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AN UNEXPECTED HIGH PREVALENCE OF INTRONIC RET PROMOTER VARIATIONS IN BLACK AFRICAN HIRSCHSPRUNG DISEASE PATIENTS

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Introduction: The RET promoter region contains common ancestral RET gene variations which regulate transcription and are thought to be causative by increasing the Hirschsprung (HSCR) susceptibility risk. Hirschsprungs disease is not uncommon in African patients but Inter-ethnic variation of the predisposing intronic *RET* susceptibility alleles exists and is reported to be virtually absent in Africa (< 5%). This study evaluates the *RET* promoter region variations in Black African patients with HSCR and the as compared to other ethnic groups

Patients and methods: Following ethical approval, DNA was extracted from whole blood samples of comparative HSCR patients in 3 main ethnic groups. PCR products were screened for genetic variation of the *RET* by direct sequencing analysis. Black African HSCR patients(n=14)] were compared with a comparative sample of 20 HSCR patients from the other 2 main ethnic groups [viz: Caucasian (10), mixed (Coloured) (10)].

Results: HSCR patients were clinically comparative in terms of aganglionic length and syndromic expression.

Extracellular RET variations in Black HSCR patients were not dissimilar from those seen in other Hirschsprungs patients. 13 detected RET promoter variants were many of which were common to those found in other population groups

However, against expectations 79% of Black patients had RET promoter variations which included the intronic variant SNP2 (rs 2435357) in a 71%of Black HSCR patients (88% homozygous) and SNP1 (rs2506004) in 78% (70% homozygous).

However, 3 patients had a combination of different RET promoter variants and 4 of the 13 (31%) were homozygous variations were specific to the Black African population .

Conclusions: Specific disease-related *RET* variations were identified in the promoter region in an unexpectedly high proportion of Black African patients in a South African sample. This challenges previously held concepts of a low incidence and adds to our understanding in Hirschsprung pathogenesis.