

New Genome-Wide Study from Tata Memorial Centre Reveals: “Why Do Some Tobacco Chewers Develop Oral Cancer Early?”

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A landmark Genome-Wide Association Study (GWAS) conducted by the Centre for Cancer Epidemiology (CCE), ACTREC at the Tata Memorial Centre (TMC), Mumbai, has identified key genetic factors that explain why some tobacco chewers in India develop oral cancer nearly a decade earlier than others. The findings were shared during a press conference held at TMC on Saturday, where the team of expert doctors involved in the research presented the study in detail.

The new research, published in eBioMedicine, part of The Lancet Discovery Science, identifies specific genetic markers that significantly increase susceptibility to oral cavity cancer—one of the most common and preventable cancers in India, primarily linked to tobacco use.

Dr. Sudeep Gupta, Director, Tata Memorial Centre, underscored the need to examine gene–environment interactions and to develop polygenic risk scores for common cancers in India. He emphasized that although genetic susceptibility is important to understand, tobacco chewing remains the single most preventable cause of oral cancer, with more than 80% of cases potentially avoidable through effective tobacco control policies.

Dr. Pankaj Chaturvedi, Director, ACTREC, reiterated that tobacco chewing is a major risk factor for oral cancers, noting that the risk of developing oral cancer is 26 times higher among tobacco chewers compared to non-users. He added that genetic susceptibility markers further double the risk among individuals with a high genetic risk score.

Dr. Elisabete Weiderpass, Director of the International Agency for Research on Cancer (IARC), WHO, Lyon, France, highlighted the significance of the study, stating:

“This landmark study represents a significant advance in our understanding of the genetic and environmental factors driving buccal mucosa cancer, a disease that imposes a heavy burden in India and across South Asia. By conducting the largest genome-wide association study of its kind and integrating data from multiple ancestries, the authors have identified novel risk loci and illuminated the complex

interplay between genetic susceptibility and tobacco chewing. These findings deepen our knowledge of oral cancer etiology and highlight the urgent need for tailored prevention and screening strategies for high-risk populations.”

Dr. Rajesh Dikshit, Director, CCE, explained that understanding genetic predisposition can help predict oral cavity cancer development among tobacco chewers. He noted that pathway analysis from the study identified distinct immune pathways and “highly calcium-permeable nicotine receptor-encoding genes” as being involved in cancer development. Further exploration of these pathways could lead to more precise methods for early detection and prevention.

Dr. Nilanjan Chatterjee, Bloomberg Distinguished Professor, Johns Hopkins University, said:

“This article provides important insights into the genes that influence susceptibility to this cancer and how they interact with the carcinogenic effects of tobacco chewing. Individuals who chew tobacco face a substantially higher risk of developing buccal mucosa cancer. What is often less recognized is that genetic predisposition can further amplify this risk. We don’t get to choose the genes we’re born with, which makes it even more important to choose the habits that keep this cancer at bay.”

Dr. Sharayu Mhatre, Scientific Officer, CCE, and lead author of the study, stated that while tobacco use remains the strongest risk factor for Buccal Mucosa cancer, a genetic susceptibility component also plays a role. She noted a 24% relative excess of oral cavity cancer cases among tobacco chewers with a high genetic risk score compared to those with a low score. Comparisons with European populations showed both similarities and distinct differences in genetic architecture, underscoring the importance of India-specific genetic data.

Dr. Preetha Rajaraman, Executive Director (U.S.), Vice Chair, and Chief of Research, Radiation Effects Research Foundation (RERF), Hiroshima, remarked that the findings provide important insights into how behaviour interacts with genetic makeup to influence buccal mucosa cancer risk. She emphasized the potential for more personalized screening strategies by considering both tobacco-chewing habits and genetic predisposition.

Dr. Siddhartha Kar, Associate Professor, Oncology Department, Cambridge University, added:

“This landmark study advances our understanding of why oral cancer is so common in India, uncovering uniquely Indian genetic risk factors. By showing how inherited risk interacts with tobacco use, it lays the groundwork for targeted prevention and early detection.”

Dr. Rajesh Dikshit further shared that CCE is conducting GWAS research on several other common cancers in India, which will help develop genetic risk scores for those cancers as well. Dr. Sharayu Mhatre presented the study results and emphasized the need for large sample sizes to better understand genetic factors responsible for cancer causation.

How the Study Was Conducted

The study compared 2,160 cases of Buccal Mucosa cancer with 2,325 controls from various regions in India and conducted a genome-wide scan to assess genetic susceptibility. Researchers identified significant genetic risk loci on chromosomes 5 and 6, near genes including CLPTM1L-TERT, HLA-DRB1, HLA-DQB1, and CEP43. A meta-analysis incorporating data from Europe and Taiwan also identified novel risk loci near the NOTCH1 gene.

The investigators calculated a polygenic risk score and found that tobacco chewers with a high score developed Buccal Mucosa cancer 10 years earlier than those with a low score.

The Indian Scenario

India records approximately 141,342 cases of oral cancer, with an average age-standardized incidence rate of 10.0 per 100,000 population. In certain states, this rate rises to 25–33 per 100,000. Despite similar lifestyle factors, the onset and progression of the disease vary significantly among individuals. This study provides the first clear genetic explanation for these variations, demonstrating that genetic makeup plays a crucial role in elevating oral cancer risk among tobacco chewers.

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