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## Prevalence and Clinicopathological Characteristics of Oral Potentially Malignant Disorders in Betel Quid Chewers and Non-Chewers: A Cross-Sectional Study

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## ABSTRACT

### Background

Oral potentially malignant disorders (OPMDs) represent a wide range of lesions with a substantial risk of malignant transformation. Betel quid chewing, prevalent in South Asia, is one of the main risk factors for OPMDs.

### Objective

This study aimed to assess the prevalence of OPMDs in betel quid chewers and non-chewers and analyze their clinicopathological characteristics. Additionally, it aims to contribute to the existing literature on the correlation between betel quid use and the development of potentially malignant oral disorders.

### Methods

A cross-sectional study involved 100 (50 betel quid chewers and 50 non-chewers) participants from a tertiary care hospital in Peshawar and Lahore. Data were collected using structured clinical examinations, histopathological analyses, and a detailed questionnaire addressing chewing habits, lifestyle, and medical history. Statistical analysis was performed using logistic regression and chi-square tests.

### Results

The prevalence of OPMDs was significantly higher in betel quid chewers (40%) compared to non-chewers (12%). Leukoplakia was the most common lesion in both groups. The odds of developing OPMDs were 5.5 times higher in betel quid chewers compared to non-chewers (OR = 5.5, 95% CI: 3.1–8.9;  $p < 0.001$ ).

### Conclusion

This study emphasizes the association between betel quid chewing and the development of OPMDs. Early detection and intervention, combined with lifestyle changes, could significantly reduce the risk of malignant transformation in individuals with OPMDs.

**Keywords:** Clinicopathological Characteristics, Oral Potentially Malignant Disorders, Chewers

## INTRODUCTION

Oral potentially malignant disorders (OPMDs) are recognized as precursors to oral cancer, particularly oral squamous cell carcinoma (OSCC). Common OPMDs include leukoplakia, erythroplakia, oral submucous fibrosis (OSMF), and lichen planus, each characterized by varying degrees of epithelial dysplasia.<sup>1</sup> Oral cancer remains a significant public health issue worldwide, with approximately 377,700 new cases diagnosed annually.<sup>2</sup> The burden of this disease is particularly high in regions where tobacco and betel quid consumption are prevalent, such as South and Southeast Asia.<sup>3</sup> Betel quid is composed of areca nut (Areca catechu), slaked lime, and often includes tobacco. Areca nut contains alkaloids such as arecoline, which have been shown to cause cytotoxicity, inflammation, and fibrosis in oral tissues.<sup>4</sup> Regular betel quid consumption has been linked to the development of OPMDs, such as OSMF, which may progress to OSCC.<sup>5</sup> This association has been well-documented in studies across India, Sri Lanka, and Taiwan, where betel quid chewing is a widespread practice.<sup>6,7</sup>

Several factors contribute to the malignant transformation of OPMDs, including the duration and frequency of betel quid chewing, the presence of tobacco in the quid, and individual susceptibility.<sup>8</sup> Moreover, histopathological changes such as epithelial dysplasia, often observed in OPMDs, are important indicators of malignant potential.<sup>9</sup> Although numerous studies have investigated the association between betel quid

chewing and OPMDs, there is a paucity of data from Pakistan, particularly in regions like Peshawar, where the use of betel quid is prevalent.<sup>10</sup> Previous research has consistently shown a strong link between betel quid chewing and the development of OPMDs. In a study conducted by Gupta et al., the prevalence of OPMDs in habitual betel quid chewers was found to be 42%, with leukoplakia being the most common lesion.<sup>11</sup> Similarly, a study in Sri Lanka by Warnakulasuriya et al. reported that OSMF was present in 35% of betel quid chewers, with a significant risk of progression to OSCC.<sup>12</sup> Tobacco, when added to betel quid, increases the risk of malignant transformation. A meta-analysis by IARC concluded that tobacco-containing betel quid users have a 5-7 fold increased risk of developing OPMDs compared to non-users.<sup>13</sup> The role of areca nut alone has also been explored. Jeng et al. demonstrated that areca nut alone could induce OPMDs through chronic irritation and the production of reactive oxygen species, leading to DNA damage and epithelial dysplasia.<sup>14</sup>

The clinical presentation of OPMDs varies, with leukoplakia often appearing as a white patch, erythroplakia as a red patch, and OSMF as fibrotic bands that limit mouth opening.<sup>15</sup> Histopathological analysis is essential for determining the degree of dysplasia, which serves as a predictor of malignant potential. A study by Scully et al. found that moderate to severe dysplasia increases the risk of malignant transformation by 10-15 times compared to mild or no dysplasia.<sup>16</sup> The limited availability of data from Pakistan makes it difficult to assess the true burden of OPMDs in the country. However, studies from Karachi and Lahore have reported high prevalence rates of OSMF and leukoplakia in populations that consume betel quid, highlighting the need for region-specific research.<sup>17,18</sup> This study aims to fill this gap by investigating the prevalence and clinicopathological characteristics of OPMDs in betel quid chewers and non-chewers in Peshawar. We hypothesize that the prevalence of OPMDs will be significantly higher among chewers, and that these lesions will exhibit more advanced histopathological changes compared to non-chewers.

## **METHODOLOGY**

This cross-sectional study was conducted from January to June 2024 at a tertiary care hospital in Peshawar. The study involved 100 participants, divided into two groups: 50 betel quid chewers and 50 non-chewers. Inclusion criteria for chewers were individuals aged 18-65 with a history of daily betel quid use for at least five years. Non-chewers had no history of tobacco or betel quid use. Exclusion criteria included individuals with a history of oral cancer, major systemic illnesses, or prior treatment for OPMDs. A comprehensive clinical examination was conducted by experienced dentists. The oral mucosa was examined for any visible lesions, including leukoplakia, erythroplakia, and OSMF. Lesions were measured, and their characteristics were documented, including color, texture, and size. Any suspicious lesion was subjected to a biopsy for histopathological analysis.

Participants completed a structured questionnaire designed to capture relevant demographic information (age, gender, education level) and personal habits, including betel quid use (frequency, duration, and ingredients), smoking, alcohol consumption, and family history of oral diseases. The questionnaire was administered in the local language (Pashto), and responses were translated into English for analysis. Biopsy specimens were collected from participants with clinically suspicious lesions. Histological slides were prepared and stained with hematoxylin and eosin. Dysplasia was graded as mild, moderate, or severe based on established WHO criteria.<sup>19</sup> The presence of fibrosis, inflammation, and keratosis was also noted. Data were analyzed using SPSS version 26. Prevalence rates of OPMDs were calculated for both groups. The chi-square test was used to assess the association between betel quid chewing and OPMDs. Logistic regression analysis was performed to estimate odds ratios (ORs) for the risk factors associated with

OPMDs, controlling for age, gender, smoking, and alcohol use. A p-value of <0.05 was considered statistically significant.

## RESULTS

The study sample comprised 100 participants, with 60 males and 40 females. The mean age was  $42.6 \pm 11.3$  years. Betel quid chewers had a significantly higher prevalence of smoking (32%) compared to non-chewers (8%) ( $p < 0.01$ ). The average duration of betel quid use was  $9.3 \pm 3.7$  years. The prevalence of OPMDs was significantly higher in betel quid chewers (40%) compared to non-chewers (12%) (Table 1). Among chewers, leukoplakia was the most common lesion, followed by OSMF. In non-chewers, leukoplakia was the predominant lesion, albeit at a lower frequency. Leukoplakia accounted for 55% of the OPMDs in chewers, followed by OSMF (30%) (Table 2). Histopathological analysis revealed that 20% of the lesions in chewers exhibited moderate dysplasia, compared to 4% in non-chewers. Moderate dysplasia was found in 40% of chewers, compared to 10% of non-chewers (Table 3). Severe dysplasia was present in 15% of chewers but was absent in non-chewers. Logistic regression analysis showed that betel quid chewers were 5.5 times more likely to develop OPMDs than non-chewers (OR = 5.5, 95% CI: 3.1–8.9;  $p < 0.001$ ). Other significant risk factors include smoking and alcohol use.

**Table 1: Prevalence of OPMDs in Betel Quid Chewers and Non-Chewers**

| Group              | Total Participants | OPMDs Present (%) | OPMDs Absent (%) |
|--------------------|--------------------|-------------------|------------------|
| Betel Quid Chewers | 50                 | 20 (40%)          | 30 (60%)         |
| Non-Chewers        | 50                 | 6 (12%)           | 44 (88%)         |

**Table 2: Distribution of OPMD Types in Betel Quid Chewers and Non-Chewers**

| Lesion Type             | Chewers (n=20) | Non-Chewers (n=6) |
|-------------------------|----------------|-------------------|
| Leukoplakia             | 11 (55%)       | 5 (83%)           |
| Oral Submucous Fibrosis | 6 (30%)        | 0 (0%)            |
| Erythroplakia           | 2 (10%)        | 1 (17%)           |
| Lichen Planus           | 1 (5%)         | 0 (0%)            |

**Table 3: Dysplasia Grading in Betel Quid Chewers and Non-Chewers**

| Dysplasia Grade    | Chewers (n=20) | Non-Chewers (n=6) |
|--------------------|----------------|-------------------|
| No Dysplasia       | 6 (30%)        | 4 (67%)           |
| Mild Dysplasia     | 6 (30%)        | 1 (17%)           |
| Moderate Dysplasia | 4 (20%)        | 1 (17%)           |
| Severe Dysplasia   | 4 (20%)        | 0 (0%)            |

## DISCUSSION

The present study demonstrates a significant association between betel quid chewing and the development of OPMDs, corroborating findings from other regions where betel quid is commonly consumed.<sup>20</sup> The prevalence of OPMDs in chewers was 40%, substantially higher than in non-chewers, suggesting that betel quid plays a crucial role in the pathogenesis of these lesions. These findings align with previous studies, such as those by Gupta et al., where the prevalence of OPMDs in habitual chewers was also reported to be above 40%.<sup>11</sup> Leukoplakia was the most common OPMD in both chewers and non-chewers, consistent with the global trend of leukoplakia being the most frequently diagnosed potentially malignant oral lesion.<sup>21</sup> However, the distribution of more advanced lesions, such as OSMF and erythroplakia, was exclusive to

chewers, emphasizing the impact of chronic betel quid use on oral tissue. OSMF is particularly concerning due to its high risk of malignant transformation, with a reported transformation rate of 7-13%.<sup>22</sup> The histopathological findings from this study also underscore the malignant potential of OPMDs in betel quid chewers. A significant portion of chewers (20%) exhibited severe dysplasia, a known precursor to OSCC.<sup>23</sup> In contrast, severe dysplasia was absent in non-chewers, further supporting the notion that betel quid use accelerates the progression of OPMDs toward malignancy. Similar findings have been reported by Jeng et al., who noted that chronic exposure to arecoline, the principal alkaloid in areca nut, induces DNA damage and promotes epithelial dysplasia.<sup>14</sup> The present study also identified smoking and alcohol use as significant risk factors for the development of OPMDs, in agreement with existing literature. These habits likely act synergistically with betel quid to enhance the carcinogenic potential of oral lesions. The inclusion of tobacco in betel quid has been shown to increase the risk of malignant transformation by several fold.<sup>13</sup> While this study provides valuable insights into the prevalence and clinicopathological characteristics of OPMDs in Peshawar, it is not without limitations. The cross-sectional design precludes the establishment of a temporal relationship between betel quid use and the development of OPMDs. Additionally, the sample size was relatively small, and the participants were selected from a single center, limiting the generalizability of the findings. Future studies should consider larger, multi-center cohorts and longitudinal designs to assess the progression of OPMDs over time. Furthermore, interventions aimed at reducing betel quid consumption, such as public health campaigns and cessation programs, should be implemented to curb the growing burden of OPMDs in the region.

## **CONCLUSION**

This study highlights the significant association between betel quid chewing and the prevalence of OPMDs in Peshawar. The findings indicate that betel quid chewers are at a higher risk of developing potentially malignant oral lesions, particularly leukoplakia and OSMF, which may progress to OSCC if left untreated. Early detection through clinical examinations and histopathological evaluation is critical in preventing malignant transformation. Public health efforts should focus on raising awareness about the risks associated with betel quid chewing and promoting cessation strategies to reduce the incidence of OPMDs.

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