BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue10

DOI:10.58240/1829006X-2025.21.10-386

ORIGINAL RESEARCH

THE ROLE OF GENETIC FACTORS IN THE PATHOGENESIS OF ORAL AND MAXILLOFACIAL DISEASES

Omar Abdul Jabbar Abdul Qader[1], Marwah Ayad Al-Hamadani[2] , Maha Mohammed Abd Ali[3]

[1] Lecturer Doctor, College of Dentistry, University of Al Mashreq, Baghdad 10023, Iraq dromarqader@gmail.com
[2] Lecturer, Department of Pharmacy, The University of Mashreq, Baghdad 10023, Iraq, marwaayad2006@yahoo.com
[3]Al Hadi University, Baghdad 10023, Iraq maha.m@huc.edu.iq
Corresponding author: Omar Abdul Jabbar Abdul Qader Lecturer Doctor, College of Dentistry, University of Al Mashreq, Baghdad 10023, Iraq dromarqader@gmail.com
Received: Oct 14*. 2025;* ***Accepted: Nov 14*** *, 2025;* ***Published:Nov 17*** *,2025*

Abstract

Background: Both hereditary and environmental factors play essential roles in the complex diseases collectively known as oral and maxillofacial diseases. The important role genetic factors play in susceptibility, development, and treatment outcome of all sorts of diseases has been highlighted. Advances in molecular biology over the last several years have made it clear.

Materials and Methods: This study was conducted as a narrative literature review based on systematic searches across PubMed, Scopus, and Google Scholar databases. Relevant English-language articles published between 2015 and 2025 were selected using keywords such as *genetic factors*, *oral and maxillofacial diseases*, *molecular mechanisms*, *oral cancer*, and *craniofacial anomalies*.

Results: The review revealed that several oral and maxillofacial disorders have strong genetic and molecular bases. Mutations in *MSX1*, *IRF6*, and *TP63* were linked to cleft lip and palate, while *AMELX*, *ENAM*, and *DSPP* mutations contributed to hereditary enamel and dentin defects. In oral cancer, overexpression of oncogenes (*EGFR*, *RAS*) and inactivation of tumor suppressor genes (*TP53*, *RB1*) were frequently observed, alongside epigenetic alterations. Variants in inflammatory genes such as *IL-1* and *TNF-α* were associated with increased susceptibility to periodontal diseases.

Conclusions: It is crucial to understand the molecular and genetic causes of oral and maxillofacial diseases. Genetic testing is indispensable for personalized treatment, for assessing risks and for early detection of disease. Multi-omic research, gene therapy, and precision medicine advances all promise to transform the future patient care in oral and maxillofacial healthcare fields. No matter existing problems such as access, complexity or ethical, they have great prospects of accomplishment in time to save human costs.

Keywords: Molecular mechanism, genetic tests, oral and maxillofacial diseases, genetic traveler, personalized medicine

INTRODUCTION

The mouth is a key component of individual identity and the teeth and mouth are a crucial aspect of the body, supporting and facilitating vital human activities. Building on previous definitions, oral health can be described as multifaceted, encompassing social, emotional, psychological, and physical aspects that are essential to general health and wellness [1]. Subjective and ever-changing, oral health allows one to eat, speak, smile, and interact with others without experiencing pain, discomfort, or shame. A person's capacity to adjust to physiological changes over the course of their life and to take care of their own teeth and mouth through self-care on their own is reflected in their level of oral health [2].

The soft and hard tissues of the mouth are impacted by a broad range of illnesses and conditions, such as congenital abnormalities, traumas, infections, and a variety of craniofacial disorders. However, dental caries (tooth decay), periodontal (gum) disease, and oral malignancies are the main clinical disorders that are regarded as global public health issues [3]. Dental caries is the localized breakdown of dental hard tissues (dentine and enamel) by acidic byproducts of bacterial fermentation of free sugars, which are defined as sugars that are naturally found in honey, syrups, fruit juices, and fruit juice concentrates, as well as monosaccharides and disaccharides that are added to food and beverages by the producer, cook, or consumer [4].

Chronic inflammatory disorders known as periodontal diseases impact the tissues that support and surround teeth. Gingivitis, a reversible inflammation of the periodontal soft tissues that causes gingival bleeding and swelling, is the initial symptom of periodontal disease. Gingivitis may develop into periodontitis in vulnerable people with weakened immune systems, which gradually erodes the bone that surrounds the teeth and supports the periodontal tissue. This loss of periodontal tissue support, which shows up as clinical attachment loss, periodontal pocketing, gingival bleeding, and radiographically measured alveolar bone loss, is what defines periodontitis [5]. Poor oral hygiene, which results in the buildup of pathogenic microbial biofilm (plaque) at and below the gingival edge, is the primary cause of periodontal disease.

Another significant independent risk factor for periodontal disease is tobacco use [6]. According to the International Classification of Disease, 10th Revision, cancer of the lips and oral cavity is a broad category of localization for a neoplasm. It can be found in the lips, tongue, gum, floor of the mouth, palate, cheek mucosa, vestibule of the mouth, or retromolar area (malignant neoplasm topography codes C00–C06). The most prevalent kind of mouth cancer is squamous cell carcinoma. Alcohol use and tobacco use are substantial risk factors for oral malignancies. Human papillomavirus infection is the cause of a sharp increase in the incidence of oropharyngeal malignancies in young individuals in many high-income countries (HICs).

The prevalence of oral cancers is greater among men, older age groups, and individuals from poorer backgrounds, with socioeconomic inequalities observed both between and within countries [7].

Any disease that results from a change in one or more genes is considered a human genetic condition. This covers the study of both hereditary traits and DNA-regulated cellular alterations. Multiple categories of genetic illnesses are represented by oral diseases with a genetic etiology. A large number of periodontal illnesses are multifactorial, meaning that environmental influences coexist with one or more genetic factors. However, oral symptoms are present in many chromosomal and single gene disorders. A wide range of phenotypic changes, including oral symptoms, are exhibited by chromosome abnormalities. These abnormalities, which impact oral health, are either related to sex chromosomes or autosomes [8].

The function of chromosome abnormalities, single nucleotide polymorphisms (SNPs), and mutation While certain variants are associated with particular abnormalities, including heightened vulnerability to tooth caries and periodontal disease, inherited or acquired mutations can raise the risk of oral malignancies [9]. A single nucleotide in the DNA sequence varies from person to person in SNPs, which are widespread variations in the human genome. When paired with environmental risk factors like tobacco smoking, SNPs in genes like P16 can raise the risk of oral cancer and potentially malignant illnesses (OPMDs). SNPs can impact immune response-related genes in periodontal disease, increasing the risk of developing periodontitis.

In addition to its impact on tooth agenesis and cleft lip/palate. Oral cleft syndromes can result from chromosomal abnormalities, which can affect a person's entire development [10]. Malocclusion: Certain diseases, such as Turner syndrome (which has a missing X chromosome) [11], and Klinefelter syndrome (which has an additional X chromosome), are linked to unique craniofacial characteristics, like mandibular prognathism or retrognathia, which impact facial form and jaw growth [12].

- Cleft Palate and Cleft Lip: The most prevalent craniofacial abnormality associated with a family history is this one. It has to do with the lip or palate not fully fusing.

- A congenital condition called anodontia results in lacking teeth, Children with this abnormality typically have one or more primary teeth missing when they are born, but they do obtain their baby teeth. Due to the failure of lower second premolars, upper lateral incisors, and third molars to form, this disease may result in spacing abnormalities.

Defective enamel, the hard material that covers the tooth crown, is a component of amelogenesis imperfecta. As a result, teeth become more susceptible to wear and temperature changes.

Supplementary Teeth Extra permanent teeth that might not erupt are present in some people. Anywhere in your mouth can have those that do erupt. They frequently have a small root and a cone-shaped crown.

Malocclusion This condition, also referred to as bad bite, results in crowding because of an improper tooth count and jaw misalignment. Both nonsurgical and surgical methods can lessen discomfort and restore function.

- A bacterial infection that harms the tissues that support your teeth is the cause of gum disease. With the right oral cleanliness and treatment, the illness can be reversed. Your risk of developing gingivitis, which is associated with diabetes, stroke, and heart disease, is also influenced by your genetic makeup.

- Fibrosis gingival Collagen overproduction is the cause of this gum tissue overgrowth.

A white or red patch in the mouth is the initial sign of oral cancer. In individuals over 40, alcohol or tobacco use is linked to the majority of oral malignancies. But genetics also come into play. White or gray mouth ulcers with a crimson border is known as canker sores. They are brought on by bacterial infections and weaknesses in the immune system. The likelihood and frequency of developing them may also be influenced by a person's genetic makeup.

A number of oral disorders are directly linked to mutations in structural and regulatory genes. For instance, DSPP mutations result in dentinogenetic imperfecta, whereas mutations in AMELX and ENAM induce amelogenesis imperfecta. A person may also be at risk for craniofacial defects including cleft lip and palate due to chromosomal abnormalities [14].

The development of tissues and the course of disease are influenced by altered expression of important genes. Histone modification and DNA methylation are examples of epigenetic modifications that impact gene function without changing the DNA sequence. These changes have been connected to the development and advancement of periodontal disease and oral squamous cell carcinoma [15].

A disturbance in the equilibrium between oncogenes and tumor suppressor genes is the primary cause of oral malignancies. Oncogene overexpression (EGFR, RAS, etc.) encourages unchecked cell division, whereas tumor suppressor gene inactivation (TP53, RB1) eliminates growth regulation checkpoints and speeds up malignant transformation [16].

Environmental risk factors like alcohol consumption, nicotine use, and virus infections interact with genetic predisposition. For example, people with particular polymorphisms in detoxifying enzymes (CYP, GST) are more susceptible to carcinogens, which raises their chance of developing cancer. [17]

Similarly important signal transduction pathways include those that control the balance of organismal dynamics and development of the craniofacial region, such as Wnt signalling pathway Hedgehog signal transduction pathway TGF-β. These cascades underpin many diseases including cancer and developmental abnormalities. Understanding this molecular rhythm becomes essential for developing targeted therapies in future years ahead. (Source: Journal Reference 14)

Although the oral and maxillofacial disease diagnosis and treatment are now subject to giant leaps because of genetics testing which updates it for the 21st century, the functions of genetics in precision oral healthcare will only become more important as sequencing technologies and analytics continue to improve. It can not only help stop disease at its outset with early detection methods that look for affected genes but also furnish that vital prerequisite to do so Scientific classification; and finally

Its benefits are even more pronounced in the dental clinic of the future.

- Comprehensive: Examines all genes known to be associated with a specific disorder regardless of whether there is direct evidence about their relationship.

- The second category contains the miscellaneous functions–it studies more than 30 genes associated with disorders which can affect development or hereditary disease. There are two methods to consider here, with complementary information that is suited for different situations.

- The third method is Whole Exome/Genome Sequencing (WES/WGS), which finds a range of genomic alterations in both coding and non-coding regions.

With its long history and large number of cases, cytogenic analysis can provide information regarding the chromosomal abnormalities that underlie malformations of craniofacial area.

- **Congenital Disorders:** Developmental abnormalities and cleft lip/palate disorders can be diagnosed with genetic testing.

- **Hereditary Dental Disorders:** Identifying genetic flaws in the development of enamel and dentin.
  Oral Cancer: Determining TP53, EGFR, and other oncogene mutations to direct focused treatment.

- **Periodontal Diseases:** Assessing susceptibility by looking for polymorphisms in genes linked to inflammation and immunity [18].

GWAS, or genome-wide association studies To find novel genetic variations connected to periodontal disease, craniofacial abnormalities, and oral cancer, extensive research is required.

- **Combining Various Omics Methods:** A more thorough understanding of disease mechanisms will be possible by combining genomes, transcriptomics, proteomics, and epigenomics.

- **Regenerative medicine and gene therapy:** It may be possible to repair defects and regenerate oral tissues thanks to developments in CRISPR-Cas9 and stem cell technologies.

- **Precision and Personalized Medicine:** Individual risk can be predicted, treatment options can be guided, and therapy response can be tracked by genetic testing.

The use of bioinformatics and artificial intelligence Large genomic databases can be analyzed by AI technologies, which enhance prediction models and support early diagnosis [20].

MATERIALS AND METHODS

This research was carried out as a review of narrative literature. Systematic searches in the PubMed, Scopus, and Google Scholar databases yielded pertinent scholarly papers. The terms "genetic factors," "oral and maxillofacial diseases," "molecular mechanisms," "oral cancer," "periodontal disease," and "craniofacial anomalies" were used in various combinations.

The requirements for inclusion were:

- Articles released from 2015 to 2025.
- English-language studies.
- Original, peer-reviewed publications and review papers that discuss the molecular and genetic components of disorders of the mouth and jaw.

Key findings were grouped by disease type, genetic factors implicated, and reported molecular pathways after all chosen research were examined.

RESULTS

According to the literature review, the pathophysiology of oral and maxillofacial disorders is influenced by a number of genetic and molecular factors.

- Cleft Palate and Lip: It has been often documented those non-syndromic cleft disorders are largely caused by mutations in MSX1, IRF6, and TP63.

- Hereditary Dental Disorders: Amelogenesis imperfecta was linked to mutations in AMELX and ENAM, whereas dentinogenetic imperfecta was linked to mutations in DSPP.

- Oral Cancer (Oral Squamous Cell Carcinoma): Overexpression of oncogenes (EGFR, RAS) and inactivation of tumor suppressor genes (TP53, RB1) were frequent observations. The development of tumors was also influenced by epigenetic changes such DNA methylation.

Genetic variations in IL-1 and TNF-α have been associated with heightened inflammatory reactions and heightened vulnerability to periodontal diseases.

TMJ diseases: Mutations in the genes associated with cartilage metabolism and inflammatory mediators suggested a genetic predisposition for joint damage and pain.

Taken together, the study identified that these diseases are not only multifactorial (influenced by such environmental risks as smoking, drinking, poor dental hygiene and viral infections), but also genetic.

DISCUSSION

This study demonstrated how critical the influence of genetic and molecular factors is in bringing about disorders of the mouth and jaw. However, while changes in regulatory genes and tumor suppressors such as TP53 and RB1 cogently support that they are involved in oral carcinogenesis, mutations of structural genes like AMELX, ENAM, and DSPP explain the genetic causes underlying those inherited dental afflictions.

These findings are consistent with research earlier this year that introduced genetic predisposition as a significant factor in the development of oral-related disease.

The role of gene– environment interactions in disease is perhaps one of the most important findings. For instance, those who have polymorphisms in inflammatory cytokines (IL-1, TNF-α) or detoxifying enzymes (GST,

CYP) are more prone to periodontal disease and oral cancer when risk factors like alcohol abuse and tobacco addiction are present -- pointing out how important it is that both genetic predisposition and lifestyle choices be considered in avoiding disease.

Another essential factor at work here is the function of epigenetic changes which with DNA methylation and histone modifications regulate gene expression without changing the DNA sequence. In these ways people who are molecularly close may suffer from completely different conditions, because episodes – as a connecting link between genetic susceptibility and environmental chance exposure

At present the clinical application of gene tests in oral surgery and dental treatment offers considerable room for development. Early diagnosis of genetic disorders by clinicians can provide for individualized treatment plans from precision-targeted therapy to preventive measures in people who show signs of them starting at an early stage: For example, when TP53 mutations found in patients with oral squamous carcinoma lead to the use of precision oncology techniques.

Problems remain, especially when resources are limited and genetic testing techniques or bioinformatic tools cannot be used.

Finally, although recent studies have provided significant new evidence to understanding diseases like periodontitis and cancer, many questions still remain unanswered. The bulk of research concentrates on certain groups of people, which limits how much the results can be broadly generalizable Moreover, mostly because most of these studies have small samples to begin with it is difficult establish strong causative correlations. Future work to drive home the real details behind pathology to provide a more comprehensive understanding of disease pathophysiology should incorporate multiple omics technologies and put large-scale multiethnic association studies (GWAS) on solid footing.

CONCLUSION

However, this requires a new understanding of what genes and molecules can do. Such illnesses span from cleft lip and palate to hereditary dental problems, periodontitis or temporomandibular joint disease, and oral cancer. They are determined more by mutations, chromosomal aberrations, and epigenetic changes than by life-style or environmental factors. The material also highlights the importance of gene-environment interactions, where behaviour and outside risk factors alter genetic susceptibility in a way that is conducive to disease. A number of practical examples are given in each instance for illustration purposes only. When these ideas described above are taken into account, we can easily see that early diagnosis may be made, precise risk evaluation is possible and individualized treatment programs made.BinContent According to argument, molecular profiling or genetic tests may be adopted into the practice of medicine and then successively prompt these advances.There are still issues, nevertheless, such as the intricacy of multifactorial illnesses, the restricted availability of sophisticated genetic testing, and moral dilemmas.

Future developments in gene therapy, multi-omics techniques, and genome-wide association studies could help close these gaps. In order to improve patient outcomes and advance precision medicine in oral and maxillofacial healthcare, genetic research can be turned into useful clinical applications by overcoming current restrictions.

DECLARATIONS

The authors declare that this manuscript is an original work and has not been submitted or published elsewhere. All authors have read and approved the final version of the manuscript and agree to its submission. There are no conflicts of interest related to this work.

REFERENCES

1.National Institutes of Health. (2021). Oral health in America: advances and challenges. *Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Institute of Dental and Craniofacial Research*.

2.Rouxel P, Tsakos G, Chandola T, Watt RG. Oral Health-A Neglected Aspect of Subjective Well-Being in Later Life. J Gerontol B Psychol Sci Soc Sci. 2018 Mar 2;73(3):382-386. doi: 10.1093/geronb/gbw024

3.Peres, M. A., Macpherson, L. M., Weyant, R. J., Daly, B., Venturelli, R., Mathur, M. R., ... & Watt, R. G. (2019). Oral diseases: a global public health challenge. *The Lancet*, *394*(10194), 249-260.

4.Rathee, M., & Sapra, A. (2024). Dental Caries.[Updated 2023 Jun 21]. *StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*.

5.Gasner, N. S., & Schure, R. S. (2021). Periodontal Disease.[Updated 2020 May 18]. *StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*.

6.Lertpimonchai A, Rattanasiri S, Arj-Ong Vallibhakara S, Attia J, Thakkinstian A. The association between oral hygiene and periodontitis: a systematic

review and meta-analysis. Int Dent J. 2017 Dec;67(6):332-343. doi: 10.1111/idj.12317.

7.Watters C, Brar S, Pepper T. Cancer of the Oral Mucosa. [Updated 2024 Mar 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK565867/

8.Tettamanti L, Gaudio RM, Iapichino A, Mucchi D, Tagliabue A. Genetic susceptibility and periodontal disease: a retrospective study on a large italian sample. Oral Implantol (Rome). 2017 Apr 10;10(1):20-27. doi: 10.11138/orl/2017.10.1.020.

9.Opal, S., Garg, S., Jain, J., & Walia, I. (2015). Genetic factors affecting dental caries risk. *Australian dental journal*, *60*(1), 2-11.

10.Laytragoon Lewin N, Karlsson JE, Robinsson D, Fagerberg M, Kentsson M, Sayardoust S, Nilsson M, Shamoun L, Andersson BÅ, Löfgren S, Rutqvist LE, Lewin F. Influence of single nucleotide polymorphisms among cigarette smoking and non-smoking patients with coronary artery disease, urinary bladder cancer and lung cancer. PLoS One. 2021 Jan 28;16(1):e0243084. doi: 10.1371/journal.pone.0243084.

11.Zou J, Meng M, Law CS, Rao Y, Zhou X. Common dental diseases in children and malocclusion. Int J Oral Sci. 2018 Mar 13;10(1):7. doi: 10.1038/s41368-018-0012-3.

12.Belling K, Russo F, Jensen AB, Dalgaard MD, Westergaard D, Rajpert-De Meyts E, Skakkebæk NE, Juul A, Brunak S. Klinefelter syndrome comorbidities linked to increased X chromosome gene dosage and altered protein interactome activity. Hum Mol Genet. 2017;26(7):1219-1229. doi: 10.1093/hmg/ddx014.

13.Joy-Thomas A, Lalwani Z, Guajardo L, Valenza J, Fakhouri WD. The Role of Genetics in Human Oral Health: A Systematic-Narrative Review. Dent J (Basel). 2025 Mar 16;13(3):133. doi: 10.3390/dj13030133.

14.Al Eid, R. The Role of Molecular Biology in the Oral and Maxillofacial Surgical Practices. *Medical Science: Recent Advances and Applications2025. 7*, *7*, 1-27.

15.Al-Eid, R. (2018). Molecular Biology Applications in Oral and Maxillofacial Surgery. *Cosmetol & Oro Facial Surg*, *4*(131), 2.

16.Manvikar V, Kulkarni R, Koneru A, Vanishree M. Role of human papillomavirus and tumor suppressor genes in oral cancer. J Oral Maxillofac Pathol. 2016 Jan-Apr;20(1):106-10. doi: 10.4103/0973-029X.180958.

17.Mbemi, A., Khanna, S., Njiki, S., Yedjou, C. G., & Tchounwou, P. B. (2020). Impact of gene–environment interactions on cancer development. *International journal of environmental research and public health*, *17*(21), 8089.

18.Kang, J., Le, V. N. T., Lee, D. W., & Kim, S. (2024). Diagnosing oral and maxillofacial diseases using deep learning. *Scientific Reports*, *14*(1), 2497.

19.Lixandru CI, Maniu I, Cernuşcă-Miţariu MM, Domnariu CD. Oral infections - a retrospective study of patients treated in the Oral and Maxillofacial Surgery clinic of the Emergency County Clinical Hospital in Sibiu. Med Pharm Rep. 2024 Jul;97(3):380-389. doi: 10.15386/mpr-2759. Epub 2024 Jul 30.

20.Abdul NS, Shenoy M, Reddy NR, Sangappa SB, Shivakumar GC, Di Blasio M, Cicciù M, Minervini G. Gene sequencing applications to combat oral-cavity related disorders: a systematic review with meta-analysis. BMC Oral Health. 2024 Jan 17;24(1):103. doi: 10.1186/s12903-023-03541-7.