



## Personalized Dentistry: The Role of Genetics and Pharmacogenomics in Clinical Decision-Making

Dr. Suyog Savant<sup>1</sup>, Dr. Farheen Tafti<sup>2\*</sup>, Dr. Mrunmayee Soman<sup>3</sup>, Dr. Amrut Shete<sup>4</sup>, Dr. Ankita Kadam<sup>5</sup>, Dr. Swapnil Kurhade<sup>6</sup>

<sup>1</sup>Associate Professor, Public Health Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Navi Mumbai.

<sup>2\*</sup>Assistant Professor, Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Navi Mumbai.

<sup>3</sup>PG Student, Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Navi Mumbai.

<sup>4</sup>PG Student, Prosthodontics, Crown & Bridge and Implantology, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Navi Mumbai.

<sup>5</sup>Assistant Professor, Prosthodontics, Crown & Bridge and Implantology, YMT Dental College and Hospital, Navi Mumbai.

<sup>6</sup>Assistant Professor, Prosthodontics, Crown & Bridge and Implantology, Dr. D Y Patil Dental College and Hospital, Pimpri, Dr. D Y Patil Vidyapeeth, Pune.

### \*Corresponding Author:

Dr. Farheen Tafti

Assistant Professor, Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Navi Mumbai.

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### ABSTRACT:

Underpinned by the understanding that interindividual heterogeneity in genetic and epigenetic composition strongly impacts illness risk, development, and treatment response, personalized medicine is becoming a key component of healthcare in the twenty-first century. By integrating patient-specific genetic, molecular, and pharmacogenomic data into clinical processes, this emerging paradigm in dentistry known as personalized or precision dentistry is completely changing the diagnosis, prevention, and treatment of oral illnesses. The strategy makes use of technologies including salivary biomarkers, next-generation sequencing, and genome-wide association studies to facilitate earlier identification, more precise risk assessment, and tailored treatment plans. With an emphasis on how genetic polymorphisms, gene-environment interactions, and pharmacogenomic profiles influence clinical judgments in fields like periodontology, orthodontics, implantology, oral pathology, and pharmacotherapy, this review examines the principles and uses of personalized dentistry. It also discusses the difficulties in integrating these innovations into standard dentistry practice, including those related to ethics, logistics, and education. In order to improve long-term results and patient happiness, personalized dentistry seeks to move the emphasis from reactive to predictive, from generalized to individualized, by matching dental care with each patient's biological uniqueness.

### Introduction

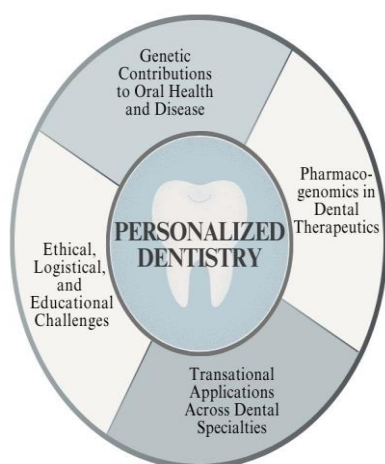
Historically, standard clinical procedures based on demographic averages and evidence-based recommendations have served as the foundation for conventional dental treatment. Large-scale clinical studies, which are the foundation of these recommendations, are reliable but frequently underrepresent individual-level variability.[1] This kind

of standardization ignores important biological variations across patients, which can have a significant impact on treatment results and disease susceptibility. For example, due to variations in immune-inflammatory gene expression or bone remodelling capability, two individuals with comparable dental hygiene habits may show radically different rates of periodontal disease development.[2] Similar to this, people with different drug-metabolizing enzymes may experience negative



side effects or less than ideal results from the same prescription medications, such as antibiotics or nonsteroidal anti-inflammatory drugs (NSAIDs). These differences point to the increasing need for customized dental treatment paths that go beyond radiographic diagnosis and visual clinical evaluation.[3]

By incorporating multi-omics technologies genomics, transcriptomics, proteomics, and metabolomics into the clinical workflow, customized dentistry is filling this gap. Single nucleotide polymorphisms (SNPs), copy number variations (CNVs), and epigenetic markers that contribute to oral disease phenotypes may now be found by clinicians thanks to the advent of salivary and buccal swab-based tests and the growing accessibility of genetic screening platforms. Loci linked to periodontitis risk (e.g., IL-1 cluster, TNF- $\alpha$ ), caries susceptibility (e.g., AMELX, DEFB1), and even orthodontic responses (e.g., RANKL, OPG) have been found by genome-wide association studies (GWAS).[4] Clinicians can customize therapeutic and preventative measures to each patient's distinct molecular profile by combining these findings with pharmacogenomic data. To reduce the possibility of insufficient pain relief or unfavourable medication effects, a patient with a known CYP2D6 poor metabolizer genotype, for instance, could be prescribed an analgesic other than codeine. By incorporating these precise techniques into normal dentistry, proactive, preventative care replaces reactive therapy, improving patient satisfaction and efficacy [Figure 1].[5]



### Genetic Contributions to Oral Health and Disease

It is now recognized that genetic susceptibility factors, in conjunction with environmental triggers, play a role in the pathogenesis of several common and complicated oral disorders.[6] An excellent illustration of this interplay is found in periodontal disorders, where the immune-inflammatory response of the host, fuelled by genetic differences, is crucial to the development and course of the illness.[7,8] Polymorphisms in genes that encode cytokines including IL-1A, IL-1B, TNF- $\alpha$ , and IL-6 have been linked in several studies to increased inflammatory responses, which result in the fast loss of alveolar bone and periodontal attachment.[9] In North American and European populations, a particular haplotype called the IL-1 composite genotype has been commercially tested and linked to a higher risk of developing severe periodontitis. Enzymes that aid in the breakdown of extracellular matrix and tissue damage, such as matrix metalloproteinases (MMPs) and cathepsins, may have their expression altered by these genetic variants.[10]

Once primarily seen through a nutritional and microbiological lens, dental caries is now understood to be a complex disease impacted by genetic variables that control immunological competence, salivary function, and enamel production.[11] Increased susceptibility to caries and enamel hypoplasia have been associated with mutations in genes that encode proteins necessary for enamel biomineralization, such as AMELX and ENAM. Caries risk is further influenced by changes in the PRH1 and PRH2 salivary glycoprotein genes, which alter bacterial adherence and the makeup of the acquired enamel pellicle. Additionally, potential loci on chromosomes 1q42.3, 13q31.1, and 14q32.2 have been linked to dental caries phenotypes in a variety of populations by recent genome-wide investigations.[12]

Classical instances of genetically driven oral developmental problems include craniofacial abnormalities like cleft lip and palate. Mutations in genes such IRF6, MSX1, TBX22, and BMP4 many of which are involved in neural crest cell migration and craniofacial morphogenesis have been connected to these abnormalities.[13] Furthermore, mutations in DLX3 and EDA1 may result in taurodontism and other structural abnormalities of the dentition, whereas polymorphisms in the PAX9 and AXIN2 genes are linked to tooth



agenesis and hypodontia. In orthodontic diagnosis, treatment planning, and multidisciplinary management including paediatricians, surgeons, and genetic counsellors, it is essential to acknowledge these hereditary factors.[14]

## Pharmacogenomics in Dental Therapeutics

One of the most practical areas of personalized dentistry is pharmacogenomics, which enables physicians to improve medication therapy by taking genetic variation in drug-metabolizing enzymes, transporters, and receptors into consideration. The cytochrome P450 enzyme system, in particular CYP2D6, CYP2C9, and CYP3A4, is one of the most investigated gene families in this area. These enzymes mediate the metabolism of a significant number of medications used in dentistry practice.[15] For example, different metabolic phenotypes like as poor, moderate, extensive, or ultra-rapid metabolizers are caused by CYP2D6 polymorphisms, and each has unique clinical consequences for the toxicity and effectiveness of analgesics. Ineffective in poor metabolizers and dangerously strong in ultra-rapid metabolizers, codeine is a prodrug that needs CYP2D6 to bioactivate to morphine. This risk is especially significant for juvenile children having tooth extractions.[16]

Genetic variations in the OPRM1 gene, which codes for the  $\mu$ -opioid receptor, affect the analgesic response to substances like morphine and fentanyl by influencing the opioid binding affinity and effectiveness.[17] Likewise, variations in pain thresholds and vulnerability to chronic orofacial pain disorders have been linked to the SCN9A gene, which codes for the Nav1.7 sodium channel involved in nociception.[18] By being aware of these differences, analgesic prescriptions may be made more precisely, lowering the possibility of reliance, oversedation, or undertreatment.

Pharmacogenomic insights can also help with antibiotic therapy, especially when it comes to prophylaxis and orofacial infections. For instance, when exposed to certain antibiotics like nitrofurantoin or sulfonamides, people with G6PD deficiency run the risk of hemolysis. The effectiveness and risk of adverse effects of systemic antibiotic exposure may be impacted by genetic variations in the SLCO1B1 and ABCB1 genes.[19] Furthermore, CYP2C19 and CYP2D6 metabolize antidepressants like amitriptyline, which are

occasionally recommended for neuropathic pain, and pharmacogenetic testing may help determine dose to enhance therapeutic results in the setting of chronic orofacial pain.[20]

The most important pharmacogenomic use in dentistry may be for bisphosphonate-related osteonecrosis of the mandible (BRONJ or MRONJ). According to genetic research, individuals receiving antiresorptive medication are more susceptible to MRONJ because of polymorphisms in the VEGFA, COL1A1, and MMP2 genes, which are linked to changes in bone turnover, angiogenesis, and extracellular matrix remodeling.[21] Dentists may be able to use preventative measures, including medication vacations or less invasive alternatives to extractions, if these patients have preemptive genotyping.

## Translational Applications Across Dental Specialties

Numerous dental subspecialties are witnessing the clinical effect of customized dentistry. Genetic profiling is starting to influence treatment intensity and maintenance regimes in periodontology. Individuals who have been shown to carry high-risk polymorphisms may benefit from early host-modulatory therapy, such as new anti-inflammatory drugs that target certain cytokine pathways or sub-antimicrobial doses of doxycycline.[22] Furthermore, the combination of host genotyping and precision microbiomics may make it easier to create tailored antibiotic regimens that more successfully restore oral microbial equilibrium.[23]

In implantology, risk assessment and treatment planning are progressively taking into account genetic characteristics that affect osseointegration, immunological response, and wound healing. Gene variations have been linked to peri-implantitis, implant failure, and impaired bone regeneration.[24] These genes include TNFRSF11B (osteoprotegerin), IL-10, and TGF- $\beta$ 1. In vulnerable people, genetic risk assessment can guide the use of adjuvant therapy including growth factors, platelet-rich plasma, or certain implant surface modifications.[25]

Another area where genetic information is starting to guide personalized treatment is orthodontics. Genetic variations in the IL-1 $\beta$  and P2RX7 genes have been linked to a higher risk of orthodontically induced inflammatory root resorption (OIIRR), a frequent side



effect of therapy.[26] Furthermore, alveolar bone remodeling in response to orthodontic pressures is regulated by genes implicated in the RANK/RANKL/OPG pathway; mutations in these genes may predict variations in treatment stability or duration. Clinicians can use this information to help them choose force levels, appliance kinds, and retention techniques that are specific to the patient's biologic profile.[27]

The molecular profiling of oral squamous cell carcinoma (OSCC) in oral oncology is making it possible to switch from standard treatment regimens to tumour genotype-based targeted therapy.[28] Together with epigenetic indicators like promoter methylation of tumour suppressor genes, mutations in TP53, NOTCH1, and CDKN2A provide prognostic information and direct the application of certain chemotherapeutic drugs.[29] In line with the more general objectives of precision oncology, salivary diagnostics employing mRNA, microRNA, and proteomic markers provide a non-invasive way for the early identification and tracking of precancerous lesions.[30,31]

**Ethical, Logistical, and Educational Challenges**

There are several difficulties in using genetics into dentistry. There are serious ethical issues with informed consent, genetic privacy, and the possibility of genetic data misuse. Dental practitioners must follow stringent guidelines for data protection and ethical usage, and patients must get sufficient counselling regarding the consequences of genetic testing.[32] Furthermore, inequities in oral health care that already exist might be made worse by differences in access to genetic technology. Barriers to wider adoption include the expense of testing, the absence of insurance coverage, and regionally disparate regulatory regimes.[33]

The dental workforce's willingness to embrace new technology is another crucial concern. According to surveys, a large number of practitioners do not have formal training in pharmacogenomics and genomics, which restricts their capacity to understand test results and use them in a clinical setting.[34] The successful integration of customized dentistry into standard practice requires multidisciplinary cooperation with geneticists, pharmacologists, and bioinformaticians, as well as continuing education initiatives and revised dental curriculum.

**Table 1: Challenges faced.**

Category	Challenges	Explanation
<b>Ethical &amp; Legal Considerations</b>	Risk of data exploitation and lack of transparency in consent processes	Patients may fear discrimination based on genetic risk profiles; laws like GINA (in the U.S.) offer limited global coverage.
<b>Patient Communication &amp; Education</b>	Limited patient understanding of genetic implications	Misinterpretation of test results can lead to anxiety or non-compliance without appropriate pre- and post-test counseling.
<b>Healthcare Inequity</b>	Unequal access to precision tools and testing	Socioeconomic disparities may prevent marginalized communities from benefiting equally from advancements in personalized care.
<b>Cost &amp; Reimbursement</b>	High upfront costs and limited third-party payer support	Genetic tests and interpretation services are often not covered under conventional dental insurance models.
<b>Regulatory Inconsistencies</b>	Variability in genetic testing regulations between regions and countries	Lack of standardized guidelines creates ambiguity for clinical adoption and cross-border collaborations.



<b>Workforce Preparedness</b>	Insufficient genomic literacy among dental professionals	Most curricula lack modules on interpreting genetic markers relevant to oral health (e.g., periodontitis risk genes).
<b>Clinical Utility &amp; Interpretation</b>	Difficulty integrating complex genetic data into decision-making	Many practitioners lack tools to translate genetic findings into actionable treatment modifications.
<b>Interdisciplinary Collaboration</b>	Fragmented interaction between dental and medical genetics professionals	A siloed healthcare system limits team-based approaches needed for effective personalized care plans.
<b>Technological Infrastructure</b>	Lack of integration with electronic health records (EHRs)	Seamless data sharing is essential for utilizing pharmacogenomic data in real-time chairside decision-making.
<b>Continuing Education &amp; Training</b>	Limited access to structured professional development in genomics	Few accredited dental CPD (Continuing Professional Development) programs currently offer modules in genetics or bioinformatics.

## Conclusion

Based on the ideas of genetic medicine, personalized dentistry is a significant advancement in oral healthcare. This method improves overall patient outcomes, optimizes therapeutic approaches, and increases diagnostic accuracy by taking individual diversity in genetic composition and medication response into consideration. There are still issues with cost-effectiveness, ethical governance, and professional readiness, but there is no denying the clinical and scientific momentum behind customized dentistry. The future of dentistry will be more and more characterized by accuracy, forecasting, and customization as molecular diagnostic techniques become more widely available and combined with digital technology like artificial intelligence. Adopting this paradigm underlines dentistry's dedication to patient-centred treatment while also bringing it into line with contemporary biological science.

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