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RESEARCH TOPIC:

Endocrine Profiling in Black South African Fanconi Anaemia Patients, Homozygous for a FANCG Founder Mutation.

RESEARCH PROPOSAL ABSTRACT

Fanconi anaemia (FA) is an uncommon, phenotypically diverse hereditary condition associated with bone marrow failure, multiple congenital abnormalities and an increased susceptibility to malignancy. Although it is thought to be a rare genetic disorder (estimated prevalence 1-5 per million), the prevalence in certain South African population groups has been found to be much higher with a proposed birth incidence of 1 in 40 000 in the Black South African population. The proposed reason for this higher incidence is a genetic founder mutation in the FANCG gene. Based on this data Black South African patients with FA thus represent a unique patient cohort from a genetic homogeneity perspective.

In addition to the classic features of FA (bone marrow failure, physical abnormalities and cancer risks) endocrine dysfunction, albeit a less recognised manifestation of FA, is also a significant contributor to morbidity and impaired quality of life for patients with FA. Numerous international research studies have documented in detail the major endocrine abnormalities (including short stature and/or growth hormone deficiency, gonadal dysfunction, hypothyroidism and abnormal glucose and insulin metabolism) in patients with FA and have highlighted the widespread nature of these irregularities. These studies have assessed individuals with FA of various genotype to give general frequencies of these disorders. Very little genotype-specific information has yet been documented in the literature.

To date there is no previous comprehensive study that has evaluated the endocrine abnormalities in Black South African patients with FA. As such there are currently no standard protocols for the investigation and management of endocrine abnormalities in this patient group. The Black South African population is a unique cohort from a genetic perspective. Such a study would allow for further genotype-phenotype correlations and will hopefully show the benefit of endocrine screening to guide standards of care for these patients in South Africa. By means of a cross-sectional, descriptive study of between approximately 25 – 30 patients, the aim of the proposed research report is to evaluate the need for routine screening of endocrine status in Black South African patients with FA based on the frequency of the endocrine disorders. The objectives of this research report are firstly to evaluate thyroid function, glucose and insulin metabolism, growth hormone (GH) status, growth and pubertal stage in Black South African patients with FA; and secondly to determine the frequency and nature of endocrine abnormalities in Black South African patients with FA; specifically those homozygous for the FANCG founder mutation.