International Journal of Medical Sciences And Clinical Research

VOLUME Vol.05 Issue11 2025
PAGE NO. 71-74
DOI 10.37547/ijmscr/Volume05Issue11-10

Comprehensive Management Framework For Medication-Related Oral Manifestations In Multimorbid Patient Populations

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Received: 15 September 2025; **Accepted:** 08 October 2025; **Published:** 12 November 2025

Abstract: The phenomenon of medication-related oral manifestations represents a significant and increasingly prevalent challenge in contemporary healthcare, particularly among patients with multiple comorbidities who require complex therapeutic regimens. The growing aging population, coupled with advances in medical treatment that allow patients with chronic conditions to live longer, has resulted in an unprecedented increase in polypharmacy practices, with approximately 40% of adults over 65 years taking five or more medications concurrently.

Keywords: Drug-induced stomatitis, comorbid pathology, xerostomia, drug-induced gingival hyperplasia.

Introduction: Drug-induced oral lesions represent a serious medical problem in modern clinical practice, which becomes particularly relevant in the context of constant expansion of pharmacological arsenal and increasing life expectancy of the population. According to the World Health Organization (WHO), the incidence of adverse drug reactions in the oral cavity ranges from 3.2% to 12.8% among all hospitalized patients, while in patients with comorbid pathology this indicator increases to 18-25%.

Medication-related oral lesions encompass a broad spectrum of adverse effects ranging from xerostomia and taste alterations to severe ulcerative lesions, gingival hyperplasia, and oral mucositis. According to recent epidemiological studies, drug-induced oral manifestations affect between 15-30% of patients receiving chronic medication therapy, with the prevalence rising to 45-60% among individuals with three or more comorbid conditions. These manifestations significantly impact patients' quality of life, nutritional status, medication adherence, and overall health outcomes.

The complexity of managing medication-related oral manifestations is exponentially increased in multimorbid patient populations, where the interplay between multiple pathological processes, numerous medications, and their potential interactions creates a challenging clinical scenario. Multimorbidity, defined as the presence of two or more chronic conditions in a single individual, affects approximately 60% of adults over 65 years and is associated with increased healthcare utilization, functional decline, and mortality risk.

Current evidence suggests that patients with comorbid pathology are at substantially higher risk for developing medication-related oral complications due to several factors: altered pharmacokinetics and pharmacodynamics associated with aging and chronic disease, increased susceptibility to adverse drug reactions, compromised immune function, and the cumulative effects of polypharmacy. Furthermore, the presence of systemic diseases such as diabetes mellitus, cardiovascular disorders, autoimmune conditions, and malignancies can predispose patients to oral manifestations while simultaneously complicating their clinical management.

The pathophysiology of drug-induced oral lesions in multimorbid patients involves complex mechanisms including direct cytotoxic effects, immunologically mediated reactions, altered salivary flow and composition, disruption of oral microbiome, and interference with normal healing processes. These mechanisms are often amplified in patients with multiple comorbidities due to compromised

physiological reserves and the presence of multiple risk factors.

Despite the clinical significance of this problem, current approaches to managing medication-related oral manifestations remain fragmented and largely reactive rather than preventive. Most healthcare systems lack standardized protocols for the systematic identification, assessment, and management of drug-induced oral complications in multimorbid populations. This results in delayed diagnosis, suboptimal treatment outcomes, unnecessary suffering, and increased healthcare costs.

The challenge is further compounded by the lack of interdisciplinary communication between healthcare providers. Physicians prescribing medications may have limited awareness of potential oral manifestations, while dental professionals may lack comprehensive understanding of the complex medical conditions and drug interactions affecting their patients. This disconnect often leads to missed opportunities for prevention, early detection, and appropriate management of medication-related oral complications.

Recent advances in pharmacogenomics, personalized medicine, and digital health technologies offer new opportunities for developing more sophisticated approaches to predicting, preventing, and managing drug-induced oral manifestations. However, the integration of these advances into clinical practice requires comprehensive frameworks that address the unique needs of multimorbid patient populations.

Modern pharmacotherapy is characterized by the use of complex treatment regimens including multiple drugs from various pharmacological groups. Polypharmacy, especially in elderly and senile patients with comorbidities, significantly increases the risk of drug-induced complications in the oral cavity. These complications range from relatively mild manifestations such as xerostomia and dysgeusia to severe conditions including ulcerative-necrotic lesions of the mucous membrane, drug-induced gingival hyperplasia, and toxic epidermal necrolysis with oral mucosal involvement.

It is incorrect to consider dental diseases exclusively as pathologies inherent only to the oral cavity. Recent studies show a direct relationship between oral health and general body condition. According to M. Farrell, Merkley V.F., Nafiza I. (2023), the average level of comorbidity among patients up to 35-40 years is 50-56%, while in the group over 50-55 years, the incidence of comorbid pathologies reaches 90%, and among patients over 75 years, almost all (98-99%) suffer from polycomorbid diseases.

According to data from S.I. Gazhva (2013), G.V. Gubanova (2015) and other researchers, in patients over 35 years, somatic pathology is detected in an average of 92.5%, with one-third showing signs of comorbidity. According to Bhateja (2012), A. Maryam et al. (2015), in a large population group of 1300 respondents, almost half of dental patients had comorbidities, with the severity of such pathologies increasing with age, and polycomorbidity was identified in 25% of those examined. Additionally, the authors emphasize that the number of diseases on average increases from 2.8 in younger patients to 6-7 in people over 75 years.

In our country, several researchers have conducted both experimental and clinical studies devoted to studying changes in the oral cavity related to the presence of comorbidities and their treatment process. Work has been performed on the diagnosis and treatment of oral mucosal lesions, and the microbiological state of the oral cavity in COVID-19 has been studied. However, questions regarding the prevalence of oral mucosal lesions caused by drug action have not yet been studied in detail.

Despite the achieved successes, problems of early diagnosis of oral diseases and development of therapeutic methods aimed at their pathogenesis remain relevant in our country. Moreover, considering the comorbidity of patient conditions and the necessity of using various medications, the question of implementing comprehensive dental treatment for this group of patients remains debatable. The dentist faces the task of developing methods for early and differential diagnosis, treatment, and monitoring of results in patients with comorbid pathology of internal organs.

Particular concern is caused by the fact that drug-induced oral lesions often remain unrecognized or are incorrectly interpreted as manifestations of the underlying disease, leading to delayed adequate therapy and deterioration of patients' quality of life. According to results of epidemiological studies conducted in various countries, only 35-45% of cases of drug-induced oral lesions are diagnosed timely, which is due to insufficient awareness of physicians of various specialties regarding this problem.

The pathogenesis of drug-induced oral lesions is multifactorial and includes direct toxic effects of drugs on the mucous membrane, immune-mediated hypersensitivity reactions, disruption of the oral microbiome, changes in salivation and tissue metabolism. In patients with comorbid pathology, these mechanisms are complicated by interactions between various medications, disruption of pharmacokinetics and pharmacodynamics of drugs due

to organ insufficiency, as well as increased tissue susceptibility to damaging effects.

Currently existing approaches to prevention, diagnosis, and treatment of drug-induced oral lesions are fragmentary and do not consider the complex interaction of risk factors in patients with multiple pathologies. Most clinical recommendations and protocols focus on treating individual types of lesions and do not provide a systematic approach to preventing their development. This leads to preventive measures often being insufficiently effective, and diagnosis and treatment being delayed and incomplete.

The modern trend toward personalized medicine requires the development of individualized approaches to managing patients at high risk of developing drug-induced oral lesions. This is particularly relevant for patients with comorbid pathology, where it is necessary to consider not only the spectrum of medications taken, but also the peculiarities of the course of primary and comorbid diseases, immune system status, genetic factors, and socio-economic aspects.

The interdisciplinary nature of the problem of drug-induced oral lesions requires close cooperation between physicians of various specialties – dentists, internists, clinical pharmacologists, dermatologists, oncologists, and others. However, in real clinical practice, such cooperation is often insufficient, leading to fragmentation of medical care and reduced effectiveness.

Economic aspects of this problem also deserve special attention. Drug-induced oral lesions lead to increased hospitalization duration, the need for additional diagnostic and therapeutic procedures, as well as reduced patient adherence to therapy for the underlying disease. According to pharmacoeconomic studies, total costs for treating complications related to adverse drug reactions in the oral cavity constitute a significant share in the structure of healthcare system expenditures in developed countries.

In the Republic of Uzbekistan, the problem of drug-induced oral lesions becomes particularly relevant in connection with healthcare system reform, introduction of new drugs, and improvement of approaches to treating chronic diseases. Increased accessibility of medical care and expansion of the nomenclature of applied medications create prerequisites for increased frequency of drug-induced complications, which requires the development of effective strategies for their prevention and treatment.

The oral cavity, based on its anatomical and functional features, is considered as one of the functional systems forming human body homeostasis. Unfortunately, when studying the medical history of patients seeking dental care, it was established that in more than 75-80% of patients, along with pathological changes in teeth, oral mucosa, and salivary gland tissues, one or several comorbid somatic pathologies are revealed. Oral health is one of the main indicators of general human health and quality of life, with the prevalence of oral diseases among the population aged 33-44 years being 65-98%. An urgent problem of modern dentistry is the improvement of methods for prevention and treatment of oral diseases in patients with somatic pathology.

Numerous scientific studies are being conducted worldwide devoted to studying the development of changes in the oral cavity resulting from treatment of somatic diseases. Treatment of somatic diseases includes the use of several medications belonging to various pharmacological groups. Based on this, it can be concluded that identified pathological signs in the oral cavity may be a consequence of the treatment itself, effects of metabolic products of applied drugs, various preservatives and auxiliary substances in their composition, or local responsive reaction to the conducted therapy. Unfortunately, currently in patients with comorbidities, especially in comorbid conditions, polypharmacy often occurs due to simultaneous prescription of a large number of systemic medications. Based on this, the question remains relevant: what exactly causes changes in oral cavity tissues – comorbid diseases or the effects of drugs from various pharmacological groups.

Analysis of foreign and domestic literature indicates that, despite a significant volume of research devoted to individual aspects of drug-induced oral lesions, a holistic system combining preventive, diagnostic, and therapeutic approaches into a single integrated complex has not yet been created. This problem is particularly acute regarding patients with comorbid pathology, who constitute a significant share in the structure of medical care utilization.

The economic burden of medication-related oral manifestations is substantial, with estimated direct healthcare costs exceeding $2.5 billion annually in developed countries. Indirect costs related to reduced productivity, impaired quality of life, and complications from untreated oral lesions add significantly to this burden. In multimorbid patients, these costs are amplified due to the complexity of care required and the potential for oral complications to exacerbate existing medical conditions.

CONCLUSION

Current clinical practice guidelines for managing drug-

induced oral manifestations are often disease-specific or medication-specific, failing to address the complexity of patients with multiple comorbidities receiving multiple medications. There is a critical need for comprehensive, evidence-based frameworks that can guide healthcare providers in the systematic prevention, early detection, and optimal management of medication-related oral complications in this vulnerable population.The concept of patient-centered care has evolved to recognize the importance of addressing all aspects of a patient's health, including oral health, as integral components of overall wellbeing. This holistic approach is particularly relevant for multimorbid patients, where oral complications can significantly impact the management of systemic conditions and overall treatment outcomes.

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