The genomic landscape of aplastic anaemia, myelodysplastic neoplasms, and myelodysplastic/myeloproliferative neoplasms in a South African setting

Dr Claudia Ferreira Nunes

Student number: 351286

A research report (in the format of a "submissible" paper) submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Haematological Pathology.

Johannesburg, 6 February 2024

ABSTRACT

Background

Aplastic anaemia (AA), Myelodysplastic neoplasms (MDS) and Myelodysplastic/Myeloproliferative neoplasms (MDS/MPN) are genetically related clonal myeloid neoplasms which carry a risk of evolution to acute myeloid leukaemia.

Aim

Our study aimed to investigate the molecular-genetic profile of these disorders in South Africa.

Setting

The South African public and private sector.

Methods

Next generation sequencing (NGS) results from confirmed AA, MDS and MDS/MPN referred for testing at Charlotte Maxeke Johannesburg Academic Hospital and Oncolab Diagnostics, South Africa, between January 2019 and December 2022 were retrospectively reviewed. The laboratory information system was used to retrieve clinical and laboratory data.

Results

One hundred and forty cases were tested by NGS with an equal number from both the public and private sector and included 13 AA, 25 MDS/MPN and 102 MDS cases. Variants in genes involved in epigenetic regulation were most prevalent in MDS, with *ASXL1* and *RUNX1* mutations more common in high-risk MDS. High risk MDS was significantly more common in the public sector (69% versus 21% in the private sector) and presented at a younger age ($p < 0.0001$) with lower haemoglobin levels ($p < 0.0010$). Non-severe aplastic anaemia predominated (54%) and implicated gene variants were typically in epigenetic modifier and transcription regulation functional groups.

Conclusion:

In South Africa DNA variants in MDS more frequently involve genes in epigenetic pathways in contrast to RNA splicing pathways seen internationally. Higher risk disease was prevalent in public sector patients, which was unaccounted for in the variant profile, suggesting that other factors may be implicated.

Contribution:

This provides the first nationwide description of the genetic landscape of AA, MDS and MDS/MPN in South Africa.

Keywords:

Aplastic anaemia, Myelodysplastic neoplasm, Myelodysplastic/Myeloproliferative neoplasm, South Africa, molecular, next generation sequencing