Genetic clues to tackle oral cancer among Indian women revealed

प्रविष्टि तिथि: 29 NOV 2025 8:19PM by PIB Delhi

Indian scientists have discovered oral cancer-causing driver gene mutations in women patients of southern India. India carries one of the world's heaviest burdens of oral cancer with alarmingly high rates witnessed among women in certain regions, especially in southern and northeast India, due to the widespread habit of chewing tobacco-infused betel quid, gutka, and related products. While the disease is widely studied in men, oral cancer in women has often remained under the radar.

A team of researchers from the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru and the BRIC-National Institute of Biomedical Genomics (NIBMG), Kalyani, in collaboration with clinicians from Sri Devraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, has conducted a female-centric study on oral cancer in India with a unique tobacco chewing habit**.**

This study led by Prof. Tapas K Kundu, JNCASR, Bengaluru aimed to understand what makes cancers in women unique, how the disease manifests and progresses in female patients and how we can treat them better.

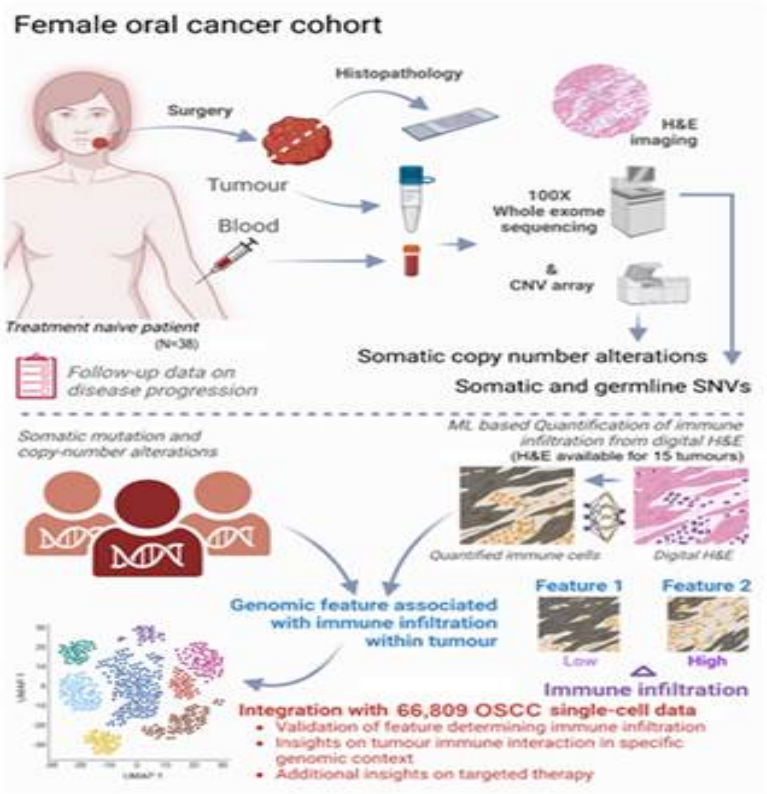

Fig - Sequencing of Patients` Gene: *Whole-exome sequencing (WES) and copy-number array profiling were performed on paired tumour and blood samples from female OSCC-GB patients with a unique regional tobacco-chewing habit (Kaddipudi), commonly observed among women in the Kolar district of*

Karnataka. Analysis of this women-centric cohort has revealed a unique driver mutation implicated in oral tumorigenesis.

This investigation published in the *Clinical and Translational Medicine Journal* was specifically designed to uncover the biological underpinnings of the disproportionately aggressive, highly recurrent, and life-threatening forms of oral cancer that affect Indian women.

Using cutting-edge whole-exome sequencing, the researchers identified ten key genes with significant mutations in the female oral cancer cohort from Kolar, Karnataka (SDUAHER).

Although two of the major genes, CASP8 and TP53, were found to be highly mutated in these patients, uniquely, CASP8 seems to be the driver mutation (cancer-causing), which is quite different compared to previously studied mutations in oral cancer patients (largely men).

Despite the limited cohort size (N=38), the findings suggest that co-occurring TP53 and CASP8 mutations confer a markedly aggressive and lethal phenotype in oral cancer. These observations warrant further investigation, and the team is now focused on delineating the molecular mechanisms of oncogenesis driven by this novel driver mutation within the background of TP53 alterations for the next phase of the research. The team also used artificial intelligence (deep learning) to digitally analyze tumor tissues. This revealed two distinct groups of female patients, each with a different immune response in their tumors. This insight is crucial because it suggests that some patients might respond better to certain treatments based on their tumor profile.

This groundbreaking study sets a new benchmark in cancer research. It not only highlights the urgent need to include more women patients in biomedical research but also provides a roadmap for personalized medicine in tackling oral cancer—a disease that has claimed many lives in India. However, these findings need to be further confirmed in a larger number of patients.

Publication link- doi: 10.1002/ctm2.70386

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