). Furthermore, males had higher average HO-1 levels (85.5 ng/ml) relative to females (63.1 ng/ml) ($p<0.001$). Our data show for the first time that children with SCD have significantly elevated HO-1 levels relative to adults, with a sharp decline in HO-1 levels during adolescence. HO-1 may serve as a protective SCD factor, contributing to enhanced ACS survival rates in children versus adults. To the best of our knowledge, this is the first study of HO-1 levels in patients with SCD at different ages. Our future work aims to establish whether baseline blood HO-1 levels can predict ACS incidence and severity, in addition to further investigating genetic and epigenetic mechanisms controlling HO-1 expression.

Disclosures No relevant conflicts of interest to declare.

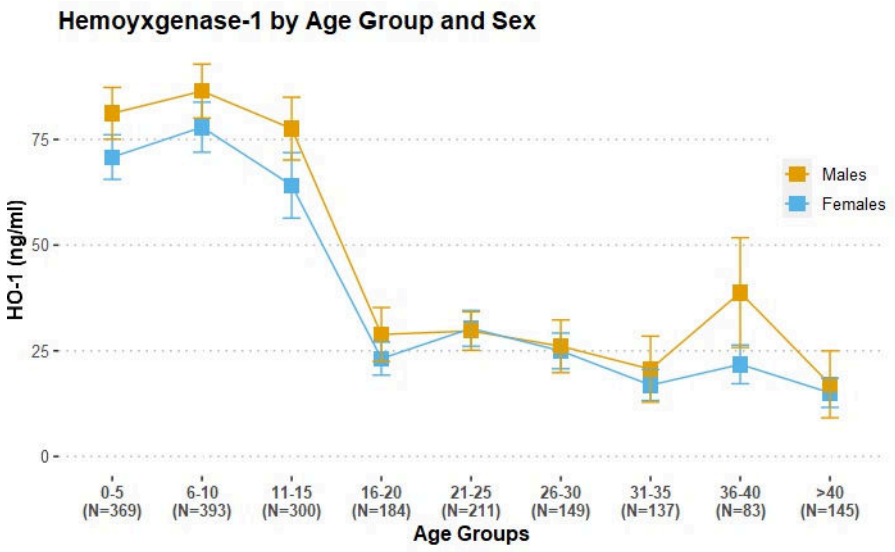

Figure 1

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