

PREVALENCE AND CLINICOPATHOLOGICAL CHARACTERISTICS OF MICROSATELLITE INSTABILITY IN GASTRIC CARCINOMA: INSIGHTS FROM A SOUTH AFRICAN COHORT

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Background: Gastric carcinoma (GC) is a biologically heterogeneous malignancy with diverse molecular profiles. The identification of microsatellite instability (MSI), driven by deficient DNA mismatch repair (dMMR), has significantly advanced GC classification. MSI-high (MSI-H) tumours are highly immunogenic and predictive of response to PD-1 blockade therapy. However, data on MSI in sub-Saharan African populations remain limited. This study aimed to determine the prevalence and clinicopathological characteristics of MSI in a South African cohort and assess the relevance of routine molecular stratification.

Methods: A retrospective analysis was performed on formalin-fixed paraffin-embedded tissue from 64 patients diagnosed with gastric adenocarcinoma between 01 January 2018 and 31 December 2022 at a tertiary laboratory in Pretoria. MSI status was assessed using a mononucleotide pentaplex PCR assay (NR-21, NR-24, NR-27, BAT-25, BAT-26). Tumours were classified as MSI-high (≥ 2 markers), MSI-low (1 marker), or microsatellite stable (MSS). Immunohistochemistry for mismatch repair proteins (MLH1, PMS2, MSH2, MSH6) was conducted on MSI-H cases.

Results: MSI was identified in 21.9% (n=14) of cases. Of these genomically unstable tumours, 42.9% were classified as MSI-H and 57.1% as MSI-L. MSI cases demonstrated a male predominance and a younger mean age of onset (59.3 years). Immunohistochemistry revealed predominant MLH1/PMS2 loss. No significant association was found between MSI status and clinicopathological features such as Lauren classification or tumour differentiation ($p>0.05$) suggesting that molecular phenotype in this population cannot be accurately predicted by histopathology alone.

Conclusion: This study demonstrates a relatively high prevalence of MSI in South African GC, with distinct demographic patterns. The lack of correlation between MSI status and histopathological features highlights the limitation of morphology-based prediction. Routine MSI testing is recommended to ensure accurate identification of patients eligible for

immunotherapy and to support the development of population-specific precision oncology strategies.