ABSTRACT

Phosphatase and tensin homolog (*PTEN*) is a critical tumor suppressor gene frequently inactivated in various malignancies. This study aimed to investigate the DNA methylation profile of the *PTEN* gene promoter in oral cancer (OC) patients. A total of 101 OC patients clinically diagnosed at Shaukat Khanum Memorial Hospital and Research Centre (SKMCH&RC), Lahore, Pakistan, along with 101 healthy control (HC) samples obtained from diverse geographic regions of the country. The methylation status of the *PTEN* gene promoter region was assessed using methylation-specific polymerase chain reaction (MS-PCR). Binary logistic regression analysis and chi square test were performed to evaluate the association between *PTEN* methylation and oral cancer risk. The results revealed no statistically significant association between *PTEN* promoter methylation and the development of oral cancer. However, methylation patterns varied with clinicopathological parameters. A higher frequency of *PTEN* methylation was observed in males potentially linked to lifestyle factors such as smoking and tobacco use. Furthermore, individuals aged 50–70 years showed a higher methylation rate (56.4%) compared to those under 50 (42.6%). Among OC patients, 43.6% displayed full methylation, 51.5% partial methylation, and none were unmethylated. The present findings indicate that *PTEN* promoter methylation does not show a significant association with oral cancer development. Nevertheless, the high prevalence of partial *PTEN* promoter methylation observed in peripheral blood suggests possible biological significance. However, its variation across demographic factors limits its value as a standalone biomarker for oral cancer. Therefore, extensive tissue-based studies with larger cohorts are warranted to further explore its role in disease progression and prognostic evaluation.