RESEARCH ARTICLE

Evaluation of Serum Lactate Dehyderogenase Level as a potential marker of Dysplasia in Oral Submucous Fibrosis and Leukoplakia

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ABSTRACT

Background: Oral submucous fibrosis (OSMF) and leukoplakia are oral potentially malignant disorders associated with an increased risk of malignant transformation. Lactate dehydrogenase (LDH), an intracellular enzyme released during cellular injury and increased turnover, may serve as a potential biomarker for assessing disease severity and epithelial dysplasia.

Objectives: To estimate and compare serum LDH levels across different clinical grades of OSMF, homogeneous and non-homogeneous leukoplakia, and healthy controls, and to evaluate their association with histopathological features and dysplasia.

Materials and Method: A prospective, comparative study was conducted involving 70 participants divided into seven groups of 10 each: OSMF Grades I–IV according to the Khanna and Andrade classification based on clinical features, homogeneous leukoplakia, non-homogeneous leukoplakia, and healthy controls. Clinical examination, serum LDH estimation using the enzymatic UV kinetic method, and histopathological examination of biopsy specimens were performed. The collected data were analysed using appropriate statistical tests to compare serum LDH levels among the study groups and assess their association with histopathological findings.

Results: Results showed male predominance and peak prevalence in the 20–40-year age group in both OSMF and leukoplakia groups. Mean serum LDH levels showed highly significant variation with age, gender and habit-associated OPMDs [p=0.001*], where higher levels observed in non-homogeneous leukoplakia and higher grades of OSMF compared to controls. Histopathologically, Early OSMF grades showed no dysplasia, while mild dysplasia was observed in higher grades; homogeneous leukoplakia showed an equal distribution of mild and moderate dysplasia, whereas non-homogeneous leukoplakia showed a predominance of moderate dysplasia [p=0.1]. Mean serum LDH levels significantly increased with the severity of epithelial dysplasia according to WHO criteria and were highest in non-homogeneous leukoplakia, followed by homogeneous leukoplakia and OSMF, which was statistically highly significant [p=0.0001*].

Conclusion:- In conclusion, the majority of participants affected by OSMF and leukoplakia in this study were male, accounting for 80% (56) cases, which indicates a clear male predominance in the occurrence of the disease. Furthermore, the condition was most commonly observed in the 20–40year age group. Notably, the study demonstrates that as clinical severity of OSMF and leukoplakia progresses and with increasing grades of epithelial dysplasia according to WHO criteria, serum LDH levels show a statistically significant increase compared to the control group, suggesting its potential role as a cost-effective biomarker for assessing disease severity and dysplastic changes in oral potentially malignant disorders.

Keywords: Oral submucous fibrosis; leukoplakia; serum LDH; lactate dehydrogenase; oral potentially malignant disorders; epithelial dysplasia.

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Introduction: -

Oral Submucous Fibrosis (OSMF) is a chronic, progressive oral potentially malignant disorder predominantly affecting the Indian subcontinent and Southeast Asia.[1] It is defined as "an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx, characterized by a juxta-epithelial inflammatory reaction followed by fibro-elastic changes in the lamina propria, with epithelial atrophy leading to mucosal stiffness, trismus and difficulty in eating" (Pindborg J.J., 1966).[2] OSMF is strongly associated with areca nut and tobacco consumption. Arecoline stimulates fibroblast proliferation and collagen synthesis, while other areca nut constituents inhibit collagen degradation and promote collagen cross-linking, resulting in progressive fibrosis.[3] Clinically, OSMF presents with a burning sensation, mucosal blanching, palpable fibrous bands and restricted mouth opening. Histopathologically, it is characterized by juxta-epithelial inflammation, dense collagen deposition, varying degrees of hyalinization and epithelial atrophy, with or without epithelial dysplasia. OSMF carries a significant risk of malignant transformation, particularly into oral squamous cell carcinoma, and requires early diagnosis, cessation of areca nut and tobacco habits, and regular long-term follow-up.[4,5,6]

Leukoplakia is defined as "A white plaque of questionable risk for malignant transformation, having excluded other known white lesions or disorders that carry no increased risk for cancer" (Warnakulasuriya et al.).[7] Oral leukoplakia is broadly classified into homogeneous and non-homogeneous types. Homogeneous leukoplakia presents as a uniformly white, well-demarcated plaque, whereas non-homogeneous leukoplakia includes speckled (erythroleukoplakia), nodular and verrucous forms. Histopathologically, leukoplakia may exhibit hyperkeratosis, acanthosis and varying degrees of epithelial dysplasia, ranging from mild to severe; invasive squamous cell carcinoma may occasionally be identified. Homogeneous leukoplakia generally has a lower malignant potential than non-homogeneous leukoplakia, particularly speckled lesions. Proliferative verrucous leukoplakia (PVL) is a progressive, multifocal form with frequent recurrence and a particularly high risk of malignant transformation. Overall, malignant potential depends on the clinical type, lesion size, anatomical site and presence and severity of epithelial dysplasia.[7,8]

Lactate dehydrogenase (LDH) assessment may provide a simple, minimally invasive and cost-effective approach for evaluating cellular injury and metabolic alterations in oral potentially malignant disorders, including OSMF and leukoplakia. LDH is a cytoplasmic glycolytic enzyme released into body fluids following cellular damage and increased membrane permeability. Chronic inflammation, oxidative stress, tissue hypoxia and increased glycolytic activity may alter LDH levels in these conditions. Its assessment may provide insights into epithelial turnover, tissue damage and disease pathogenesis, with potential diagnostic and prognostic significance. However, further research is required to establish LDH as a reliable biomarker for disease progression, risk stratification and malignant transformation in OSMF and leukoplakia.This comparative biochemical analysis addresses a critical gap by evaluating serum LDH levels across all four grades of OSMF and both subtypes of leukoplakia along with healthy controls in a single cohort, which is scarcely reported. Serum LDH estimation by enzymatic UV kinetic method is simple, cost-effective and reproducible. Assessing its correlation with histopathological dysplasia will help validate its utility as a potential marker for early detection, clinical grading and monitoring of OPMDs in routine Oral Medicine practice.[9,10]

MATERIALS AND METHOD: -

The present purposive, prospective and comparative study was conducted in the Department of Oral Medicine and Radiology, Government Dental College and Hospital, Jamnagar, after obtaining Institutional Ethics Committee clearance (EC/NEW/INST/1896/191/03/2025). Participants were recruited from the outpatient department according to predefined inclusion and exclusion criteria after obtaining written and verbal informed consent. The sample size was calculated using G*Power software version 3.1.9.4, considering an effect size of 0.5, a significance level of 5% and a statistical power of 80%. The calculated sample size was 63, which was rounded to 70 participants. Participants were equally divided into seven groups (n = 10 each): OSMF Grades I, II, III and IV, homogeneous leukoplakia, non-homogeneous leukoplakia and age and gender matched healthy controls.

Participants aged 20–70 years with a history of areca nut or tobacco consumption, including cigarettes and bidis, and clinically diagnosed OSMF or leukoplakia.Healthy controls were individuals without harmful oral habits or systemic or genetic disorders. Participants unwilling to participate, those with systemic diseases, pregnant women, and patients undergoing chemotherapy or radiotherapy were excluded. Detailed habit history and clinical examination were performed. Clinical grading of OSMF was performed according to the Khanna and Andrade[11] classification, while leukoplakia was categorized into homogeneous and non-homogeneous types according to clinical appearance. Homogeneous leukoplakia was characterized by a uniformly white or greyish-white, well-demarcated plaque with a smooth, thin, cracked mud,leathery or fissured

surface and was usually asymptomatic. In contrast, non-homogeneous leukoplakia exhibited variations in colour, thickness or texture, presenting as mixed red and white areas (speckled or erythroleukoplakia), nodular lesions or thick, verrucous plaques (Figure1).

Under aseptic precautions, 2 mL of venous blood was collected in a plain vacuette and centrifuged at 2500 rpm for 4–5 minutes using a REMI PR 23 centrifuge. Serum was used for pre-biopsy investigations, including complete blood count (CBC), bleeding time (BT), clotting time (CT), random blood sugar (RBS), hepatitis B surface antigen (HBsAg), human immunodeficiency virus (HIV), hepatitis C virus (HCV) testing, as well as LDH estimation using an Altgenix LDH kit by the enzymatic UV kinetic method at 340 nm using a semi-automated analyser. A biopsy was obtained from the most clinically affected site under local anaesthesia using a biopsy punch and preserved in 10% formalin for histopathological evaluation. Epithelial dysplasia was assessed according to WHO[12] criteria (Figure 2). Data were analysed using SPSS version 25.0, Descriptive statistics, one-way ANOVA, two-way ANOVA, Chi-square and Fisher's exact tests were applied, with statistical significance set at $p<0.05$. where P value > 0.05 was considered nonsignificant, P value < 0.05 was considered significant*, and P value < 0.01 was considered highly significant**.

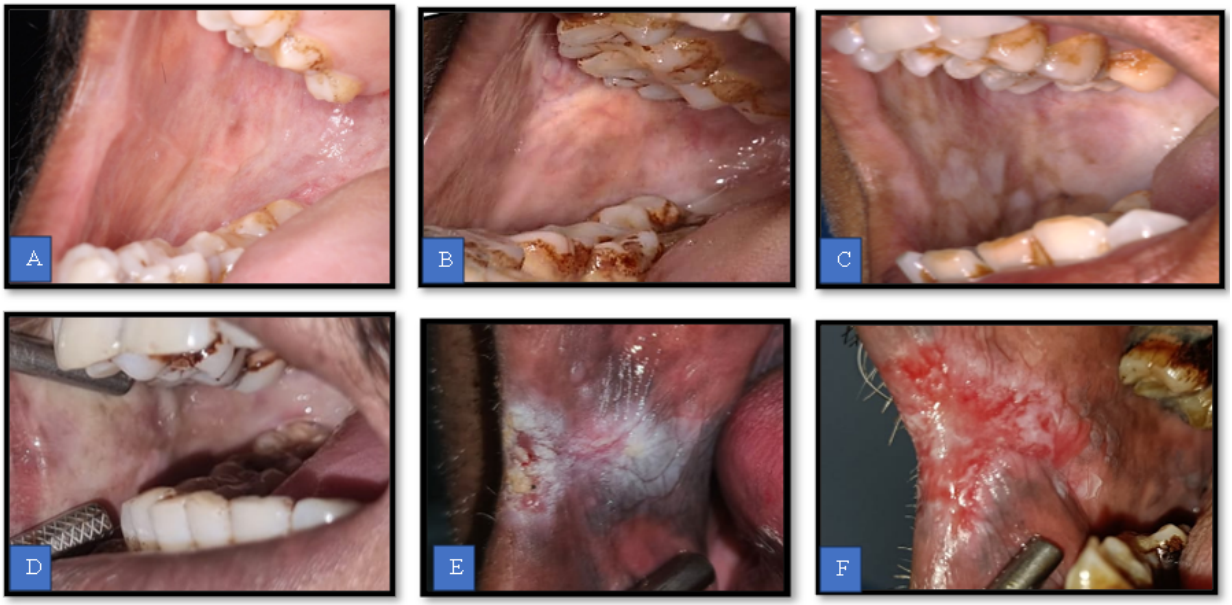


Figure 1: Clinical features of different grades of OSMF and leukoplakia

(A- OSMF Grade I, B- OSMF Grade II, C- OSMF Grade III, D- OSMF Grade IV, E- Homogenous leukoplakia, F- Non-Homogenous leukoplakia)

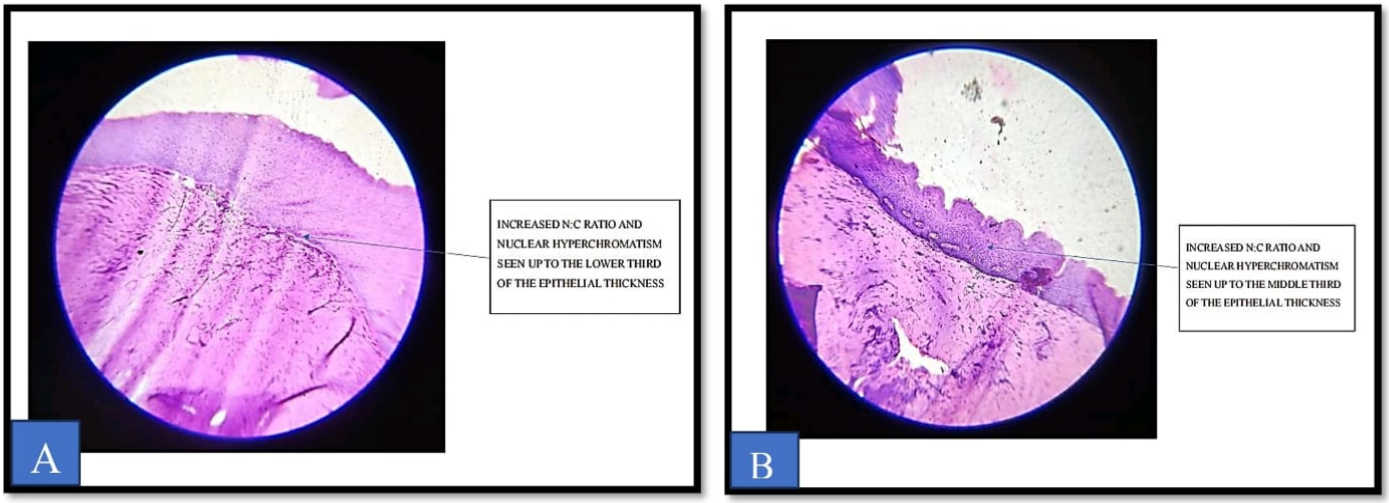


Figure 2: Histopathological grading of epithelial dysplasia according to WHO criteria (A- Mild epithelial dysplasia, B- Moderate epithelial dysplasia)

Results: -

Out of total 70 participants showing a male predominance, most belonged in the 20-40 years age group, with no significant difference in age and gender distribution among the groups [p=0.1] [Table 1]. Mean serum LDH levels showed significant variation, being higher in non-homogenous leukoplakia and higher grades of OSMF, which was highly significant [p=0.001] [Table 2]. On histopathological evaluation, no dysplasia was observed in OSMF Grade I and III, while mild dysplasia was noted in OSMF Grade II and IV. In homogenous leukoplakia, mild and moderate dysplasia were equally distributed, whereas non-homogenous leukoplakia showed a predominance of moderate dysplasia, with no severe dysplasia in any group [p=0.1] [Table 3]. Comparison of mean serum LDH levels across WHO grades of dysplasia revealed higher LDH levels in non-homogenous leukoplakia compared to homogenous leukoplakia and OSMF, and LDH levels increased with severity of dysplasia, which was statistically highly significant [p=0.0001] [Table 4].

TABLE 1: AGE- AND GENDER-WISE DISTRIBUTION OF PARTICIPANTS ACROSS DIFFERENT CLINICAL GRADES OF OSMF, LEUKOPLAKIA AND CONTROL GROUP

AGE GROUP (YEARS)	GENDER	OSMF GRADE I	OSMF GRADE II	OSMF GRADE III	OSMF GRADE IV	HOMOGENOUS LEUKOPLAKIA	NON HOMOGENOUS LEUKOPLAKIA	CONTROL	TOTAL
20-40	MALE	5	5	8	3	1	4	4	30
	FEMALE	2	0	1	4	0	0	2	9
41-60	MALE	2	1	0	3	7	5	2	20
	FEMALE	1	3	0	0	0	0	1	5
>60	MALE	0	1	1	0	2	1	1	6
	FEMALE	0	0	0	0	0	0	0	0
TOTAL	MALE	7	7	9	6	10	10	7	56
	FEMALE	3	3	1	4	0	0	3	14
	TOTAL	10	10	10	10	10	10	10	70
p VALUE	0.1								

TABLE 2: AGE AND GENDER WISE VARIATIONS IN MEAN LDH LEVELS (IU/L) AMONG OSMF, LEUKOPLAKIA AND CONTROL PATIENTS

AGE GR	GENDER	OSMF GR	OSMF GR	OSMF GRAD	OSMF GRAD	HOMOGE	NON HOMO	CONTROL

20-40	MALE	342.6	342	339.12	369	394	391.75	347.25
	FEMALE	387	0	442	355	0	0	386
41-60	MALE	298.5	356	0	369.33	375	379.4	287.5
	FEMALE	398	363	0	0	0	0	362
>60	MALE	0	406	445	0	390.5	476	377
	FEMALE	0	0	0	0	0	0	0
p value		0.001**						

TABLE 3: DISTRIBUTION OF ORAL EPITHELIAL DYSPLASIA ACCORDING TO WHO GRADING CRITERIA ACROSS DIFFERENT OSMF GRADES AND LEUKOPLAKIA

DYSPLASIA GRADING ACCOEDING TO WHO	OSMF GRADE I	OSMF GRADE II	OSMF GRADE III	OSMF GRADE IV	HOMOGENOUS LEUKOPLAKIA	NON HOMOGENOUS LEUKOPLAKIA	p value
MILD	0	1	0	1	5	3	0.1
MODERATE	0	0	0	0	5	7	
SEVERE	0	0	0	0	0	0	

TABLE 4: COMPARISON OF MEAN SERUM LDH LEVELS (IU/L) ACROSS WHO GRADES OF EPITHELIAL DYSPLASIA IN OSMF AND LEUKOPLAKIA PATIENTS

DYSPLASIA GRADING ACCOEDING TO WHO	OSMF GRADE I	OSMF GRADE II	OSMF GRADE III	OSMF GRADE IV	HOMOGENOUS LEUKOPLAKIA	NON HOMOGENOUS LEUKOPLAKIA	p value
MILD	0	317	0	365	380.8	398	0.0001**
MODERATE	0	0	0	0	379.2	392.28	
SEVERE	0	0	0	0	0	0	

DISCUSSION: -

Oral potentially malignant disorders, such as OSMF and leukoplakia, carry a variable potential for malignant transformation, necessitating the exploration of reliable biomarkers for early identification of high-risk lesions. [13] LDH, an enzyme associated with cellular metabolism and tissue injury, has emerged as a promising biochemical marker for evaluating metabolic alterations and cellular damage in these disorders. [14]

In the present study, male predominance was observed, with males accounting for 80% of the total participants. This finding is consistent with Panda et al.[15], who also reported male predominance among patients with OSMF and leukoplakia. This predominance may be attributed to differences in areca nut and tobacco consumption patterns, occupational exposures, and health-seeking behaviour. Regarding age distribution, the majority of participants in the present study belonged to the 20–40-year age group, whereas Panda et al.[15] reported the highest representation in the 40–49-year age group. This difference may partly be attributed to variations in geographical location, socioeconomic status, duration and type of harmful oral habits, and participant selection criteria. Furthermore, the two studies used different age classifications. Panda et al.[15] divided participants into five age groups: 20–29, 30–39, 40–49, 50–59, and 60–69 years, whereas the present study classified participants into three broader age groups: 20–40, 41–60, and above 60 years. These differences in age categorization may have influenced the observed distribution of participants across age groups. Additionally, Panda et al.[15] included 120 participants divided into three groups of 40 each: healthy controls, patients with OSMF, and patients with leukoplakia. However, the OSMF group was not further stratified according to clinical grades, and the leukoplakia group was not subdivided into homogeneous and non-homogeneous types. In contrast, the present study adopted a more systematic classification, with equal numbers of participants assigned to each clinical grade of OSMF and separate groups for homogeneous and non-homogeneous leukoplakia.

In the present study, age- and gender-wise variations in mean serum lactate dehydrogenase (LDH) levels were observed across different clinical grades of OSMF, homogeneous and non-homogeneous leukoplakia, and healthy controls. Higher LDH levels were generally observed in patients with leukoplakia, particularly non-homogeneous leukoplakia, compared with healthy controls. These findings are consistent with Panda et al.[15], who reported higher mean serum LDH levels in patients with OSMF and leukoplakia than in healthy controls. In contrast, Shah et al.[16] reported lower mean serum LDH levels in patients with oral potentially malignant disorders than in individuals with oral habits and patients with oral squamous cell carcinoma, with no statistically significant differences among the groups. These differences may be attributed to variations in study populations, clinical grouping, sample size, disease characteristics, and laboratory methodologies. Shah et al. measured LDH levels in both saliva and serum using spectrophotometry at 340 nm, whereas the present study estimated serum LDH levels using an Altgenix LDH kit based on the enzymatic UV kinetic method at 340 nm with a semi-automated analyser. Differences in assay kits, sample processing, calibration, and analytical conditions may have contributed to the variation in findings between the studies.

In the present study, according to WHO grading criteria, mild epithelial dysplasia was observed in OSMF Grades II and IV, whereas no dysplasia was identified in Grades I and III. These findings were compared with Jani Y et al.[17], who reported dysplasia in 53 out of 100 OSMF patients, including 30 mild, 22 moderate, and 1 severe case. Unlike their study, no moderate or severe dysplasia was observed in the present OSMF group. This difference may be attributed to the smaller sample size of the present study, which included 40 OSMF patients, with only 2 exhibiting mild dysplasia, as well as variations in patient selection and areca nut or tobacco exposure. Among leukoplakia cases, homogeneous leukoplakia showed an equal distribution of mild and moderate dysplasia, while non-homogeneous leukoplakia exhibited a predominance of moderate dysplasia, with no severe dysplasia observed in any group. The predominance of moderate dysplasia in non-homogeneous leukoplakia is consistent with Evren et al.[18] and Rubert et al.[19] found that non-homogeneous leukoplakia was associated with higher-grade epithelial dysplasia.

In the present study, higher serum LDH levels were observed in patients with leukoplakia than in those with OSMF. Among cases with mild dysplasia, the highest mean LDH level was observed in non-homogeneous leukoplakia 398 IU/L, followed by homogeneous leukoplakia 380.8 IU/L. In cases with moderate dysplasia, the mean LDH levels were 392.28 IU/L and 379.2 IU/L in non-homogeneous and homogeneous leukoplakia, respectively. No cases of severe dysplasia were identified in the study population. These findings suggest a possible direct association between serum LDH levels and epithelial alterations in OPMDs. Similar findings were reported by Panda et al.[15], who observed differences in serum and salivary LDH levels among patients with OSMF, leukoplakia, and healthy controls, with higher levels in the disease groups than in healthy controls. In contrast, Shah et al.[16] reported no statistically significant differences in serum LDH levels among the study groups, despite investigating LDH as a potential biomarker for OPMDs. These differences may be attributed to variations in sample size, study design, clinical classification, and disease severity. Shah et al. included 30 participants divided into three groups: individuals with oral habits, patients with OPMDs, and patients with oral squamous cell carcinoma (OSCC), with 10 participants in the OSCC group. Furthermore, Shah et al.[16] measured LDH levels in both saliva and serum using spectrophotometry at 340 nm, whereas the present study

estimated serum LDH levels using an Altgenix LDH kit based on the enzymatic UV kinetic method at 340 nm with a semi-automated analyser. Differences in assay kits, sample processing, and analytical conditions may also have contributed to the variations in findings between the studies.

Limitations: The present study was limited by a relatively small sample size, single-centre recruitment, cross-sectional design, and unequal representation of demographic characteristics across the study groups. The absence of severe epithelial dysplasia and the limited number of participants in each group restricted the assessment of serum LDH across the full spectrum of dysplastic changes.

Future prospects: Future studies should include larger, multicentric populations with longitudinal follow-up to validate serum LDH as a potential biomarker for disease severity and malignant transformation in OSMF and leukoplakia. Further research should establish diagnostic cut-off values, determine sensitivity and specificity, assess the influence of systemic and metabolic factors, and incorporate molecular studies to clarify the role of LDH in disease progression and identify potential diagnostic and therapeutic targets.

Conclusion: Based on the results of the present study, it can be concluded that OSMF and leukoplakia predominantly affected males, with the majority of participants belonging to the 20–40-year age group. Serum LDH levels showed significant variations across age and gender categories and were generally higher in patients with leukoplakia, particularly non-homogeneous leukoplakia, and higher clinical grades of OSMF compared with healthy controls. Serum LDH levels showed a highly significant association with the grades of epithelial dysplasia, suggesting its potential role as an adjunctive biomarker for assessing disease severity and epithelial alterations in oral potentially malignant disorders.

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There are no conflicts of interest.

REFERNECES:-

1) Shih YH, Wang TH, Shieh TM, Tseng YH. Oral Submucous Fibrosis: A Review on Etiopathogenesis, Diagnosis, and Therapy. Int J Mol Sci. 2019;20(12):2940.

2) Shafer, textbook of oral pathology, 9th edition, 1st volume, 2020, chapter no 5, page

no 164-166.

3) Maheswari TNU, Ramakrishnan K, Senthilnathan K, Prathiba N, Ganapathy N, Ramani P. Prevalence of Different Stages of Oral Submucous Fibrosis In India: A Cross-Sectional Study. Educ Adm Theory Pract. 2024;30(5):4750-4756.

4) Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263.

5) Kumari P, Debta P, Dixit A. Oral Potentially Malignant Disorders: Etiology, Pathogenesis, and Transformation Into Oral Cancer. Front Pharmacol. 2022;13:825266.

6) Iocca O, Sollecito TP, Alawi F, Weinstein GS, Newman JG, De Virgilio A, Pellini R, Spriano G, Villa A. Potentially malignant disorders of the oral cavity and oral dysplasia: A systematic review and meta-analysis of malignant transformation rate by subtype. Head Neck. 2020;42(3):539-555.

7) Alajbeg I, Challacombe SJ, Holmstrup P, Jontell M. Red and white lesions of the oral mucosa. In: Glick M, Greenberg MS, Lockhart PB, Challacombe SJ, editors. Burket's Oral Medicine. 13th ed. Hoboken (NJ): Wiley; 2021. p. 85-138.

8) George A, Sreenivasan BS, Sunil S, Varghese SS, Thomas J, Gopakumar D, et al. Potentially malignant disorders of oral cavity. Oral Maxillofac Pathol J. 2011;2(1):95–100.

9) Iglesias-Velázquez Ó, López-Pintor RM, González-Serrano J, Casañas E, Torres J, Hernández G. Salivary LDH in oral cancer and potentially malignant disorders: A systematic review and meta analysis. Oral Dis. 2022;28(1):44-56.

10) Shah FY, Shetty DC, Kaur G, Gupta S, Pathak A, Aggarwal V. Serum and Saliva LDH Levels in Patients with Habit, Oral Potentially Malignant Disorders (OPMDs), and Oral Squamous Cell Carcinoma (OSCC): A Spectrophotometry Study. J Pharm Bioallied Sci. 2023;15(Suppl 2):S881-S884.

11) Khanna JN, Andrade NN. Oral submucous fibrosis: a new concept in surgical management. Report of 100 cases. Int J Oral Maxillofac Surg. 1995;24(6):433-9.

12) El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (Eds). (2017). WHO Classification of Head and Neck Tumours. International Agency for Research on Cancer, Lyon, France. Page 112-113.

13) Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, González-Moles MÁ, Kerr AR, et al. Oral potentially malignant disorders: a consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021;27(8):1862-80.

14) Barbi W, Purohit BM. Serum lactate dehydrogenase enzyme as a tumor marker in potentially malignant disorders: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2022;23(8):2553-9.

15) Panda A, Behura SS, Bhuyan L, Dash KC, Kumar V, Mukherjee S. Assessment of lactate dehydrogenase

enzyme levels in saliva and serum of oral submucous fibrosis and leukoplakia patients. J Oral Maxillofac Pathol. 2020;24(1):183.

16) Shah FY, Shetty DC, Kaur G, Gupta S, Pathak A, Aggarwal V. Serum and saliva LDH levels in patients with habit, oral potentially malignant disorders (OPMDs), and oral squamous cell carcinoma (OSCC): a spectrophotometry study. J Pharm Bioallied Sci. 2023;15(Suppl 2):S881–S884.

17) Jani YV, Dudhia BB. The clinicohistopathologic study of oral submucous fibrosis: A new staging system with treatment strategies. J Indian Acad Oral Med Radiol 2016;28:111-8.

18) Evren I, Brouns ER, Poell JB, Wils LJ, Brakenhoff RH, Bloemena E, et al. Associations between clinical and histopathological characteristics in oral leukoplakia. Oral Dis. 2023;29(2):696–706.

19) Rubert A, Bagán L, Bagán JV. Retraction: Oral leukoplakia, a clinical-histopathological study in 412 patients. J Clin Exp Dent. 2021;13(5):e426-e432. Published 2021 May 1. doi:10.4317/jced.532746