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Original Article

Diagnostic Accuracy of Toluidine Blue-Assisted Clinical Screening for Oral Potentially Malignant Disorders and Cancer in a High-Risk South Indian Cohort: A Field-Based Study

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ABSTRACT

Southeast Asian nations, particularly India, report a substantial burden of oral cancer and oral potentially malignant disorders. This investigation evaluated how well screening findings align with histopathological outcomes and estimated the specificity and sensitivity of chair-side or field-level evaluations of oral lesions. In the first phase, 40,852 individuals aged 20–60 years were examined. Suspicious lesions were stained with toluidine blue (Otto Chemicals Pvt. Ltd., India) at two intervals; cases showing positive staining on both occasions proceeded to biopsy. The initial clinical impressions were subsequently compared with the histopathological results. The average age of patients who received biopsies was 49.01 ± 9.8 years. Among users of tobacco, leukoplakia (1.5%) emerged as the most frequent lesion, yet demonstrated the lowest diagnostic agreement (39.6%). Overall sensitivity reached 88%, while the positive predictive value was 80% for the clinical identification of OPMD. The concordance between clinical and histological diagnoses in this study indicates a higher proportion of true-positive findings during screening efforts in remote and underserved groups, ultimately supporting improved quality of life.

Keywords: Cancer, Toluidine, Oral potentially malignant disorders, Indian

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Introduction

India accounts for nearly one-third of global oral cancer cases and approximately one-fourth of the world's oral cancer-related deaths. A notable share of these cases is detected at later disease stages. Identifying potentially malignant conditions early improves outcomes and long-term well-being [1–3].

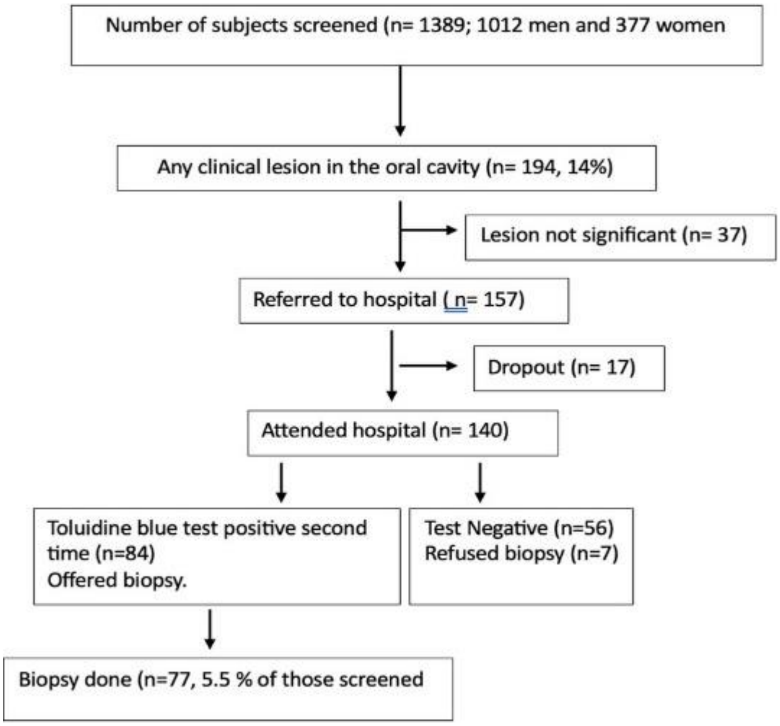

Figure 1. presents the flow sequence of screened participants, clinical diagnoses, referrals, and biopsy confirmations.

The rising rate of oral cancer is a significant public health concern, becoming the country's most prevalent cancer despite awareness campaigns and regulations aimed at reducing exposure to risk factors [4]. Screening strategies have shown variable success in identifying symptom-free individuals, raising questions about practicality [2]. Evidence suggests that risk-based screening is more efficient than population-wide programs. Effectiveness increases when trained healthcare workers (HCWs) are engaged to perform initial examinations and direct suspicious cases to hospitals for further evaluation [5, 6].

Although histopathology remains the definitive diagnostic method, proper referral based on a meticulous clinical examination is essential. When clinicians or trained HCWs recognize lesions accurately, unnecessary procedures and resource expenditure can be minimized [7].

There is limited literature comparing screening-based diagnoses of oral cancer or OPMD against histopathology. Only a few earlier studies have attempted similar assessments using retrospective datasets [8, 9]. Understanding the sensitivity and specificity of chair-side evaluations is crucial for standardizing screening methods, ensuring consistent reporting, and optimizing limited healthcare resources. While earlier papers addressed other primary objectives of this work, the present manuscript focuses on evaluating the accuracy of visual screening in relation to histological confirmation, regarded as the "gold standard" [10].

This study was carried out among a large "high-risk" cohort in the industrial locality of Ranipet, Tamil Nadu, India. Its objective was to measure the agreement between screening findings and biopsy results and estimate the specificity and sensitivity of field-based lesion assessments.

Materials and Methods

Ranipet, a district in Tamil Nadu with a semi-urban setting, includes a mixed population and serves as a center for tannery-related industries. Tobacco and alcohol consumption are highly prevalent in this area.

For this community-level screening initiative, a memorandum of understanding (MOU) was established between Thirumalai Mission Trust Hospital in Vanapadi village (Ranipet district) and Ragas Dental College and Hospital, Chennai. The trust hospital provides care for roughly 142,150 residents across 315 villages and 35,000 families and has been functioning in the region for over ten years.

The trust hospital conducts routine awareness activities supported by a structured team including family care volunteers (FCVs)—one for about 50 households—supervised by multipurpose workers (MPWs) who oversee 500–1,000 households each. Because FCVs are community members themselves, their involvement enhanced local participation and understanding during screening. Using this workforce and the hospital's infrastructure, the oral cancer screening project was initiated collaboratively. Population screening (cross-sectional) occurred from August 2018 to December 2019. Ethical approval was obtained from both institutions (project 20180703, approved July 30, 2018). Study reporting followed STROBE guidelines [11].

Written informed consent was secured from every participant before their inclusion, and all details regarding participation and expected outcomes were explained in the local language (Tamil) to ensure clarity and cooperation. The study adhered to the ethical standards of the Declaration of Helsinki, Good Clinical Practice guidelines, and the norms set by the Indian Council of Medical Research.

Adults, regardless of whether they had oral risk habits, were initially checked for oral lesions. From the target population, 71,356 individuals aged 21–60 years were considered eligible. For operational ease, the study area was separated into ZONE I and ZONE II, consisting of 40,852 and 30,504 people, respectively. A 1:2 case-to-control ratio was used. Potential confounders—age, sex, habits, and occupation—were evenly matched between cases and controls. Controls came from the same community but had no adverse oral habit history. Dental practitioners performed the intra-oral examinations in community locations such as anganwadis and nearby schools. The American Dental Association (ADA) Type III oral examination method was used with artificial lighting. When a suspicious lesion was detected, expert input was obtained through images shared via WhatsApp. Normal mucosal variations or clinically insignificant mucosal findings (e.g., mucosal keratosis variants, smoker's palate, denture-related stomatitis) were excluded from further evaluation. Suspected lesions underwent toluidine blue staining at two distinct times: first in the field, and again at the hospital clinic. Only lesions staining positive on both occasions were biopsied (5 mm punch biopsy), which was carried out by a trained dentist. Samples were placed in 10% formaldehyde, transported within 3–4 hours, and sent to the oral pathology department at Ragas Dental College and Hospital for microscopic assessment. Biopsy sites were sutured, and sutures were removed after one week to confirm proper healing.

Participants reporting tobacco use received counseling at the hospital de-addiction center. Nicotine replacement therapy was provided free of charge as part of their cessation support.

Individuals with confirmed oral malignancies were referred to the Aringar Anna Cancer Treatment Center, Kanchipuram, Tamil Nadu, for appropriate therapy and follow-up. Data were cleaned and entered into Microsoft Excel. Descriptive statistics summarized frequency distributions. Sensitivity and specificity from initial screening were compared with the histopathological gold standard. Statistical analyses were performed using SPSS (Version 20.0, SPSS Inc., Chicago, IL, USA) and Microsoft Excel.

Results and Discussion

Outcomes from the screening initiative were previously described by the authors [10]. In this phase, 77 biopsies were taken, of which 74 were examined histologically; 3 were excluded because they were insufficient for evaluation.

Table 1 outlines key variables, including the total number screened (40,852, 28.7%), mean age of biopsied participants (49.01 ± 9.8 years), average duration of tobacco exposure (15.2 ± 11.9 years), and the exposure index (173.80 ± 213.6). Among individuals using tobacco, leukoplakia (1.5%) appeared most frequently, with the left buccal mucosa accounting for 36.4% of OPMD cases.

Table 1. Variables of interest in the screened population.

Variable of Interest	Observation
Total population screened	40,852 (28.7% of 142,150 targeted individuals)
Mean age of participants who underwent biopsy	49.01 ± 9.8 years
Mean duration of tobacco use among biopsied patients	15.2 ± 11.9 years
Mean exposure factor (daily consumption × years of use)	173.80 ± 213.6
Most common oral potentially malignant disorder (OPMD)	Leukoplakia • 21/41 (51.2%) of all diagnosed OPMDs • 21/1,389 (1.5%) of all tobacco users
Most frequent anatomical site of OPMDs	Left buccal mucosa: 27 cases (36.4%)

Table 2 compares clinical and histopathological findings. Of the 43 (58.1%) clinically diagnosed leukoplakia cases, only 21 displayed dysplasia on histological review. Except for fibroma and frictional keratosis (which showed hyperkeratosis with acanthosis), dysplastic alterations were confirmed among those clinically identified with potentially malignant lesions.

Table 2. Frequency correlation of clinical and histopathological diagnosis of OPMD.

Clinical (Provisional) Diagnosis	**Histopathological Diagnosis**	**Total**
	Mild Dysplasia	Moderate Dysplasia
Leukoplakia	16	1
Erythroleukoplakia	3	–
Verrucous leukoplakia	2	–
Oral submucous fibrosis	1	–
Fibroma	–	–
Tobacco pouch keratosis	5	–
Lichen planus	1	–
Frictional keratosis	–	–
Total	**28 (37.8%)**	**1 (1.4%)**

Overall clinical diagnostic sensitivity was 88%, but individual values varied—ranging from 39.6% for leukoplakia to 100% for verrucous leukoplakia and lichen planus. Positive predictive values exceeded 80% for all clinically identified conditions **(Table 3).**

Table 3. Sensitivity and positive predictive value (PPV) for clinical diagnosis of OPMD in the study.

Clinical (Provisional) Diagnosis	**Sensitivity (%)**	**Positive Predictive Value (PPV) (%)**
Leukoplakia	39.6	80.9
Erythroleukoplakia	50.0	100
Verrucous leukoplakia	100	100
Oral submucous fibrosis	90.0	90.0
Tobacco pouch keratosis	55.5	100
Lichen planus	100	100

Multiple studies indicate that when true-positive cases are detected early, patients experience far better outcomes, including higher survival and improved daily functioning [12, 13]. A recent systematic review also highlighted that screening programs targeting high-risk groups may prevent two to three times more deaths than screening the general population [14, 15]. In this project, we focused on an industrial community considered to be at elevated risk.

The individuals who were eventually biopsied had a mean age of 49.01 ± 9.8 years, a figure closely matching that reported by Torabi *et al*. [15]. Comparable investigations by Maia *et al*. and Mehrotra *et al*. described slightly older averages of 56 and 55 years, respectively.

Leukoplakia represented the most frequently identified OPMD in the current screening activity. Similar observations were made by Chher *et al*. and Pentenero *et al*. [16, 17] in population-level exams in Cambodia and Italy. In contrast, research conducted by Oivio *et al.* [18] and Feng *et al.* [19] in Finland and China indicated that oral lichen planus predominated in their screened cohorts.

In the present dataset, OPMDs were most often found on the left buccal mucosa; the right buccal mucosa and right vestibule followed next. This mirrors patterns described by Torabi *et al*. [15] and M. Bokor-Bratic *et al.* [20]. The updated classification issued by the WHO Collaborating Centre on Oral Cancer includes oral leukoplakia, oral lichen planus, oral lichenoid lesions, proliferative verrucous leukoplakia, and oral submucous fibrosis as OPMDs [15], each carrying a malignant transformation risk that ranges from 5% to 18%.

Among those selected for biopsy, the average duration of harmful oral habits—whether smoking, smokeless tobacco, betel quid, or areca nut—was 15.2 years. A clear upward trend in OPMD diagnoses was observed as the daily frequency of these habits increased (from <5 to >20 times per day). This trend aligns with results from Shivakumar *et al*. [21], who reported 7.31 ± 6.94 years of tobacco use among their OPMD patients along with an average daily exposure of 4.92 ± 4.02.

An additional indicator, the exposure factor (daily usage multiplied by total years), also rose in tandem with OPMD occurrence. The mean exposure factor recorded here was 173.80. This resembles the person-years habit calculations made by Sankaranarayanan *et al*. [22] in Kerala, where longer cumulative exposure was tied to higher rates of cancer incidence and mortality.

A noticeable inverse relationship was detected with respect to lesion size: most lesions measuring 1–1,000 sq mm did not fall into the OPMD category. This particular pattern has not been documented elsewhere. Similarly, lesion texture did not differ significantly between groups—OPMDs comprised 33 soft and 8 firm lesions, while non-OPMD lesions consisted of 27 soft and 6 firm.

The sensitivity of OPMD detection during screening reached 88%, a figure consistent with earlier work comparing clinical observations with microscopic confirmation. For instance, Abidullah *et al.* [23] reported a 78% clinical–histological agreement for white lesions.

Lichen planus and verrucous leukoplakia demonstrated perfect clinical–histological concordance (100% each), followed by oral submucous fibrosis (90%). Paradoxically, although leukoplakia was the most frequently identified OPMD, its clinical sensitivity was only 39.6%. This likely reflects the broad and non-specific nature of the clinical term "leukoplakia," which does not always correspond well with the underlying tissue changes. Erythroleukoplakia also showed inconsistent matching, probably due to the close resemblance between severe dysplasia and carcinoma in situ.

There is a strong justification for sustained nationwide oral cancer screening. Taiwan remains the only country with an ongoing national program, focusing particularly on individuals who currently or previously chewed betel nut or who smoke [2]. Implementing similar programs would be especially important in South and Southeast Asia, where OPMD rates are notably high.

Improved examiner training is another essential step, as disparities in skill and calibration can reduce diagnostic consistency and affect screening efficiency. The current study reinforces previous evidence showing that visual screening correlates well with histopathological findings. Given its high sensitivity, it remains a practical first-line method for communities with limited access to specialized healthcare. Nonetheless, the study was limited by dropouts during biopsy referrals—likely driven by anxiety—as well as inadequate tissue samples that required exclusion. These issues should be carefully addressed in future research designs.

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Conflict of Interest: None

Financial Support: None

Ethics Statement: The studies involving humans were approved by IRB, Ragas Dental College and Hospital, Chennai IRB, Thirumalai Mission Hospital, Ranipet. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

References

1. Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in India. Sens Int. (2020) 1:100046. doi: 10.1016/j.sintl.2020.100046
2. Warnakulasuriya S, Kerr AR. Oral cancer screening: past, present, and future. J Dent Res. (2021) 100(12):1313–20. doi: 10.1177/00220345211014795
3. Seoane J, Takkouche B, Varela-Centelles P, Tomás I, Seoane-Romero JM. Impact of delay in diagnosis on survival to head and neck carcinomas: a systematic review with meta-analysis. Clin Otolaryngol. (2012) 37(2):99–106. doi: 10.1111/j.1749-4486. 2012.02464.x
4. Sharma S, Satyanarayana L, Asthana S, Shivalingesh KK, Goutham BS, Ramachandra S. Oral cancer statistics in India on the basis of first report of 29 population-based cancer registries. J Oral Maxillofac Pathol. (2018) 22(1):18–26. doi: 10.4103/jomfp.JOMFP_113_17
5. Awan KH. Oral cancer: early detection is crucial. J Int Oral Health. (2014) 6 (5):1–8.
6. Mariño R, Haresaku S, McGrath R, Bailey D, Mccullough M, Musolino R, et al. Oral cancer screening practices of oral health professionals in Australia. BMC Oral Health. (2017) 17(1):151. doi: 10.1186/s12903-017-0439-5
7. Soyele OO, Aborisade A, Adesina OM, Olatunji A, Adedigba M, Ladeji AM, et al. Concordance between clinical and histopathologic diagnosis and an audit of oral histopathology service at a Nigerian tertiary hospital. Pan Afr Med J. (2019) 34:100. doi: 10.11604/pamj.2019.34.100.19388
8. Acharya S, Tayaar AS. Analysis of clinical and histopathological profiles of oral squamous cell carcinoma in young Indian adults: a retrospective study. J Dent Sci. (2012) 7(3):224–30. doi: 10.1016/j.jds.2012.05.005
9. Rahaman SMU, Mujib BA. Histopathological correlation of oral squamous cell carcinoma among younger and older patients. J Oral Maxillofac Pathol. (2014) 18 (2):183–8. doi: 10.4103/0973-029X.140734

10. Madan Kumar PD, Iyer K, Soni S, Nagarajan L, Kumar K, Solomon S, et al. A simple screening program for oral cancer in a defined geographic area in southern India: a community-based cross-sectional study. Cancer Res Stat Treat. (2022) 5:226–31. doi: 10.4103/crst.crst_92_22
11. Available at: https://www.strobe-statement.org/checklists/ (Accessed Auguest 07,2023).
12. Parak U, Lopes Carvalho A, Roitberg F, Mandrik O. Effectiveness of screening for oral cancer and oral potentially malignant disorders (OPMD): a systematic review. Prev Med Rep. (2022) 30:101987. doi: 10.1016/j.pmedr.2022. 101987
13. Bouaoud J, Bossi P, Elkabets M, Schmitz S, Van Kempen LC, Martinez P, et al. Unmet needs and perspectives in oral cancer prevention. Cancers. (2022) 14(7):1815. doi: 10.3390/cancers14071815
14. González-Moles MÁ, Aguilar-Ruiz M, Ramos-García P. Challenges in the early diagnosis of oral cancer, evidence gaps and strategies for improvement: a scoping review of systematic reviews. Cancers. (2022) 14(19):4967. doi: 10.3390/cancers14194967
15. Torabi M, Afshar MK, Afshar HM, Mohammahzadeh I. Correlation between clinical and histopathologic diagnosis of oral potentially malignant disorder and oral squamous cell carcinoma. Pesqui Bras Odontopediatria Clín Integr. (2021) 21. doi: 10.1590/pboci.2021.068
16. Chher T, Hak S, Kallarakkal TG, Durward C, Ramanathan A, Ghani WMN, et al. Prevalence of oral cancer, oral potentially malignant disorders, and other oral mucosal lesions in Cambodia. Ethn Health. (2018) 23(1):1–15. doi: 10.1080/ 13557858.2016.1246431
17. Pentenero M, Broccoletti R, Carbone M, Conrotto D, Gandolfo S. The prevalence of oral mucosal lesions in adults from the Turin area. Oral Dis. (2008) 14(4):356–66. doi: 10.1111/j.1601-0825.2007.01391.x
18. Oivio UM, Pesonen P, Ylipalosaari M, Kullaa A, Salo T. Prevalence of oral mucosal normal variations and lesions in a middle-aged population: a northern Finland birth cohort 1966 study. BMC Oral Health. (2020) 20:357. doi: 10.1186/ s12903-020-01351-9
19. Feng J, Zhou Z, Shen X, Wang Y, Shi L, Wang Y, et al. Prevalence and distribution of oral mucosal lesions: a cross-sectional study in Shanghai, China. J Oral Pathol Med. (2015) 44(7):490–4. doi: 10.1111/jop.12264
20. Bokor-Bratíc M, Vucković N, Mirković S. Correlation between clinical and histopathologic diagnosis of potentially malignant oral lesions. Arch Oncol. (2004) 12(3):145–7. doi: 10.2298/AOO0403145B
21. Shivakumar KM, Raje V, Kadashetti V. Prevalence of oral potentially malignant disorders (OPMD) in adults of Western Maharashtra, India: a cross-sectional study. J Cancer Res Ther. (2022) 18(Supplement):S239–43. doi: 10.4103/jcrt.JCRT_1444_20
22. Sankaranarayanan R, Ramadas K, Thomas G, Muwonge R, Thara S, Mathew B, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster- randomised controlled trial. Lancet. (2005) 365(9475):1927–33. doi: 10.1016/S0140-6736(05)66658-5
23. Abidullah M, Raghunath V, Karpe T, Akifuddin S, Imran S, Dhurjati VN, et al. Clinicopathologic correlation of white, non scrapable oral mucosal surface lesions: a study of 100 cases. J Clin Diagn Res. (2016) 10(2):ZC38–41. doi: 10.7860/JCDR/ 2016/16950.722