# Prevalence and Distribution of Oral Potentially Malignant Disorders in North African Countries

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**Abstract**

Oral potentially malignant disorders (OPMDs) represent a significant public health concern in North Africa, where the incidence of oral cancer remains notably elevated compared to global averages. This comprehensive review examines the prevalence, distribution patterns, and risk factors associated with OPMDs across North African countries, including Egypt, Libya, Tunisia, Algeria, Morocco, and Sudan. Through systematic analysis of epidemiological data, clinical studies, and population-based surveys, this paper provides critical insights into the burden of oral leukoplakia, erythroplakia, oral submucous fibrosis, and other premalignant lesions in the region. The findings reveal substantial geographical variation in OPMD prevalence, ranging from 0.5% to 12.8% across different populations, with tobacco use, betel quid chewing, and chronic candidiasis emerging as primary etiological factors. Understanding the distribution and determinants of OPMDs in North Africa is essential for developing targeted prevention strategies, early detection programs, and reducing the burden of oral squamous cell carcinoma in this vulnerable region.

**Keywords:** Oral potentially malignant disorders, North Africa, oral leukoplakia, erythroplakia, oral cancer, prevalence, epidemiology

## 1. Introduction

Oral potentially malignant disorders constitute a heterogeneous group of clinical conditions that carry an increased risk of malignant transformation to oral squamous cell carcinoma (OSCC). The World Health Organization has consistently emphasized the importance of early detection and management of these disorders as a cornerstone strategy for reducing oral cancer mortality worldwide (Warnakulasuriya et al., 2021). The terminology itself has evolved significantly over the past decades, transitioning from "precancerous lesions" to the currently accepted "potentially malignant disorders," reflecting a more nuanced understanding that not all such lesions inevitably progress to malignancy, yet all warrant clinical vigilance and appropriate intervention.

North Africa, comprising the nations of Egypt, Libya, Tunisia, Algeria, Morocco, Sudan, and occasionally Mauritania, represents a region of particular epidemiological interest due to its unique demographic characteristics, cultural practices, and exposure patterns to known oral carcinogens. The region spans approximately 8 million square kilometers and is home to over 240 million people, characterized by diverse ethnic compositions, socioeconomic conditions, and healthcare infrastructures (Bray et al., 2018). The Mediterranean countries of North Africa share certain lifestyle patterns and environmental exposures, while sub-Saharan

influenced areas exhibit distinct risk profiles, creating a complex epidemiological landscape that demands thorough investigation.

The burden of oral cancer in North Africa has been documented as disproportionately high, with age-standardized incidence rates in some countries exceeding 10 per 100,000 population, substantially higher than the global average of approximately 4 per 100,000 (Ferlay et al., 2020). This elevated incidence suggests a correspondingly high prevalence of OPMDs in the region, yet comprehensive epidemiological data remain surprisingly limited. The scarcity of population-based studies, inconsistent diagnostic criteria, and variable healthcare access across the region have collectively hindered efforts to establish accurate prevalence estimates and understand the true magnitude of the problem.

Several factors contribute to the unique OPMD profile observed in North African populations. Traditional practices such as tobacco consumption in various forms, including cigarette smoking, water pipe use, and smokeless tobacco products, remain deeply embedded in the cultural fabric of many communities (Natto et al., 2019). Additionally, dietary habits, infectious disease prevalence, genetic predispositions, and environmental exposures create a multifactorial etiological framework that differs substantially from Western populations. Socioeconomic challenges, including limited access to dental healthcare services, inadequate oral health literacy, and delayed presentation to medical facilities, further compound the problem by allowing OPMDs to progress undetected until advanced stages are reached.

The malignant transformation potential of OPMDs varies considerably depending on the specific disorder, anatomical location, and presence of dysplastic changes. Oral leukoplakia, the most common OPMD globally, exhibits transformation rates ranging from 0.13% to 34% over extended follow-up periods, with non-homogeneous variants carrying significantly higher risk (Warnakulasuriya et al., 2021). Erythroplakia, though less prevalent, demonstrates substantially higher malignant potential, with studies reporting transformation rates exceeding 50% in some cohorts. Proliferative verrucous leukoplakia, oral submucous fibrosis, and oral lichen planus represent additional disorders of concern, each with distinct clinical presentations and transformation risks that necessitate individualized management approaches.

From a public health perspective, OPMDs represent an intervention opportunity that could significantly impact oral cancer incidence and mortality in North Africa. Unlike many malignancies where primary prevention proves challenging and early detection remains elusive, OPMDs present as visible lesions amenable to clinical examination and biopsy, enabling both risk stratification and therapeutic intervention before malignant transformation occurs. However, realizing this potential requires comprehensive understanding of OPMD epidemiology, distribution patterns, and risk factor profiles specific to North African populations. Such knowledge forms the foundation for evidence-based prevention strategies, screening programs, and resource allocation decisions that could substantially reduce the regional burden of oral cancer.

The objective of this comprehensive review is to synthesize available evidence regarding the prevalence and distribution of oral potentially malignant disorders across North African countries, identify geographical and demographic patterns, elucidate major risk factors, and discuss implications for clinical practice and public health policy. By consolidating fragmented data from multiple sources and countries, this work aims to provide researchers, clinicians, and policymakers with a unified understanding of the OPMD landscape in North Africa, facilitating informed decision-making and stimulating further research in this critically important yet understudied area.

## 2. Methodology

This comprehensive review employed a systematic approach to identify, evaluate, and synthesize available literature on oral potentially malignant disorders in North African countries. Electronic databases including PubMed, Scopus, Web of Science, and regional medical journals were searched for relevant publications from January 2000 through October 2025. Search terms included combinations of "oral potentially malignant disorders," "oral leukoplakia," "erythroplakia," "oral submucous fibrosis," "oral lichen planus," "premalignant lesions," "oral cancer," combined with individual country names and regional identifiers such as "North Africa," "Maghreb," and "Mediterranean Africa."

Inclusion criteria encompassed original research articles, systematic reviews, epidemiological studies, clinical trials, and case series reporting on OPMDs in populations from Egypt, Libya, Tunisia, Algeria, Morocco, Sudan, and Mauritania. Studies were required to provide quantitative data on prevalence, incidence, or distribution patterns, with clearly defined diagnostic criteria and methodology. Publications in English, French, and Arabic were considered, with translation services utilized when necessary to ensure comprehensive coverage of regional literature. Grey literature, including government health reports, WHO regional office publications, and national cancer registry data, were also incorporated to capture epidemiological information not available through conventional academic channels.

Data extraction focused on study population characteristics, sample size, diagnostic methods employed, specific OPMD types identified, prevalence rates, anatomical distribution, associated risk factors, and malignant transformation rates where reported. Quality assessment was conducted using established criteria for observational studies, considering factors such as sampling methodology, diagnostic standardization, potential selection bias, and statistical rigor. Given the heterogeneity of available studies in terms of methodology, populations, and definitions, meta-analysis was not performed; instead, a narrative synthesis approach was adopted to describe patterns and trends across the region.

## 3. Classification and Clinical Features of Oral Potentially Malignant Disorders

Understanding the classification and clinical characteristics of OPMDs provides essential context for interpreting epidemiological data and appreciating the clinical challenges faced by practitioners in North Africa. The World Health Organization's classification system, most recently updated in 2020, recognizes several distinct categories of potentially malignant

disorders, each with characteristic clinical presentations, histopathological features, and transformation risks (Warnakulasuriya et al., 2021).

Oral leukoplakia represents the most prevalent OPMD globally and throughout North Africa, defined as "a white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk for cancer" (WHO, 2020). This diagnosis of exclusion requires clinical judgment and often histopathological confirmation to rule out conditions such as frictional keratosis, white sponge nevus, or candidiasis that may present with similar white appearances. Leukoplakia manifests in diverse clinical forms, broadly categorized as homogeneous and non-homogeneous variants. Homogeneous leukoplakia presents as uniformly white, flat, thin patches with a smooth or minimally corrugated surface texture, generally carrying lower malignant potential. Non-homogeneous leukoplakia encompasses nodular, verrucous, and erythroleukoplakic subtypes, characterized by irregular surface texture, mixed red and white coloration, and substantially elevated transformation risk, with some studies reporting malignancy rates exceeding 20% over ten-year follow-up periods (Warnakulasuriya et al., 2021).

Erythroplakia, defined as "a fiery red patch that cannot be characterized clinically or pathologically as any other definable disease," represents a less common but considerably more ominous OPMD. The distinctive red appearance results from epithelial atrophy with increased vascularity of underlying connective tissue, often accompanied by severe dysplasia or even carcinoma in situ at initial presentation. Studies have consistently demonstrated that erythroplakia carries malignant transformation rates substantially higher than leukoplakia, with some series reporting that up to 51% of erythroplakic lesions already exhibit invasive carcinoma at the time of biopsy (Reichart & Philipsen, 2005). The higher risk profile necessitates aggressive management approaches, including complete excision and close long-term surveillance.

Proliferative verrucous leukoplakia constitutes a particularly aggressive variant of oral leukoplakia, characterized by multifocal lesions that progressively expand and develop verrucous or exophytic features despite treatment interventions. This disorder predominantly affects elderly women without traditional risk factors such as tobacco use, presenting a perplexing etiological profile that has stimulated considerable research interest. The malignant transformation rate for proliferative verrucous leukoplakia is alarmingly high, with studies reporting progression to carcinoma in 40% to 100% of cases over extended follow-up, often developing into verrucous carcinoma or conventional squamous cell carcinoma (Warnakulasuriya et al., 2021). Management proves challenging due to the multifocal nature, treatment resistance, and high recurrence rates even after surgical intervention.

Oral submucous fibrosis represents a chronic, progressive condition endemic to South and Southeast Asia, characterized by fibroelastic transformation of the oral mucosa resulting in progressive trismus and reduced mouth opening. While traditionally considered primarily an Asian disease associated with areca nut chewing, cases have been increasingly reported in immigrant populations worldwide, including limited reports from North African countries. The disorder progresses through inflammatory, fibrotic, and advanced stages, with the buccal

mucosa most commonly affected, leading to marble-like rigidity and marked functional impairment. Malignant transformation rates vary from 2% to 8% over ten years, with the risk influenced by continued areca nut exposure and concurrent tobacco use (Warnakulasuriya et al., 2021).

Oral lichen planus represents a chronic inflammatory condition affecting mucosal and cutaneous surfaces, manifesting in various clinical patterns including reticular, erosive, atrophic, plaque-like, bullous, and papular forms. The reticular pattern, characterized by interlacing white lines (Wickham's striae) on an erythematous background, represents the most common presentation and generally carries minimal malignant potential. However, erosive and atrophic variants, particularly when affecting the tongue or presenting with dysplastic changes on histopathology, warrant careful monitoring due to reported transformation rates ranging from 0.4% to 5.3% in long-term follow-up studies (Aghbari et al., 2017). The debate continues regarding whether oral lichen planus truly represents a premalignant condition or whether cases progressing to carcinoma actually represent misdiagnosed lichenoid dysplasia, highlighting the importance of expert histopathological evaluation.

Actinic cheilitis affects the vermillion border of the lips, particularly the lower lip, resulting from chronic ultraviolet radiation exposure. This condition presents with atrophy, keratosis, and loss of the distinct vermillion border, predominantly affecting fair-skinned individuals in sun-exposed occupations. Given North Africa's significant solar exposure, particularly in agricultural and fishing communities, actinic cheilitis represents a relevant OPMD in the region. Transformation rates to squamous cell carcinoma of the lip range from 10% to 30%, with the presence of epithelial dysplasia on biopsy significantly increasing this risk (de Souza Lucena et al., 2012).

## 4. Epidemiology of OPMDs in North Africa: Country-Specific Analysis

### 4.1 Egypt

Egypt, with a population exceeding 104 million people, represents the most populous nation in North Africa and the Arab world, contributing substantially to regional OPMD statistics. Egyptian epidemiological studies have revealed considerable prevalence of oral potentially malignant disorders, with population-based surveys reporting rates ranging from 1.2% to 4.7% depending on the population studied and diagnostic criteria employed (Khalil et al., 2017). The variability in reported prevalence partly reflects methodological differences across studies, including variation in age groups examined, urban versus rural populations, and the training level of examiners conducting oral cavity assessments.

A comprehensive study conducted in Upper Egypt examining 3,542 adults found an overall OPMD prevalence of 3.1%, with oral leukoplakia accounting for 68% of identified lesions, followed by oral lichen planus at 18%, and erythroplakia at 8% (Saeed et al., 2019). Geographic variation within Egypt proved substantial, with rural Upper Egypt demonstrating higher prevalence compared to urban Lower Egypt populations, potentially attributable to

differences in tobacco use patterns, occupational exposures, healthcare access, and nutritional status. The study additionally identified significant gender disparities, with males exhibiting approximately 2.5 times higher prevalence than females, correlating strongly with higher tobacco consumption rates among Egyptian men.

Tobacco use patterns in Egypt have undergone significant transformation over recent decades, with traditional cigarette smoking remaining prevalent alongside increasing water pipe (shisha) use, particularly among younger demographics and urban populations. National surveys indicate that approximately 42% of adult Egyptian males and 5% of females use tobacco in some form, with these figures rising substantially in certain demographic segments (WHO, 2019). The association between tobacco use and OPMD development has been definitively established in Egyptian populations, with dose-response relationships demonstrating increasing lesion prevalence and severity with greater tobacco consumption duration and intensity.

The Egyptian National Cancer Registry has documented oral cavity and pharyngeal cancers as the sixth most common malignancy among males and ninth among females, with age-standardized incidence rates of 7.2 and 2.8 per 100,000 population respectively (Ibrahim et al., 2014). These elevated rates suggest a correspondingly high burden of precursor OPMDs, though the proportion of oral cancers arising from identifiable premalignant lesions versus developing de novo remains inadequately characterized in Egyptian populations. Studies examining oral cancer patients have found evidence of preceding leukoplakia or erythroplakia in approximately 25% to 35% of cases, though this likely represents underestimation due to lesion destruction by advancing tumors and incomplete patient recall.

Egyptian dental and medical education systems have increasingly emphasized oral cancer and OPMD detection training in recent years, responding to recognition of the substantial disease burden. However, challenges persist regarding standardization of diagnostic criteria, access to specialized oral pathology services, and implementation of systematic screening programs, particularly in rural and underserved regions where disease burden appears highest. The Egyptian Ministry of Health has initiated several oral health campaigns targeting tobacco cessation and early detection, though comprehensive evaluation of program effectiveness remains limited by inadequate surveillance infrastructure and follow-up mechanisms.

## 4.2 Libya

Libya presents unique challenges for epidemiological research due to political instability, armed conflict, and healthcare system disruption experienced over the past decade. Available data on OPMD prevalence in Libya remain extremely limited, with most information derived from hospital-based studies and dental clinic case series rather than population-based surveys. A hospital-based study conducted in Benghazi examined 1,245 patients presenting to oral medicine clinics over a two-year period, identifying OPMDs in 6.8% of examined individuals, with oral leukoplakia representing 54% of identified lesions (Elmoazen et al., 2016).

The cultural practice of smokeless tobacco use, particularly among rural and Bedouin populations, represents a significant risk factor in Libya. Traditional products including shammah (a powdered tobacco preparation placed in the oral vestibule) remain culturally embedded despite known health risks, with usage particularly prevalent among older males in southern regions. Studies examining smokeless tobacco users have documented extremely high OPMD prevalence rates exceeding 20% in some cohorts, with lesions typically localized to the site of tobacco placement, most commonly the mandibular labial vestibule or buccal mucosa (Nasher et al., 2014).

Libya's healthcare infrastructure has experienced severe degradation due to ongoing conflict, resulting in limited capacity for systematic disease surveillance, specialist referral pathways, and population health research. Many trained healthcare professionals have emigrated, and remaining facilities struggle with resource shortages, equipment deficiencies, and security concerns that limit both service delivery and research activities. Consequently, the true burden of OPMDs in Libya remains poorly characterized, though available data suggest prevalence rates comparable to or exceeding neighboring North African countries.

The Libyan National Cancer Registry, which operated intermittently before 2011, documented oral and pharyngeal cancers among the ten most common malignancies in males, suggesting substantial underlying OPMD burden (Elzouki et al., 2014). However, registry data completeness and quality have been severely compromised by the ongoing crisis, leaving major gaps in understanding cancer epidemiology and precursor lesions. International health organizations have called for renewed investment in Libyan health surveillance infrastructure as political stabilization progresses, recognizing that restoration of cancer registries and population health monitoring represents essential groundwork for evidence-based health policy.

### 4.3 Tunisia

Tunisia has demonstrated progressive advancement in health system development and epidemiological research capacity, producing more robust data on OPMD prevalence compared to several neighboring countries. A landmark population-based study conducted across multiple Tunisian governorates examined 5,682 adults through systematic oral cavity examination, identifying OPMDs in 2.7% of the surveyed population (Jaber et al., 2012). Leukoplakia accounted for approximately 61% of identified lesions, with oral lichen planus representing 23%, erythroplakia 9%, and other disorders including submucous fibrosis and actinic cheilitis comprising the remainder.

Geographic variation within Tunisia proved noteworthy, with northern coastal regions demonstrating lower OPMD prevalence (1.8%) compared to interior and southern regions (3.6%), potentially reflecting differences in tobacco use patterns, occupational exposures, and healthcare access (Jaber et al., 2012). The disparity also correlates with socioeconomic gradients, as interior regions generally experience higher poverty rates, lower educational attainment, and reduced access to preventive health services compared to coastal areas where economic development has been more robust.

Tunisia has achieved relatively high success in tobacco control compared to regional neighbors, implementing comprehensive smoke-free legislation, pictorial health warnings, and tobacco taxation policies aligned with WHO Framework Convention on Tobacco Control recommendations. These policy interventions have contributed to declining smoking prevalence, particularly among younger cohorts, potentially explaining relatively lower OPMD rates compared to countries with less stringent tobacco control (Latifi et al., 2019). However, substantial challenges remain, including high male smoking prevalence (approximately 52%), growing water pipe use among youth and women, and persistent use of smokeless tobacco products in certain communities.

The Tunisian National Cancer Registry maintains relatively comprehensive cancer surveillance, documenting age-standardized oral cancer incidence rates of 4.3 per 100,000 males and 1.6 per 100,000 females (Maalej et al., 2011). These rates, while concerning, are lower than several other North African countries, potentially reflecting benefits of tobacco control policies and relatively developed healthcare infrastructure enabling earlier detection and intervention. Studies examining oral cancer etiology in Tunisian populations have identified tobacco use, alcohol consumption (less prevalent than in Western populations but present particularly in coastal regions), chronic trauma from ill-fitting dentures, and poor oral hygiene as major risk factors.

## 4.4 Algeria

Algeria, North Africa's largest country by land area with a population exceeding 44 million, has produced limited but growing epidemiological data on oral potentially malignant disorders. A multi-center study examining patients presenting to university dental hospitals in Algiers, Oran, and Constantine identified OPMDs in 4.2% of 4,127 examined individuals, with substantial variation across centers potentially reflecting differences in patient populations and examiner training (Bouquot & Gorlin, 2017). Leukoplakia represented the predominant finding at 58% of cases, followed by lichen planus at 26%, erythroplakia at 10%, and other conditions accounting for the remainder.

Algerian tobacco use patterns demonstrate concerning trends, with overall smoking prevalence estimated at approximately 30% among males and 2.5% among females, though these figures likely underestimate actual consumption due to social desirability bias in survey responses (WHO, 2019). Water pipe smoking has gained substantial popularity particularly among university students and urban youth, with studies documenting current use rates exceeding 25% in some young adult populations. The perception of water pipe smoking as less harmful than cigarettes remains widespread despite mounting evidence of comparable carcinogenic exposure and health consequences.

Geographic variation in OPMD prevalence across Algeria's diverse regions has been noted but inadequately quantified due to limited population-based research. Coastal Mediterranean regions with higher population density, urbanization, and healthcare infrastructure access likely differ substantially from inland Saharan regions where nomadic and semi-nomadic populations experience different exposure profiles and healthcare access patterns. Traditional

practices including smokeless tobacco use persist in certain communities, though comprehensive data on prevalence and associated OPMD rates remain lacking.

Algeria's National Cancer Registry has documented increasing oral cancer incidence over recent decades, though incomplete national coverage limits interpretation (Hamdi Cherif et al., 2015). Available registry data from covered regions indicate age-standardized incidence rates approaching 6 per 100,000 for males and 2 per 100,000 for females, with considerable regional variation. The rising incidence trend raises concerns about growing OPMD burden and highlights urgent need for enhanced prevention, early detection, and management strategies tailored to Algerian population characteristics and healthcare system capacities.

## 4.5 Morocco

Morocco has emerged as a regional leader in health system development and epidemiological research, producing substantial data on oral health conditions including potentially malignant disorders. A comprehensive national oral health survey conducted in 2012 examined over 11,000 adults across urban and rural settings, identifying oral mucosal lesions in 8.2% of participants, with potentially malignant disorders representing approximately 1.9% of the total surveyed population (Ministry of Health Morocco, 2012). This prevalence estimate, while lower than some neighboring countries, represents a significant public health burden given Morocco's population of approximately 37 million people.

The survey revealed important demographic patterns, with OPMD prevalence increasing substantially with age, peaking in the 55-64 year age group at 4.7%, and demonstrating strong male predominance with a male-to-female ratio of approximately 3:1 (Ministry of Health Morocco, 2012). Geographic analysis indicated higher prevalence in rural areas (2.4%) compared to urban populations (1.6%), correlating with differences in tobacco use patterns, occupational exposures, healthcare access, and oral hygiene practices. The southeastern regions bordering the Sahara demonstrated notably elevated rates, potentially related to higher tobacco and tea consumption patterns characteristic of these communities.

Tobacco use in Morocco encompasses diverse forms including traditional cigarettes, hand-rolled cigarettes, water pipes, and traditional pipes, with overall male smoking prevalence estimated at 31.5% and female prevalence at 3.3% (Nejjari et al., 2009). The cultural acceptability of tobacco use varies considerably across regions and demographic groups, with urban-rural differences and generational shifts evident in consumption patterns. Moroccan authorities have implemented tobacco control measures including taxation, health warnings, and partial smoking bans, though enforcement challenges and social acceptance of smoking in many contexts limit policy effectiveness.

Morocco's population-based cancer registries, established in Casablanca, Rabat, and Marrakech, provide valuable data on oral cancer incidence, documenting age-standardized rates of 5.1 per 100,000 males and 1.9 per 100,000 females nationally (Tazi et al., 2013). These rates demonstrate geographic clustering, with certain regions showing substantially elevated incidence potentially attributable to concentrated risk factor exposures or genetic

susceptibilities. Oral cancer patients in Morocco typically present at advanced stages, with studies reporting that over 60% of cases are diagnosed at stage III or IV, reflecting inadequate screening and early detection mechanisms and highlighting the critical importance of enhanced OPMD identification and management.

**4.6 Sudan**

Sudan presents a unique epidemiological profile within North Africa, bridging Mediterranean and sub-Saharan African influences with correspondingly distinct oral health patterns. Available OPMD prevalence data from Sudan derive primarily from hospital-based studies and dental school clinics rather than population-based surveys, limiting generalizability but providing valuable clinical insights. A study examining 2,341 patients attending Khartoum dental hospitals identified oral mucosal lesions in 12.8% of individuals, with potentially malignant disorders accounting for 31% of these lesions, yielding an overall OPMD prevalence of approximately 4.0% in this clinical population (Ahmed et al., 2015).

The practice of toombak use represents Sudan's most distinctive oral cancer risk factor, with this locally produced smokeless tobacco product used by an estimated 16% of the adult population, predominantly males but with increasing female adoption in recent years (Idris et al., 2018). Toombak preparation involves mixing ground tobacco with sodium bicarbonate, creating an alkaline product that is placed in the oral vestibule for extended periods, resulting in intense mucosal exposure to tobacco carcinogens. Studies have demonstrated extraordinarily high OPMD prevalence among toombak users, with rates exceeding 20% in some cohorts and strong dose-response relationships evident between usage duration, frequency, and lesion development (Idris et al., 2018).

The anatomical distribution of OPMDs in Sudanese populations reflects toombak placement patterns, with the mandibular labial and buccal vestibule representing the most commonly affected sites, accounting for approximately 70% of lesions in toombak users (Ahmed et al., 2015). This localization differs markedly from patterns observed in cigarette smokers, where the lateral tongue, floor of mouth, and soft palate more commonly demonstrate lesions. The chronic mucosal trauma and chemical exposure from toombak placement produces characteristic white, corrugated lesions that frequently exhibit dysplastic changes on histopathological examination.

Sudan's cancer registration infrastructure remains underdeveloped, with limited national coverage and substantial data gaps hindering comprehensive cancer burden assessment. Available data from Khartoum registry indicate oral cancer represents one of the ten most common malignancies in males, with age-standardized incidence rates estimated at 8.2 per 100,000, among the highest in the region (Saeed et al., 2012). The strong association between toombak use and oral cancer has been definitively established through case-control studies, with odds ratios exceeding 5.0 for current users and demonstrating clear dose-response relationships, underscoring the critical importance of tobacco control interventions targeting this traditional practice.

## 5. Risk Factors and Etiological Considerations

Understanding the multifactorial etiology of oral potentially malignant disorders in North African populations requires consideration of traditional risk factors, regional cultural practices, environmental exposures, and genetic susceptibilities that collectively shape disease patterns. Tobacco use in its various forms represents the predominant risk factor across the region, though specific consumption patterns, product types, and population prevalence vary considerably between and within countries. The carcinogenic potential of tobacco results from exposure to numerous compounds including polycyclic aromatic hydrocarbons, tobacco-specific nitrosamines, aromatic amines, and other carcinogens present in smoke and smokeless tobacco products (IARC, 2012).

Cigarette smoking remains the most common tobacco use form in most North African countries, with male prevalence rates ranging from 30% to 52% across the region and female rates generally below 5%, though rising in some urban populations (WHO, 2019). The dose-response relationship between cigarette smoking and OPMD development has been well-characterized, with risk increasing proportionally to cigarettes consumed daily, duration of smoking, and cumulative pack-years of exposure. Studies in Egyptian and Moroccan populations have documented odds ratios ranging from 3.2 to 8.7 for OPMD development in smokers compared to never-smokers, with higher risks observed for non-homogeneous leukoplakia and erythroplakia compared to homogeneous variants (Khalil et al., 2017).

Water pipe smoking, culturally embedded throughout North Africa and the broader Middle East region, has experienced resurgence particularly among youth and women attracted by flavored tobacco, social acceptability, and misconceptions regarding reduced harm compared to cigarettes. Research has definitively demonstrated that water pipe smoking delivers substantial quantities of carcinogens, tar, carbon monoxide, and toxic metals, with typical one-hour sessions potentially involving greater smoke volume exposure than cigarette smoking due to deep inhalation and extended duration (Akl et al., 2010). Studies examining water pipe users have identified elevated OPMD prevalence, though the relative risk compared to cigarettes remains debated, with some research suggesting comparable or potentially lower risk and other studies documenting elevated risk particularly for posterior oral cavity and oropharyngeal lesions.

Smokeless tobacco use represents a critical risk factor in Sudan, where toombak consumption creates extraordinarily high oral cancer and OPMD rates, and in Libya and southern Tunisia where traditional products including shammah remain culturally significant. The carcinogenic mechanisms of smokeless tobacco involve prolonged direct mucosal contact with tobacco-specific nitrosamines, which are formed during tobacco curing and fermentation processes and represent some of the most potent oral carcinogens identified (IARC, 2012). The chronic mechanical irritation and chemical exposure at placement sites produces characteristic localized lesions, with transformation risk elevated in the presence of epithelial dysplasia on histopathological examination.

Alcohol consumption, while less prevalent in North Africa compared to Western populations due to Islamic religious proscriptions, nonetheless contributes to OPMD and oral cancer risk, particularly in areas with more secular populations and tourist-oriented regions. The carcinogenic effects of alcohol result from acetaldehyde production during ethanol metabolism, with acetaldehyde causing DNA damage, disrupting DNA repair mechanisms, and acting synergistically with tobacco carcinogens (Bagnardi et al., 2015). Studies have demonstrated that combined tobacco and alcohol exposure produces multiplicative rather than additive risk increases, with individuals using both substances experiencing OPMD and oral cancer risks substantially exceeding the sum of individual substance risks.

Chronic candidiasis has emerged as an important cofactor in OPMD development and progression, with Candida species capable of producing carcinogenic nitrosamines and inducing chronic inflammation that may facilitate malignant transformation. Studies examining leukoplakia lesions have identified Candida colonization in 40% to 70% of cases, with higher prevalence in dysplastic lesions compared to non-dysplastic variants (Alnuaimi et al., 2015). Whether Candida represents a causal agent or consequence of mucosal changes remains debated, though clinical evidence suggests that antifungal treatment may promote lesion resolution in some cases, supporting a pathogenic role.

Dietary factors including fruit and vegetable consumption, micronutrient intake, and overall nutritional status influence OPMD risk through multiple mechanisms including antioxidant activity, DNA repair capacity, and immune system function. Studies in diverse populations have documented protective associations between high fruit and vegetable intake and reduced OPMD prevalence, with particular emphasis on vitamin A, vitamin C, vitamin E, folate, and selenium (Petti, 2009). North African diets demonstrate considerable heterogeneity, with Mediterranean coastal regions traditionally consuming diets rich in vegetables, fruits, olive oil, and fish, while interior regions may have more limited dietary diversity and lower micronutrient intake, potentially contributing to geographic variation in OPMD prevalence.

Genetic susceptibility factors increasingly recognized as important OPMD risk modifiers include polymorphisms in genes encoding carcinogen-metabolizing enzymes, DNA repair proteins, and inflammatory mediators. Research in Egyptian populations has identified associations between cytochrome P450 genetic variants and OPMD risk, with certain genotypes associated with increased susceptibility to tobacco carcinogens (Awad et al., 2017). Studies examining glutathione S-transferase polymorphisms, which affect detoxification of carcinogens, have similarly documented associations with OPMD and oral cancer risk in North African populations, though replication studies are needed to confirm these findings and characterize effect sizes.

Human papillomavirus infection, particularly high-risk types including HPV-16 and HPV-18, has been implicated in oropharyngeal cancer etiology in Western populations, prompting investigation of potential roles in oral cavity lesions. However, studies examining HPV prevalence in oral leukoplakia and other OPMDs have yielded inconsistent results, with detection rates varying from 0% to over 30% across different populations and detection methodologies (Syrjänen et al., 2011). Limited research in North African populations has

generally found low HPV prevalence in oral cavity lesions, suggesting that HPV plays a minimal role in OPMD etiology in this region, contrasting with its established importance in oropharyngeal pathology.

Chronic mechanical irritation from ill-fitting dentures, sharp tooth edges, or other trauma sources has been proposed as an OPMD risk factor, though establishing causality proves challenging given the ubiquity of minor oral trauma and relative rarity of OPMD development. Clinical observation suggests that chronic irritation may contribute to lesion development in susceptible individuals, particularly when combined with other risk factors such as tobacco use. The practice of wearing dentures during sleep, common in some populations, may create environments conducive to Candida proliferation and chronic mucosal changes that could facilitate OPMD development.

Occupational exposures relevant to North African populations include solar radiation exposure in outdoor workers, potentially increasing actinic cheilitis risk; dust and chemical exposures in agricultural, construction, and manufacturing sectors; and asbestos exposure in certain industrial settings. Research characterizing occupational OPMD risks in North Africa remains limited, though recognition of these potential contributors has increased, prompting calls for occupational health surveillance and protective measure implementation in high-risk industries.

## 6. Clinical Management and Malignant Transformation

The management of oral potentially malignant disorders requires individualized approaches balancing the goals of preventing malignant transformation, preserving function, and minimizing treatment morbidity. Risk stratification based on clinical features, histopathological findings, and patient characteristics guides management decisions, with higher-risk lesions warranting more aggressive intervention and surveillance strategies. The cornerstone of OPMD management across North African healthcare settings involves identification and elimination of causative factors, particularly tobacco cessation, which represents the most evidence-based intervention for reducing transformation risk and promoting lesion regression (Warnakulasuriya et al., 2021).

Tobacco cessation counseling and support programs constitute essential components of OPMD management, yet implementation in North African settings faces substantial challenges including limited trained personnel, cultural acceptance of tobacco use, lack of pharmacological cessation aids, and insufficient healthcare system integration. Studies examining spontaneous regression rates of leukoplakia following smoking cessation have documented complete resolution in 20% to 40% of cases within six to twelve months, with additional cases showing partial regression or stability, demonstrating the profound impact of eliminating tobacco exposure (Holmstrup et al., 2006). However, achieving sustained cessation proves difficult, with relapse rates exceeding 70% in some cohorts lacking intensive support interventions.

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Biopsy represents a critical diagnostic and risk stratification tool, with histopathological assessment determining the presence and grade of epithelial dysplasia, which constitutes the most important predictor of malignant transformation risk. The WHO classification system recognizes mild, moderate, and severe dysplasia categories based on the extent of architectural and cytological abnormalities, with transformation rates increasing progressively across dysplasia grades. Studies have documented annual transformation rates of approximately 1% to 3% for mild dysplasia, 3% to 8% for moderate dysplasia, and 7% to 30% for severe dysplasia, though considerable variation exists across different populations and follow-up durations (Warnakulasuriya et al., 2021). North African studies examining dysplasia prevalence in OPMDs have reported rates ranging from 15% to 45%, with higher proportions observed in non-homogeneous leukoplakia and erythroplakia compared to homogeneous variants.

Surgical excision represents the definitive management approach for high-risk OPMDs, particularly those exhibiting severe dysplasia, carcinoma in situ, or high-risk clinical features such as non-homogeneous appearance, size exceeding two centimeters, or location in high-risk anatomical sites including the floor of mouth, ventrolateral tongue, and soft palate. Complete excision with clear margins enables both therapeutic benefit and comprehensive histopathological assessment, addressing concerns about sampling error inherent in incisional biopsy approaches. However, surgical management poses challenges including potential functional impairment, cosmetic concerns, and technical difficulty in cases involving large or multifocal lesions that may not be amenable to complete excision without unacceptable morbidity.

Laser ablation using carbon dioxide, Nd:YAG, or other laser systems provides an alternative or adjunctive treatment modality offering advantages including precise tissue removal, hemostasis, reduced postoperative pain, and lower infection risk compared to conventional scalpel surgery. Studies examining laser treatment outcomes for oral leukoplakia have documented complete lesion resolution rates of 60% to 85%, with recurrence rates of 10% to 35% over five-year follow-up periods (van der Hem et al., 2005). The technique proves particularly valuable for superficial lesions and cases where conventional surgery might compromise function, though the absence of intact tissue specimens for histopathological examination represents a significant limitation, necessitating prior biopsy to exclude invasive carcinoma and assess dysplasia grade.

Photodynamic therapy represents an emerging treatment modality involving administration of photosensitizing agents followed by activation with specific wavelength light, generating reactive oxygen species that selectively destroy dysplastic cells. Research evaluating photodynamic therapy for oral leukoplakia has demonstrated promising complete response rates of 50% to 75%, with the advantage of minimal invasiveness and preservation of tissue architecture (Kübler et al., 2001). However, limitations including photosensitivity reactions, treatment costs, limited availability in resource-constrained settings, and insufficient long-term outcome data have restricted widespread adoption, particularly in North African

healthcare contexts where access to specialized equipment and trained personnel remains limited.

Medical management approaches for OPMDs have been extensively investigated, with agents including retinoids, carotenoids, cyclooxygenase inhibitors, and other chemopreventive compounds evaluated in clinical trials. Systemic and topical retinoids have demonstrated capacity to induce lesion regression and prevent new lesion development through modulation of epithelial differentiation and proliferation pathways, with clinical trials documenting response rates of 50% to 90% during active treatment (Lodi et al., 2016). However, significant limitations include high recurrence rates following treatment discontinuation, systemic side effects including teratogenicity requiring contraceptive measures in women of reproductive age, mucocutaneous symptoms, and lipid abnormalities that restrict long-term use and limit clinical applicability.

Surveillance strategies for OPMDs without high-risk features or following definitive treatment involve regular clinical examination at intervals determined by lesion characteristics, with typical protocols recommending evaluation every three to six months for lesions exhibiting dysplasia and six to twelve months for non-dysplastic lesions. Clinical examination should include comprehensive oral cavity assessment with palpation to detect induration suggesting early malignant transformation, photographic documentation to enable comparison across visits, and biopsy of any areas demonstrating clinical change or suspicious features. The implementation of systematic surveillance programs in North African settings faces challenges including patient loss to follow-up due to geographic barriers, financial constraints, limited specialist availability, and competing health priorities.

Adjunctive diagnostic technologies including toluidine blue staining, brush biopsy, tissue autofluorescence, and narrow-band imaging have been investigated as tools for improving OPMD detection and risk assessment, potentially enabling earlier identification of high-risk areas within heterogeneous lesions. Toluidine blue, a vital dye that preferentially stains dysplastic epithelium, has been employed in some North African centers to guide biopsy site selection, though concerns about false-positive and false-negative results limit interpretation, with reported sensitivities of 80% to 90% but specificities as low as 30% to 50% in some studies (Awan et al., 2011). More sophisticated technologies remain largely unavailable in resource-limited North African settings, though increasing research interest and declining costs may eventually enable broader implementation.

The malignant transformation rates of OPMDs in North African populations demonstrate considerable variation across studies, reflecting differences in lesion types, risk factor profiles, follow-up durations, and diagnostic methodologies. A Sudanese study examining toombak-associated leukoplakia documented transformation rates of 4.7% over a mean follow-up of 6.3 years, with presence of dysplasia significantly predicting progression to carcinoma (Idris et al., 2018). Egyptian research evaluating diverse OPMD types reported overall transformation rates of 3.2% over five years, with erythroplakia exhibiting rates exceeding 15% compared to 2.1% for homogeneous leukoplakia (Saeed et al., 2019). These

transformation rates, while lower than some Western series, nonetheless represent substantial cancer risk given the high OPMD prevalence in certain North African populations.

Factors associated with increased transformation risk identified across multiple studies include advanced patient age, female gender in some but not all studies, large lesion size exceeding two centimeters, non-homogeneous clinical appearance, location in high-risk anatomical sites particularly the floor of mouth and ventrolateral tongue, presence and grade of epithelial dysplasia, and continued tobacco use during follow-up. The development of new risk stratification models incorporating clinical, histopathological, and potentially molecular biomarkers represents an active research area, with the goal of more precisely identifying patients requiring aggressive intervention versus those amenable to conservative management and surveillance approaches.

## 7. Healthcare System Challenges and Access Barriers

The effective management of oral potentially malignant disorders in North Africa confronts substantial healthcare system challenges that limit case identification, appropriate referral, definitive treatment, and long-term surveillance. Primary healthcare infrastructure in many North African countries remains underdeveloped, particularly in rural and remote regions where population health needs often exceed available resources. The shortage of trained oral health professionals represents a critical barrier, with dentist-to-population ratios in some countries falling below one per 10,000 people, substantially lower than World Health Organization recommendations and developed country standards (Benzian et al., 2015).

The distribution of dental professionals demonstrates marked urban-rural disparities, with major cities often having adequate or even surplus dentists while rural regions experience severe shortages. This geographic maldistribution creates access barriers for rural populations who must travel substantial distances to receive oral healthcare, incurring transportation costs, losing work time, and facing other obstacles that discourage care-seeking particularly for conditions perceived as non-urgent. Studies examining healthcare utilization patterns in Morocco and Egypt have documented that rural residents are significantly less likely to receive preventive dental care and more likely to present with advanced oral diseases compared to urban counterparts (Ministry of Health Morocco, 2012).

Specialist oral medicine and oral pathology services remain scarce throughout the region, with comprehensive expertise often concentrated in university teaching hospitals located in capital cities or major urban centers. The limited availability of specialists capable of diagnosing and managing OPMDs means that many cases go unrecognized, are inappropriately managed by providers lacking specific training, or experience substantial delays in diagnosis and treatment initiation. Referral pathways from primary dental care to specialist services frequently lack formalization, contributing to patient loss to follow-up and missed opportunities for early intervention.

The absence of organized oral cancer screening programs represents another critical gap in North African healthcare systems. While opportunistic screening during dental visits

theoretically provides opportunities for OPMD detection, the reality of time-constrained appointments, focus on symptomatic complaints, and variable provider training in oral mucosal examination means that many lesions remain undetected until symptomatic or advanced. Population-based screening programs, while potentially valuable for high-risk groups such as tobacco users, have not been implemented due to resource constraints, uncertain cost-effectiveness, lack of evidence regarding optimal screening protocols, and competing health priorities.

Financial barriers significantly impact access to oral healthcare across North Africa, where out-of-pocket health expenditure remains high and insurance coverage for dental services limited or non-existent in many contexts. The costs associated with specialist consultation, biopsy, histopathological examination, and definitive treatment exceed the financial capacity of many families, particularly in countries lacking universal healthcare coverage or social safety nets. Studies examining reasons for delayed oral cancer presentation have consistently identified financial concerns as major contributing factors, with patients postponing care-seeking until symptoms become unbearable or lesions obviously malignant (Ghantous et al., 2015).

Cultural and linguistic diversity across North Africa creates additional challenges for health education, risk communication, and informed consent processes essential for appropriate OPMD management. The coexistence of Arabic, Berber, French, and English languages, along with numerous local dialects, complicates development of culturally appropriate health promotion materials and can impede provider-patient communication when language discordance exists. Cultural beliefs regarding disease causation, traditional healing practices, and gender norms around healthcare seeking influence behavior patterns in ways that may delay diagnosis and complicate management efforts.

The integration of oral health within broader healthcare systems remains inadequate in most North African countries, with dental services often operating as separate vertical programs with limited connection to medical care systems. This fragmentation means that patients with systemic conditions affecting oral health, those requiring multidisciplinary care, and individuals who primarily access medical rather than dental services may not receive appropriate oral health assessment. The lack of systematic oral cavity examination by medical providers represents a missed opportunity for OPMD detection, as many at-risk individuals regularly access general medical care but rarely visit dentists.

Training programs for healthcare providers across North Africa have increasingly incorporated oral cancer and OPMD content, reflecting growing recognition of the disease burden and importance of early detection. However, the translation of curricular content into clinical practice faces obstacles including competing clinical demands, examination time constraints, perceived lack of treatment options even when lesions are identified, and insufficient reinforcement of oral mucosal examination skills following graduation. Continuing education opportunities for practicing providers remain limited, particularly in underserved regions, contributing to knowledge gaps and missed diagnostic opportunities.

Laboratory infrastructure for histopathological diagnosis varies substantially across the region, with well-equipped pathology departments in major teaching hospitals contrasting sharply with limited or absent facilities in peripheral areas. The shortage of trained oral pathologists, who possess specialized expertise in diagnosing oral mucosal lesions and assessing dysplasia, means that many specimens receive evaluation by general pathologists who may lack confidence in distinguishing reactive lesions from dysplasia or subtle malignancy. Inter-observer variability in dysplasia grading, well-documented even among experienced oral pathologists, poses additional challenges for risk stratification and treatment planning.

## 8. Public Health Implications and Prevention Strategies

The substantial burden of oral potentially malignant disorders in North Africa carries profound public health implications, representing both a challenge demanding immediate action and an opportunity for effective intervention before progression to invasive malignancy occurs. Primary prevention through tobacco control represents the most cost-effective strategy for reducing OPMD and oral cancer burden, with comprehensive tobacco control programs demonstrated to decrease cancer incidence in populations maintaining long-term low tobacco prevalence (Hashibe et al., 2009). The WHO Framework Convention on Tobacco Control provides an evidence-based policy framework that North African countries have variably adopted, with implementation success reflecting political commitment, resource availability, and cultural factors influencing tobacco use acceptability.

Tobacco taxation represents one of the most effective tobacco control interventions, with research demonstrating that price increases achieved through taxation reduce consumption, prevent initiation, and promote cessation particularly among youth and lower-income populations most price-sensitive. However, tobacco taxation policies across North Africa remain suboptimal in many countries, with cigarette prices often affordable relative to income levels and tax structures failing to keep pace with inflation or income growth (WHO, 2019). Illicit tobacco trade, stimulated by price differentials across borders and inadequate enforcement capacity, undermines taxation effectiveness and represents a challenge requiring regional coordination and strengthened customs enforcement.

Comprehensive smoke-free policies protecting workers and the public from secondhand smoke exposure represent another evidence-based tobacco control intervention with co-benefits including social denormalization of smoking and encouragement of cessation attempts. Implementation of smoke-free legislation has progressed unevenly across North Africa, with Tunisia achieving relatively comprehensive coverage including restaurants, cafes, and workplaces, while other countries maintain more limited restrictions or face enforcement challenges that limit real-world impact (Latifi et al., 2019). Cultural factors including the social acceptability of smoking in many contexts and the economic importance of tobacco cultivation and hospitality industries complicate efforts to implement and enforce comprehensive smoke-free policies.

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Health warnings on tobacco packaging, particularly pictorial warnings depicting disease consequences, have demonstrated effectiveness in increasing risk awareness, discouraging initiation, and motivating cessation attempts. The neurobiological impact of graphic images bypasses cognitive resistance mechanisms and creates stronger emotional responses compared to text-only warnings, with larger warning size correlated with greater effectiveness (Hammond, 2011). North African countries have implemented health warnings with varying coverage, size, and graphic content, though many fall short of best practice recommendations for warnings covering at least 50% of principal display surfaces and incorporating vivid imagery depicting oral cancer and other tobacco-caused diseases.

Mass media campaigns educating populations about tobacco health risks, promoting cessation, and preventing youth initiation represent valuable components of comprehensive tobacco control strategies. Effective campaigns utilize emotional appeals, personal testimonials from individuals affected by tobacco-related diseases, and messages tailored to target audience values and concerns. Resource constraints limit the scale and reach of anti-tobacco mass media campaigns in many North African countries, with tobacco industry marketing often dramatically outspending public health communication efforts. The emergence of social media and digital platforms provides new opportunities for health communication that may prove more cost-effective than traditional broadcast media, though effective utilization requires expertise in digital marketing and strategic message development.

Cessation support services including behavioral counseling, pharmacotherapy, and quitlines represent essential infrastructure for assisting tobacco users in achieving and maintaining abstinence. The integration of brief cessation counseling into routine healthcare encounters, including dental visits, has been demonstrated to increase cessation rates at minimal cost through systematic implementation of "5 A's" protocol: Ask about tobacco use, Advise users to quit, Assess readiness to quit, Assist with cessation plan, and Arrange follow-up (Fiore et al., 2008). However, implementation in North African healthcare settings remains limited by provider training gaps, time constraints, lack of reimbursement mechanisms, and limited availability of pharmacological cessation aids including nicotine replacement therapy, varenicline, and bupropion.

Addressing smokeless tobacco use, particularly toombak in Sudan and traditional products in other countries, requires culturally tailored interventions recognizing the distinct social contexts and motivations underlying these practices. The deep cultural embedding of smokeless tobacco in certain communities, its association with masculinity and tradition, and limited awareness of health consequences necessitate multifaceted approaches combining health education, community engagement, regulatory measures, and accessible cessation support. Research evaluating smokeless tobacco control interventions in North Africa remains limited, though experiences from South Asian countries with high smokeless tobacco prevalence provide valuable lessons regarding effective strategies.

Secondary prevention through early detection of OPMDs and prompt treatment to prevent progression represents a complementary strategy to primary prevention, potentially reducing

oral cancer incidence in populations with established high OPMD prevalence. Opportunistic screening during routine dental examinations represents the most feasible approach in resource-limited settings, requiring minimal additional resources beyond provider training and systematic implementation of oral mucosal examination protocols. Studies evaluating the sensitivity and specificity of visual oral cavity examination by trained providers have documented acceptable test characteristics, with sensitivities exceeding 85% for detecting obvious lesions, though performance varies with examiner experience, examination thoroughness, and lesion characteristics (Lingen et al., 2008).

Targeted screening programs focusing on high-risk populations including current and former tobacco users, individuals with previous oral potentially malignant disorders or oral cancer, and people engaging in high-risk practices such as toombak use may represent more cost-effective approaches than population-wide screening. Risk-based screening enables concentration of resources on individuals most likely to benefit, potentially improving program efficiency and sustainability. However, implementation requires systems for identifying high-risk individuals, convincing them to participate in screening, and ensuring access to diagnostic and treatment services when lesions are identified.

Community-based screening programs utilizing trained health workers or mobile dental units to conduct examinations in underserved areas represent strategies for overcoming geographic access barriers. Such programs have been piloted in several North African countries, with reported success in detecting previously undiagnosed oral lesions and referring patients for definitive care, though sustainability challenges related to funding, human resources, and referral pathway capacity limit scalability (El-Sabrout, 2014). The integration of oral cancer screening with existing community health programs addressing diabetes, hypertension, or other chronic diseases may improve efficiency and acceptability.

Health education interventions targeting at-risk populations and the general public aim to increase awareness of oral cancer risk factors, early signs, and the importance of prompt evaluation of suspicious oral lesions. Educational approaches range from mass media campaigns and school-based programs to individual counseling during healthcare encounters and community outreach activities led by health workers or peer educators. Evaluation of oral cancer awareness studies across North Africa has revealed substantial knowledge deficits, with many individuals unable to identify key risk factors or early warning signs, underscoring the need for intensified health promotion efforts (Ghantous et al., 2015).

Healthcare provider education represents a critical element of comprehensive prevention strategies, given that dentists, physicians, and other healthcare professionals serve as front-line resources for case identification, risk counseling, and treatment facilitation. Medical and dental school curricula throughout North Africa have increasingly incorporated oral cancer and OPMD content, though the adequacy of clinical training opportunities and the translation of knowledge into routine practice remain uncertain. Continuing education programs, clinical practice guidelines, and performance feedback mechanisms represent strategies for maintaining and improving provider competency in OPMD management throughout their careers.

Policy development addressing alcohol availability and consumption, while politically sensitive in predominantly Muslim countries, represents an evidence-based strategy for reducing oral cancer burden, particularly in populations where alcohol use combines with tobacco to produce multiplicative risks. Countries with more secular populations or substantial tourism industries face particular challenges in balancing public health objectives with economic interests and cultural values. Strategies including taxation, age restrictions, advertising limitations, and drink-driving enforcement demonstrated effectiveness in other regions may warrant consideration in North African contexts where culturally appropriate and politically feasible.

Nutritional interventions promoting fruit and vegetable consumption, adequate micronutrient intake, and overall dietary quality may contribute to reduced oral cancer risk through multiple biological mechanisms. Public health nutrition programs addressing malnutrition, micronutrient deficiencies, and diet-related chronic diseases represent opportunities for integration of oral cancer prevention messages. The traditional Mediterranean diet consumed in coastal North Africa, rich in fruits, vegetables, whole grains, and olive oil, may provide protective benefits that could be promoted through public health campaigns, though dietary transitions toward more processed, Western-pattern diets threaten these potential benefits.

## 9. Future Research Directions and Knowledge Gaps

Despite growing research attention to oral potentially malignant disorders in North Africa, substantial knowledge gaps persist, limiting evidence-based policy development and clinical practice optimization. The absence of high-quality population-based prevalence studies in many countries and regions means that the true burden of OPMDs remains uncertain, with most available data derived from hospital-based or convenience samples that may not represent general population characteristics. Well-designed cross-sectional surveys employing standardized examination protocols, representative sampling strategies, and adequate sample sizes are urgently needed to establish baseline prevalence estimates and enable international comparisons.

Longitudinal cohort studies following individuals with diagnosed OPMDs over extended periods represent critical research priorities for characterizing natural history, identifying factors predicting malignant transformation, and evaluating management strategies. Such studies require substantial resources and long-term institutional commitment, posing challenges in resource-limited settings, yet provide irreplaceable information for risk stratification and treatment decision-making. International collaboration linking North African institutions with well-resourced research centers in Europe or elsewhere may enable high-quality cohort studies that would be difficult to conduct independently.

The molecular and genetic basis of OPMD development and progression in North African populations remains poorly understood, with most available research conducted in Western, Asian, or other populations that may not fully represent the genetic diversity and exposure profiles characteristic of North Africa. Investigations of genetic polymorphisms influencing carcinogen metabolism, DNA repair capacity, and inflammatory responses could identify

susceptibility markers enabling personalized risk assessment. Similarly, research examining molecular alterations in dysplastic lesions, including chromosomal aberrations, gene expression changes, and epigenetic modifications, may identify biomarkers predicting transformation risk more accurately than histopathological assessment alone.

The effectiveness of various treatment modalities for OPMDs specifically in North African populations requires rigorous evaluation through randomized controlled trials or high-quality comparative effectiveness research. Questions regarding optimal management of lesions with different dysplasia grades, the role of adjunctive treatments, appropriate surveillance intervals, and cost-effectiveness of various approaches remain inadequately addressed. Pragmatic clinical trials conducted within existing healthcare delivery systems could provide evidence directly applicable to North African contexts while building local research capacity.

Tobacco control research examining the effectiveness of policy interventions, cessation programs, and health communication campaigns specifically in North African cultural and economic contexts would inform evidence-based prevention strategies. Research questions include optimal pricing and taxation strategies accounting for illicit trade and cross-border shopping, effective cessation support models compatible with healthcare system structures, culturally appropriate messaging for diverse populations, and strategies for addressing smokeless tobacco use. Implementation science approaches examining barriers and facilitators to tobacco control policy adoption and enforcement could accelerate translation of evidence into practice.

Health services research investigating access barriers, utilization patterns, costs of care, and quality of oral healthcare delivery would inform system strengthening efforts. Questions regarding optimal models for integrating oral health into primary healthcare, effective strategies for expanding access in underserved regions, sustainable financing mechanisms, and quality improvement interventions merit systematic investigation. Patient-centered outcomes research examining factors influencing care-seeking behavior, treatment adherence, and quality of life among individuals with OPMDs could guide development of more effective, acceptable interventions.

The role of infectious agents including Candida species, human papillomavirus, and possibly other microorganisms in OPMD etiology and progression requires clarification through well-designed epidemiological and laboratory studies. Research examining the oral microbiome in health, OPMD, and oral cancer may reveal microbial community changes contributing to disease progression and potentially amenable to intervention. Similarly, investigation of host immune responses and inflammatory pathways involved in OPMD development could identify therapeutic targets for chemoprevention strategies.

Implementation research evaluating the feasibility, acceptability, and effectiveness of screening programs, early detection protocols, and surveillance systems in real-world North African healthcare settings would provide practical evidence for program design and scale-up. Comparative studies examining different screening approaches, provider training modalities, quality assurance mechanisms, and integration strategies could optimize limited

resources. Research on cost-effectiveness of various prevention and early detection strategies considering local epidemiology, healthcare costs, and system capacities would inform resource allocation decisions.

## 10. Conclusion

Oral potentially malignant disorders represent a substantial and inadequately addressed public health challenge in North Africa, with prevalence rates ranging from 0.5% to 12.8% across different populations and settings, translating to millions of affected individuals across the region. The burden is particularly severe in countries and populations with high tobacco use prevalence, especially where smokeless tobacco products such as toombak are consumed. The elevated incidence of oral cancer observed throughout North Africa reflects, in part, the high prevalence of precursor OPMDs and inadequate implementation of prevention and early detection strategies. This situation is particularly concerning given that OPMDs are clinically detectable, amenable to intervention, and associated with preventable risk factors, suggesting that much of the resulting cancer burden could be avoided through appropriate public health action.

Geographic variation in OPMD prevalence across North Africa reflects the complex interplay of cultural practices, tobacco consumption patterns, dietary factors, healthcare access, and potentially genetic susceptibilities that vary between and within countries. The concentration of disease burden in rural and socioeconomically disadvantaged populations, who face the greatest barriers to healthcare access, creates profound health equity concerns demanding targeted interventions. Understanding these distributional patterns enables evidence-based resource allocation and program design to address populations experiencing disproportionate disease burden.

The predominance of tobacco use as the primary OPMD risk factor across North Africa underscores the critical importance of comprehensive tobacco control as a cornerstone prevention strategy. Countries achieving success in reducing tobacco prevalence through taxation, smoke-free policies, health warnings, cessation support, and mass media campaigns demonstrate the feasibility and effectiveness of evidence-based tobacco control, providing models for regional emulation and adaptation. The growing epidemic of water pipe smoking, particularly among youth and women, demands urgent attention through targeted policies and health communication recognizing the specific cultural contexts and misperceptions surrounding this form of tobacco use. Addressing the distinctive challenge of smokeless tobacco, particularly toombak in Sudan, requires culturally tailored interventions developed through community engagement and informed by understanding of the social meanings and functions these products serve.

Healthcare system strengthening represents an essential component of comprehensive responses to the OPMD challenge, encompassing workforce development, infrastructure investment, service delivery model innovation, and quality improvement initiatives. The shortage of oral health professionals, particularly in rural and underserved regions, demands multifaceted solutions including enhanced training capacity, incentive structures encouraging

practice in underserved areas, task-shifting to enable non-specialist providers to perform basic oral health functions, and telemedicine consultations linking peripheral providers with specialist expertise. The integration of oral health assessment into primary healthcare and routine medical practice represents an underutilized opportunity for early detection that could be realized through systematic provider training, clinical protocol development, and performance monitoring.

The development of organized approaches to early detection, whether through population-based screening programs, targeted screening of high-risk groups, or enhanced opportunistic case-finding during healthcare encounters, represents a promising strategy for reducing oral cancer mortality through identification and treatment of OPMDs before malignant transformation. However, screening program implementation must consider resource availability, healthcare system capacity, cost-effectiveness, and potential harms including false-positive results and overtreatment. Pilot programs with rigorous evaluation could provide evidence regarding optimal approaches for North African contexts, informing subsequent scale-up decisions.

Research priorities include establishing accurate population-based OPMD prevalence estimates, characterizing natural history through longitudinal cohort studies, identifying molecular and genetic factors influencing risk and progression, evaluating treatment effectiveness, examining health services delivery models, and assessing implementation strategies for prevention and early detection programs. International collaboration, capacity building, and sustained research investment are essential for addressing these knowledge gaps and building the evidence base needed for effective action. Regional research networks linking institutions across North Africa could facilitate multi-country studies, standardization of methodology, and sharing of expertise and resources.

Policy development and implementation require political commitment, stakeholder engagement, resource mobilization, and sustained effort across multiple sectors including health, agriculture, trade, education, and finance. The complexity of oral cancer prevention, spanning primary prevention through tobacco control and healthy lifestyles, secondary prevention through early detection, and healthcare system strengthening for effective treatment, demands coordinated multisectoral action. National cancer control plans incorporating oral cancer prevention and management as priority components represent frameworks for organizing comprehensive responses, allocating resources, defining responsibilities, and monitoring progress toward defined objectives.

The opportunity to substantially reduce oral cancer burden in North Africa through effective prevention and management of oral potentially malignant disorders represents a public health imperative demanding urgent action. The tools, knowledge, and strategies needed for success exist and have been demonstrated effective in diverse contexts worldwide. What remains is the political will, resource commitment, and sustained implementation effort required to translate evidence into population health impact. The burden of oral cancer and its precursor lesions falls disproportionately on vulnerable populations who can least afford the suffering, disability, and economic consequences of this largely preventable disease. Addressing this

health inequity through evidence-based prevention and care represents not only a public health priority but a moral imperative demanding the attention of researchers, clinicians, policymakers, and society as a whole.

As North African countries continue developing their health systems and addressing evolving disease burdens, oral health must not be neglected as peripheral to core health priorities. The substantial burden of OPMDs and oral cancer, the availability of effective prevention and early detection strategies, and the profound impacts of oral diseases on quality of life and economic productivity justify prioritization within national health agendas. By building on successes achieved in countries demonstrating leadership in oral health and learning from international best practices, North Africa can substantially reduce the burden of oral potentially malignant disorders and oral cancer, improving health outcomes and quality of life for millions of people across the region.

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