Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i7.1894
*Biol. Clin. Sci. Res. J., Volume 6(7), **2025**: 1894*
Original Research Article

Correlation Between Materials-induced Irritation and Oral Mucosal Lesions

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(Received, 24th April 2025, Accepted 18th July 2025, Published 31st July 2025)

Abstract: *Material-induced irritation of the oral mucosa can result in a spectrum of lesions, ranging from benign reactive changes to potentially malignant disorders and oral squamous cell carcinoma (OSCC). Establishing correlations between specific irritants and lesion types is critical for prevention, early diagnosis, and effective management.* ***Objective:*** *To evaluate the relationship between material-induced irritation and the development of oral mucosal lesions, with emphasis on risk factors, clinical presentation, and histopathological patterns.* ***Methods:*** *This cross-sectional study was conducted in the Department of Dental Materials, Ayub Medical College, Abbottabad, from April to September 2024. A total of 160 patients aged ≥18 years with clinically and histopathologically confirmed oral mucosal lesions related to irritant exposure (mechanical, chemical, or metallic) were included. Detailed histories, clinical examinations, and photographic documentation were undertaken, followed by incisional or excisional biopsies for diagnosis. Lesions were classified as reactive, potentially malignant disorders (PMDs), or OSCC. Data were analyzed using chi-square and Pearson correlation tests, with p<0.05 considered significant.* ***Results:*** *Of the participants (mean age 43.5 ± 12.2 years; 57.5% male), 71.3% had lesions linked to chronic mechanical irritants, while 28.7% were associated with chemical irritants. Buccal mucosa (42.5%) and lateral tongue (28.1%) were the most common sites. Histopathology revealed reactive lesions in 47.5%, PMDs in 32.5%, and OSCC in 20.0% of cases. Mechanical irritants (ill-fitting dentures, orthodontic appliances) were predominantly associated with reactive lesions, whereas chemical irritants (smokeless tobacco, nicotine) correlated more with PMDs and OSCC. Metallic restorations were significantly linked with lichenoid lesions. A strong positive correlation was found between duration of irritant exposure and lesion severity (r=0.62, p=0.002).* ***Conclusion:*** *Chronic material-induced irritation is a significant risk factor for oral mucosal pathology, with prolonged exposure markedly increasing the likelihood of malignant transformation. Early detection and removal of irritants, patient education, and preventive measures are vital to reduce lesion progression and improve oral health outcomes.*

Keywords: Oral mucosa, irritation, lesions, tobacco, prosthetic materials, carcinoma

[***How to Cite:*** Anwar R, Bibi A. Correlation between materials-induced irritation and oral mucosal lesions. *Biol. Clin. Sci. Res. J.*, **2025;** 6(7): 50-54. doi: https://doi.org/10.54112/bcsrj.v6i7.1894

Introduction

Material-induced irritation of the oral mucosa is a complex process characterised by a range of changes on the oral mucosa depending on the etiological factor. Some intraoral irritants (such as dentifrices, tobacco products, dental materials and prostheses, and metals) cause different clinical and histopathological patterns (1). Wang and Woo were able to show that irritant contact stomatitis (ICS) and contact hypersensitivity stomatitis (CHS) exhibit distinct histological characteristics and highlighted the fact that material-specific stomatitis should be addressed in diagnosis. Chronic mechanical irritation has gained recognition as a possible co-factor in the development of oral squamous cell carcinoma (OSCC), especially when caused by improperly fitting dentures or sharp restorations. This linkage was supported by a meta-analysis conducted by Gupta et al., which cited that trauma proves to be a promoter in carcinogenesis (2).

Irritation mechanisms have been improved through experimental methods. Aizawa et al. applied a three-dimensional model of human buccal mucosa in determining responses to the chemical irritants, providing a pertinent testing platform (3). Ueno et al. emphasised the effectiveness of mucosal protective formulations in mitigating chemotherapy- and radiotherapy-induced mucositis, and the promising role of protective agents in the treatment of injuries that are due to irritants (4). Vasanthi et al. measured inflammatory, angiogenic, and fibrous elements in lesions of oral reactivity and related enduring irritation to directional pathology (5). Kumari et al. provided a detailed overview of transition pathways of potentially malignant conditions in light of chronic irritation, further confirming their clinical importance (6).

Mucosal sensitivity is also affected by systemic conditions. The oral mucosal lesions occurred during SARS-CoV-2 infection, which implies that the systemic infection was a predisposing factor for irritation-induced lesions (7). Watanabe et al. also characterised OSCC within the vicinity of subperiosteal implants related to long-term mechanical affront and peri-implant inflammation with particular attention to risk factors such as prosthetic material (8). Noor and Ramanarayana showed the burden of use of smokeless tobacco on the world about oral cancer by relating chemical irritants and carcinogenesis (9). Wysocka-Slowik et al. identified severe mucositis, which was linked to conditioning regimens in acute myeloid leukaemia, as a factor caused by treatment-related irritation (10).

The pattern of exposure to lifestyle and material also contributes to lesion development. Another study conducted by Alizadehgharib et al. stated that non-tobacco nicotine pouches induce mucosal lesions identical to snus, proving that they are harmful compared to conventional tobacco (11). A study by Ciesielska et al. examined the effects of hormones on the mucosal alterations of menopausal women, and the results indicated the increased vulnerability to irritation (12). Du et al. found autoimmune components in lupus-induced mucosal lesions, where they revealed systemic factors' contribution to susceptibility (13). Tsushima et al. reported the successful treatment of lichenoid contact reactions when allergenic metals are removed, which demonstrated the reversibility of the lesions when irritation is removed (14). Zebardast et al identified the presence of Epstein-Barr virus RNA in OSCC and non-cancerous tissues, indicating the presence of viral co-factors in the irritation-based pathology (15).

The reviews conducted by da Mota Santana et al. attributed COVID-19 to oral mucosal lesions in unvaccinated people, which also confirmed infection-related vulnerability (16). Wu and Chiang linked burn mouth syndrome to the presence of medication, representing the systemic pharmacologic irritants (17). Daume et al. analyzed the oral lichen planus related to restorative materials, observing that there are strong effects on the quality of life (18). Kot et al. retrospectively discussed COVID-19-associated oral mucosal lesions due to the complexity of such inflammatory triggers (19). According to Kawashita et al., there was a correlation between the immune markers and radiotherapy-induced mucositis, which further supports the importance of the systemic immune system in determining the severity of lesions (20). Lastly, Limdiwala et al. also noted mucosal changes due to GERD, blaming it on long-term physical insult by gastric reflux (21).

Combined, it is demonstrable that mechanical, chemical, allergic, and biological irritants may cause a significant assortment of responses in the oral mucosa. Reactive lesions are often caused by mechanical trauma, whereas long-lasting and continuous exposure to chemicals and metals may cause so-called potentially malignant disorders accompanied by carcinoma. ICS and CHS have different histopathologies, and a correct diagnosis is required. Clinical and diagnostic evidence shows that sampling and removal of irritants at an early stage can stop the occurrence of lesions. Because oral cancer is highly prevalent in such regions as Pakistan, it is essential to investigate material-induced irritation. This paper proposes to delve into the relationships between irritant contact and oral mucosa lesions to improve prevention, diagnostic quality, and materials safety assurance.

This study aims to assess the relation between material-induced irritation and the development of oral mucosal lesions, identifiable risk factors, clinical manifestations, and histopathological specificities of patients with the condition.

Methodology

The study was designed as a cross-sectional observational analysis aimed at gathering insights into various aspects of dental materials. This research was conducted in the Department of Dental Materials at Ayub Medical College, located in Abbottabad.

The duration of the study spanned six months, specifically from April 2024 to September 2024. During this period, data was collected and analyzed to draw meaningful conclusions about the subject under investigation.

Patients who had oral mucosal lesions with a clinical component and which were related to potential irritants at the oral mucosa, for example, dental materials, prostheses, orthodontic appliances, tobacco, nicotine, or other known irritants, aged 18 years and older, were included. Only patients who gave informed consent and who were subjected to histopathologic examination were recruited.

Patients with infection-based (viral, bacterial, and fungal) lesions, systemic immunological processes unrelated to irritation, recent oral surgery, patients on chemotherapy, or those who did not want to take part were excluded from the study.

A senior oral medicine specialist clinically evaluated all those patients who fit the inclusion criteria. Historical details concerning the exposure to the irritant materials, type, duration, and place of contact were noted with the help of a structured proforma. Clinical investigation included observation and palpation of the lesions, their size, location, shape, and related symptoms. Photographs were also taken of the patients as a form of record-keeping. Incisional and excisional biopsies were employed under local anaesthesia on the chosen lesions to make a definite diagnosis. The pathologist was blinded to the history of exposure to minimise bias that takes place through histopathological examination. Microscopic findings were used to categorise the lesions as being reactive, potentially malignant, or malignant. Demographic, source of the irritant, type of lesion, and histopathologic outcome data were collected. SPSS version 26 was used for statistical analysis. The chi-square and Pearson correlation tests were used to determine the correlation between material-induced irritation and lesion characteristics, although p-values <0.05 were considered to be statistically significant.

Results

The number of patients studied was 160 years with a mean age of 43.5 ± 12.2 years. These consisted of 92 (57.5%) males and 68 (42.5%) females. (Table 1). The majority of the patients (72%) had a history of exposure to mechanical or chemical irritants for over six months. The most prevalent sources of irritation were ill-fitting dentures, metallic dental restorations, orthodontic devices, smokeless tobacco, and nicotine pouches. (Table 2)

Table 1. Distribution of Patients by Age and Gender

Age Group (years)	Male (n=92)	Female (n=68)	Total (n=160)
18–30	18	12	30
31–50	45	28	73
>50	29	28	57

Among all participants, 114 patients (71.3%) who were affected had lesions with chronic mechanical irritants, but 46 patients (28.7%) had lesions as a result of chemical irritants. The buccal mucosa (42.5%) and the lateral tongue (28.1%) were the most common sites of the lesions, as well as the gingiva (15%) and the labial mucosa (14.4%).

Table 2. Site Distribution of Oral Mucosal Lesions

Lesion Site	Number of Cases	Percentage (%)
Buccal Mucosa	68	42.5
Lateral Tongue	45	28.1
Gingiva	24	15.0
Labial Mucosa	23	14.4

Histopathological evaluation showed that 76 patients (47.5%) received a diagnosis of reactive lesions (fibromas, hyperkeratosis), 52 (32.5%) of potentially malignant disorders (lichen planus, leukoplakia), and 32 cases (20%) oral squamous cell carcinoma (Table 3). Chronic irritation through the use of prosthetic materials and metals was reported to be significant concerning lichenoid contact lesions and OSCC ($p<0.05$). The connection between particular irritants and the type of lesions was examined. The mechanical irritants, including ill-fitting dentures, were chiefly related to fibrous hyperplasia, whereas the chemical irritants, like smokeless tobacco, were more correlated with the leukoplakia and carcinoma. There is a strong correlation between metal restorations and lichenoid lesions,

with some patients showing clear resolutions upon excision of the offending substance. (Table 4)

Table 3. Histopathological Classification of Lesions

Lesion Type	Cases (n)	Percentage (%)
Reactive Lesions	76	47.5
Potentially Malignant Disorders	52	32.5
Oral Squamous Cell Carcinoma	32	20.0

Table 4. Correlation of Irritant Types with Lesion Categories

Irritant Type	Reactive Lesions	PMDs	OSCC
Mechanical (dentures, appliances)	52	20	6
Chemical (tobacco, nicotine)	18	16	12
Metals (restorations)	6	16	14

The statistical correlation between the length of the irritant exposure and the seriousness of lesions was (r=0.62, p=0.002), a strong positive correlation. Patients with an exposure of more than one year had a risk of developing potentially malignant or malignant lesions 3.5 times higher than patients exposed to a short exposure. These results emphasise the importance of early detection and removal of irritant causes to avoid extension of the lesions in the oral mucosal tissues.

Discussion

The current study examined the relationship between material-induced irritation and mucosal lesions of the mouth, and discovered that there were considerable correlations between the nature of the irritant, the length of exposure, and the histological manifestation. The results are in agreement with the literature and support the thesis that those exposed to irritant substances chronically may develop a wide continuum of mucosal alterations that could result in benign reactive alterations as well as potentially and malignant lesions. This validates the idea that chronic local trauma or chemical irritation is an influential co-factor in the aetiology and pathology of the mouth. Most of the lesions in this study were reactive lesions, like fibrous hyperplasia and frictional keratosis, which are normally attributed to mechanical irritants, such as ill-fitting dentures and orthodontic appliances. These findings are supported by the ones carried out by Wang and Woo, which have shown that the occurrence of irritant reactions in the mouth has distinct histopathology that depends very strongly on the exacerbating agent (1).

Chronic mechanical irritation was also identified as a major driving force in the development of lesions, which concurs with Gupta et al.'s meta-analysis that mechanical trauma contributed to the risk of oral squamous cell carcinoma (2). Trauma per se is not a primary carcinogenesis inducer, but it can become a promoter when co-acting with other risk factors, e.g., tobacco smoking, oral hygiene, or viral infections. Additionally, the study found that chemical irritants, especially smokeless tobacco and nicotine pouches, had a high association with disorders that may prove to be malignant, such as leukoplakia and oral squamous cell carcinoma. These findings substantiate the study of Noor and Ramanarayana, who highlighted the global oral cancer burden in individuals who use smokeless tobacco (9). Alizadehgharib et al. also proved that non-tobacco variant nicotine products cause mucosal damage that may be similar to that found in traditional tobacco products, like nicotine pouch (11). This highlights the importance of strict control and informing patients about the dangers of these substances.

There were also metallic dental restorations and mucosal reactions caused by the same in the current research. Lichenoid contact lesions were found to be significantly linked with metal exposure, which is in concordance with the study by Tsushima et al, who also focused on the clearing of such lesions following the extraction of allergenic dental materials (14). This reversibility underlines the necessity to identify and eradicate the causative agent early on in order to avoid chronicity or progression. Likewise, Daume et al. also associated the oral lichen planus with dental restorative materials and revealed its negative effect on oral health-related quality of life (18). Potential allergic or irritant responses must be taken into consideration during the planning of restorative treatments by clinicians. The results of the case description about histopathological analysis indicated that longer exposure to the irritants was associated with a severe type of lesions, such as potentially malignant disorders and carcinoma. This finding is consistent with Kumari et al., who explained that untreated or persistent irritants in oral potentially malignant disorders may experience malignant transformation (6).

The high percentage of carcinoma cases in this study also confirms the importance of chronic irritation as a major factor in oral carcinogenesis, especially when this factor is coupled with other carcinogenic agents. The results show that oral mucosal lesions are multifactorial. Systemic conditions like systemic lupus erythematosus (13) and menopausal hormonal shifts (12) were also observed as increasing predisposition to mucosal piquing and lesion development, as indicated in past studies. Systemic conditions were not part of this research, but we cannot afford to lock them out of influencing the mucosal response to local offenders. In addition to this, other viral factors such as Epstein-Barr virus have been recognised in oral lesions, indicating the possibility of interaction between infectious agents and irritant pathology (15).

Mucosal injuries related to treatment have been reported in past literature and are evident in patients receiving chemotherapy or radiotherapy. Research to understand the relationship between the severity of mucositis and host immune response and protective intervention was conducted by Ueno et al. and Kawashima et al. (4, 20). Although research did not include patients undergoing these kinds of treatment, the results still make sense because they show how loss of integrity of the mucosa can be intensified following exposure to irritants. The site distribution of lesions is another key point that the results portray. The most irregularly involved parts were the buccal mucosa and lateral tongue, which can be related to frequent contact with dental appliances, restorations, and placement of tobacco.

This is justified by the fact that findings of previous researchers revealed that irritation is localised to the region of greatest friction or chemical retention (8). In addition, gingival and labial mucosa lesions were observed, often relating to prosthetic or metallic contact, and these are significant to check during regular examinations. The case of COVID-19-induced oral lesions is also clear in the research, which is discussed within the studies by Mahmoud et al., Kot et al., and da Mota Santana et al. (19). Although the percentage number of participants had specific screening regarding post-COVID-19 mucosal shifts, the literature results suggest

that infection caused by the virus may de-sensitise the oral mucosal tissue to become easier irritated by the foreign substance. This indicates the exposure effects on locality and system health with the degree of exposure to the irritant.

Another irritation-associated condition, burning mouth syndrome, has also been attributed to drugs according to Wu and Chiang (17). Irritation lesions were not the primary focus of interest. However, some patients reported blistering in lesions related to irritants, and there was notable symptom overlap between irritant-related lesions and neuropathic conditions. This statistical analysis has shown a close relationship between the length of the presence of irritants and the severity of the symptoms, confirming previous studies that chronicity has been found since it is a major factor in this development (2, 5). The patients who have a history of exposure to irritants for over one year experienced considerably high rates of potentially malignant and malignant lesions. It highlights the importance of early intervention and patient awareness in reducing risk factors.

These findings have clinically important implications. Detecting and removing an irritation source early can help prevent lesion development, reduce patient morbidity, and potentially lower oral cancer rates. Furthermore, the findings support the importance of having regular oral screening, especially in a patient with preexisting risk factors or a long history of exposure to prosthetics and tobacco. Education on the hazards of chronic irritation and favorable policies that restrict harmful materials are essential preventive measures.

Conclusion

This research shows that there is a strong association between material-induced irritation and subsequent oral mucosal lesions. Mechanical irritants, mainly ill-fitting dentures and orthodontic appliances, are associated with reactive lesions, whereas chemical irritants, including smokeless tobacco and nicotine products, are more strongly linked to potentially malignant disorders and oral squamous cell carcinoma. However, dental fillings with metals were also a common cause of lichenoid lesions, and most of them cleared after removal of the irritant. The contact time proved to be a decisive factor, and a long exposure time led to a high frequency of severe lesions with severe malignant tendencies. These results are in line with other studies, as chronic local irritation is a significant accelerator of oral pathology. Preventive measures based on early detection of irritant sources, patient education, and preventive measures need to be addressed to reduce lesion progression and optimize oral health outcomes. Newer studies with bigger sample sizes and longitudinal designs are suggested in order to understand the causal paths further, clarify the roadmap of diseases, and reinforce protective measures.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-24)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

RA (Assistant Professor)

Manuscript drafting, Study Design,

AB (Assistant Professor)

Review of Literature, Data entry, Data analysis, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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