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Original Article

POLE mutations in endometrial carcinoma from a tertiary cancer care centre in eastern India

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Background and objectives: POLE exonuclease domain mutated tumours are a molecular subtype of endometrial carcinoma with paradoxically favourable prognosis despite high-grade histological features. Most data are from Western populations, with limited studies in Indian cohorts. This study aimed to determine the frequency, mutation spectrum, and clinicopathological characteristics of POLE-mutated endometrial carcinoma from a tertiary cancer centre in Eastern India.

Methods: This retrospective study was conducted between August 2022 to December 2024 at a tertiary cancer centre in Eastern India. Formalin-fixed, paraffin-embedded (FFPE) tumour tissue from 327 cases with endometrial carcinoma underwent DNA extraction and Sanger sequencing of exons 9–14 of the POLE gene. Only pathogenic and likely pathogenic variants were included. Fisher's exact test was used to assess associations between POLE status and tumour grade or histological type.

Results: Fifteen of 327 cases (4.6%) harboured POLE mutations, 13 of which were pathogenic. Most (12/15) showed endometrioid histology, and 40% had high-grade features. The common mutations were P286R, V411L, and S459F. No significant association was found between POLE status and histologic grade or type of endometrial carcinoma.

Interpretation and conclusions: The frequency of POLE mutations was lower than global averages but consistent with other Indian studies. Detected variants were recurrent hotspot mutations. The study underscores the importance of integrating POLE testing into routine diagnostic workflows for endometrial carcinoma in India.

Key words Endometrial cancer; Hotspot mutations; Molecular subtypes; Pathogenic POLE mutations; Sanger sequencing