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CAN CLINICAL IMAGE OF ORAL LEUKOPLAKIA ENVISAGE ITS MALIGNANT POTENTIAL?

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ABSTRACT

Background: Fractal analysis (FA) is a non-invasive method that quantifies complex geometric structures by generating a fractal dimension (FD), which can measure the complexity of mucosa. Healthy human tissue has a dense internal similarity at the micro-level. When a pathological process occurs, this internal coherence is broken down, resulting in complexity. FD increases or decreases according to the complexity of the object. Oral Leukoplakia is a potentially malignant oral disorder and the complexity in this lesion can occur due to increase in keratinisation. In such lesions fractal dimensions can be an important tool in detecting the malignant potential of Oral Leukoplakia.

Aim: To assess the fractal dimension of Oral leukoplakia and compare it with normal mucosa.by using Clinical Photographs.

Materials And Methods: Clinically the lesions were photographed and later evaluated by White and Rudolph and box count method using Image J software.

Results:The mean fractal dimension (FD) values increased progressively from normal mucosa (1.10) to normal mucosa with tobacco habits (1.32), lesional mucosa (1.37), and oral cancer (1.39), with a statistically significant difference among groups ($p < 0.05$). FD values in normal mucosa were significantly lower than in other groups, while differences between habit-associated mucosa, lesional mucosa, and oral cancer were not statistically significant. No significant differences in FD values were observed with respect to gender or type of tobacco use (smoking vs. smokeless).

A cutoff value of 1.2745 effectively differentiated normal mucosa from both habit-associated and lesional mucosa, while higher cutoffs 1.3349 and 1.3377 distinguished oral cancer from normal and lesional mucosa, respectively.

Conclusion: The present study demonstrates that fractal dimension (FD) analysis is an effective, non-invasive tool for assessing structural complexity in oral mucosa. A clear and progressive increase in FD values was observed indicating increasing disruption of tissue architecture and complexity. However, its limited ability to distinguish between habit-associated and lesional mucosa suggests that further refinement may be required for staging disease progression.

KEYWORDS: Fractal dimensions, oral leukoplakia, fractal objects, box count method.

INTRODUCTION

Fractal analysis (FA) is a mathematical and computational tool that quantitatively assesses the so-called fractal dimension (FD) of a natural or artificial thing called a “fractal object” [4]. The word fractal is derived from the Greek word fractus which means broken or fracture [2]. This word was introduced by the mathematician, Mandelbrot in the 1970s.Fractal analysis deals with the property of self-similarity of different fractal objects. The characteristic feature of fractal objects is their property of self-similarity irrespective of their complex shapes. These objects are self-similar when viewed at different magnifications and at different time scales. Fractal objects exist in nature as well as in the human body [2]. Some examples of fractal objects in the human body include heart rate, brain gyri, sulci, blood vessels and in nature it includes vegetables like broccoli, etc. Fractal dimension is the topological variant that provides very useful information on the complexity presented by the object of study when it is examined in different levels of detail [1]. These fractal dimensions are expressed as numerical value. The value of fractal dimensions increases or decreases depending upon the variations in the complexity of the fractal object. Fractal dimension analysis is a non-invasive procedure which can be carried out by the medical staff for at a primary level of healthcare to distinguish between premalignant lesions and malignant lesions [2].

Oral leukoplakia is a potentially malignant disorder involving the epithelium of the oral mucosa. Oral leukoplakia has a statistically increased risk of developing oral cancer. For this reason, early diagnosis and detection is essential in order to

prevent malignant transformation and provide necessary intervention. Oral leukoplakia has a branching pattern and fractal properties; hence, good quality clinical images of oral leukoplakia can be considered as fractal objects [2]. The fractal dimension value changes with the change in the keratinization of the mucosa in oral leukoplakia.
This study presents a software named Image J and explores it ability to evaluate the fractal dimensions of clinical images of oral leukoplakia and compare it with clinical images of heathy mucosa. White and Rudolph method and the box count method was employed under the Image J software.

AIM:
To assess the fractal dimension of Oral leukoplakia and compare it with normal mucosa.by using Clinical Photographs.

OBJECTIVES:
1.To assess fractal dimension values of normal mucosa and corelate them with the fractal dimension values of lesional mucosa.
2.To assess fractal dimension values of normal mucosa and corelate them with the fractal dimension values of mucosa of patients with tobacco habits and without any lesions.
3. To assess fractal dimension values of normal mucosa and corelate them with the fractal dimension values of malignant mucosa.
4.To assess difference in fractal dimension values of mucosa of patients consuming tobacco in smokeless and smoking form.
5.To assess fractal dimension values of mucosa of male and female patients to determine any gender predilection.

MATERIALS AND METHODS
First ethical approval was obtained from the institutional research and ethics board to conduct the study. (IREB Reference Number: IREB/2025/OMR/08). Clinical images of patients were obtained in the Department of Oral Medicine and Radiology.
The prospective study was carried out between July 2025-September 2025.As per ethical standards, patients name and details were kept confidential.

Inclusion Criteria
1.Clinical images of buccal mucosa showing oral leukoplakia lesions in patients having tobacco habits.
2.Clinical images of normal buccal mucosa of patients with tobacco habits and with no discernible lesions in oral mucosa
3.Clinical images of normal buccal mucosa of patients without tobacco habits and with no discernible lesions.
4.Clinical images of oral carcinoma in various locations within the oral cavity.

Exclusion Criteria
1. Medically compromised patients.
2.Clinical images of buccal mucosa showing any other lesions or concurrent lesions along with oral leukoplakia.
3.Images of normal mucosa of patients with or without habits showing surface irregularities due to chronic irritation, erosions or ulcerations.

Sampling Technique
The sample size was calculated using OpenEpi 3.0 software, based on data obtained from a previous study conducted by Guerrero-Sánchez Y et al. [Cancers 2022, 14, 2697]., where eligible patients presenting between July 2025 to September 2025 were consecutively recruited for the study.
The sample size formulae used are as follows:

$$n = \frac{(\sigma_1^2 + \sigma_2^2)/(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

The notation for the formulae are:
n = sample size to be determined
σ_1 = standard deviation of Group 1
σ_2 = standard deviation of Group 2
Δ = difference in group means
$z_{1-\alpha/2}$ = two-sided z value (e.g. z=1.96 for 95% confidence interval).
$z_{1-\beta}$ = power
Substituting the values from the previous study,
σ_1 = standard deviation of Group 1 = 0.10
σ_2 = standard deviation of Group 2 = 0.07
Δ = difference in group means = -0.11
k = ratio = n2/n1 = 1

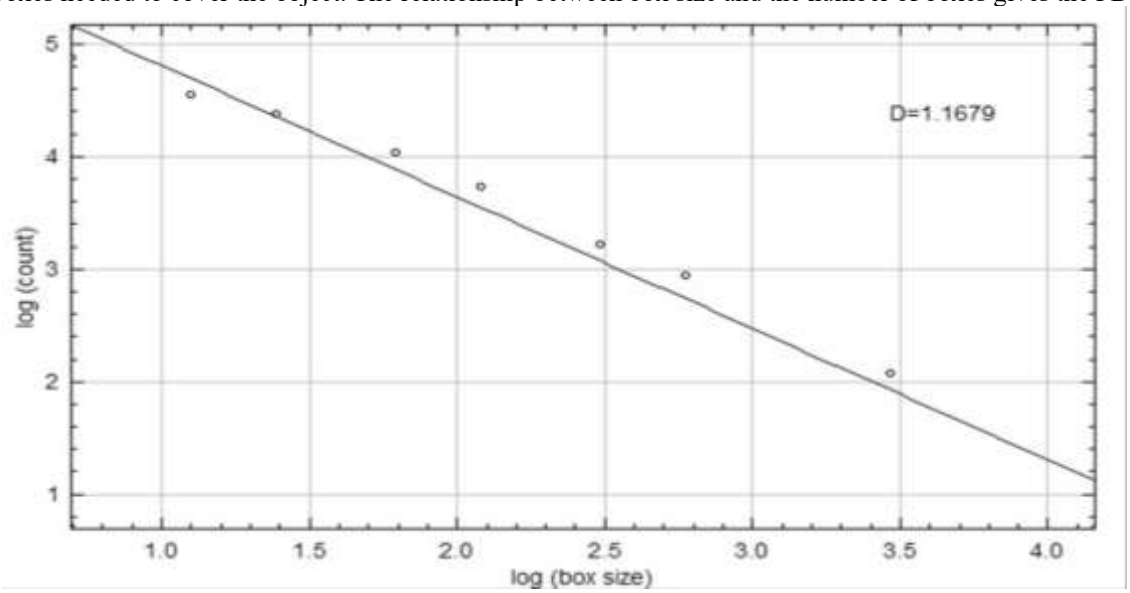
$z_{1-\alpha/2}$ = 1.96 at 95% confidence level
$z_{1-\beta}$ = 1.64 at 95% power

Substituting these values in above mentioned formula, the total sample size estimated was minimum 17 patients per group.
Digital images of normal mucosa and lesion was taken.
To achieve the same scale of photos, a focus point was locked at the same distance.
Images were stored at a maximum resolution of 4096X3512.

Image Analysis

Image J software was used. The digital images of clinically diagnosed leukoplakia were used for analysis. The image was cropped showing region of interest of size 86 X124 pixel. The image was duplicated and converted to 8-bit image as it can be analysed by the image J software. Gaussian filter was added with a diameter of 35 pixel to remove and fine and medium scale variations and retain larger density variation. The image was subtracted by 50 pixels. An image value of 128 pixel was added at each location so that we get an image of 128 irrespective of the original intensity of the image. The image was then made binary to retain an image brightness of 128, eroded to reduce noise, and dilated. The image was then skeletonized and inverted.

Fractal dimensions of all the inverted images were calculated by using the box count method. The box-counting method is based on a grid of multiple small boxes at different scales superimposed on the fractal object to analyze and count the boxes needed to cover the object. The relationship between box size and the number of boxes gives the FD.



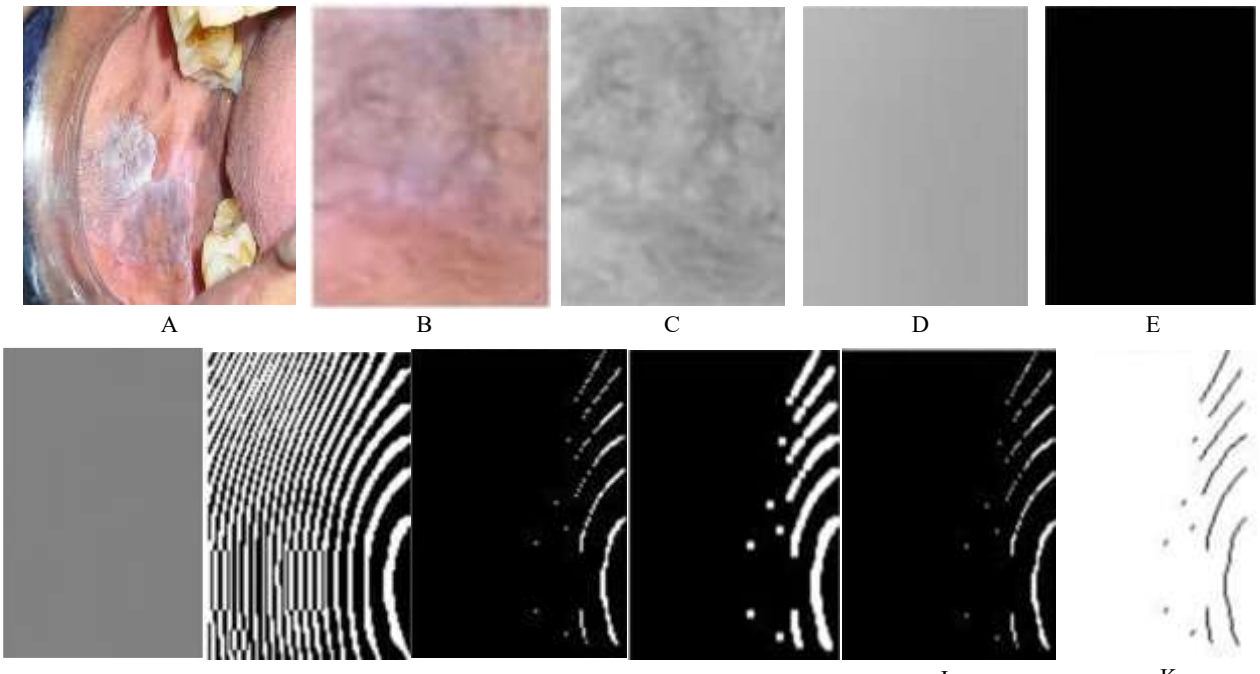


FIGURE 1: IMAGE ANALYSIS BY IMAGE J SOFTWARE

A. DIGITAL image of patient diagnosed with LEUKOPLAKIA; **B.** Cropped image showing ROI of size 86X124 PIXEL; **C.** Duplicated and converted to 8 bit IMAGE; **D.** Gaussian filter added with a diameter of 35 PIXELS; **E.** Subtract image by 50 PIXELS; **F.** Added image, with value of 128 at each pixel LOCATION; **G.** Image made Binary;**H.** Image Eroded;**I.** Image Dilated;**J.** Skeletonized Image;**K.** Inverted Image;**L**. Plot between box count and box size, showing the value of fractal dimension

RESULTS

TABLE 1: Comparison of fractal analysis among normal mucosa, normal mucosa with habits and lesional mucosa

Group	Mean	SD	SE	p-value
Normal mucosa	1.10	0.23	0.05	<0.001*
Normal mucosa with habits	1.32	0.09	0.02	
Lesional mucosa	1.37	0.16	0.03	

Kruskal Wallis test; * indicates a significant difference at p≤0.05

This table compares the fractal analysis among the three groups. The fractal dimension value in the subjects with normal mucosa and normal mucosa with habits groups was 1.10 and 1.32 respectively. The fractal dimension value in the subjects with lesional mucosa was 1.37. This difference in the fractal dimension values among the three groups was significant.

TABLE 2: Pairwise comparison of fractal analysis among normal mucosa, normal mucosa with habits and lesional mucosa

Group	Mean difference	p-value
Normal mucosa vs Normal mucosa with habits	-0.22	0.001*
Normal mucosa vs Lesional mucosa	-0.27	<0.001*
Normal mucosa with habits vs Lesional mucosa	-0.05	1.000

Kruskal Wallis test; * indicates a significant difference at p≤0.05

This table presents the pairwise comparison of the fractal analysis among the three groups. The fractal dimension value in the subjects with normal mucosa group was significantly lower than the other two groups, and the difference in the fractal dimension values of subjects with normal mucosa with habits and subjects with lesional mucosa was non-significant.

TABLE 3: Comparison of fractal analysis among males and females

Group	Gender	N	Mean	SD	p-value
Normal mucosa	**Male**	10	1.11	0.23	0.739
	Female	10	1.08	0.25	
Normal mucosa with habits	**Male**	13	1.34	0.09	0.097
	Female	7	1.28	0.08	
Lesional mucosa	**Male**	25	1.38	0.17	0.562
	Female	4	1.32	0.11	

Mann-Whitney test

This table compares the fractal analysis among males and females. There was a non-significant difference in the fractal dimension values of males and females in each study group.

TABLE 4: Comparison of fractal analysis according to the habits

Group	Habit	N	Mean	SD	p-value
Normal mucosa with habits	**Tobacco smoking**	5	1.34	0.09	0.098
	Tobacco chewing	15	1.28	0.08	
Lesional mucosa	**No habit**	2	1.35	0.03	0.736
	Tobacco smoking	4	1.47	0.36	
	Tobacco chewing	22	1.35	0.12	
	Both habits	1	1.46	.	

Mann-Whitney test; Kruskal Wallis test

This table compares the fractal analysis according to the habits. There was a non-significant difference in the fractal dimension values of tobacco smokers and tobacco chewers in each study group.

TABLE 5: Diagnostic accuracy of fractal dimension analysis

	Normal mucosa v/s Normal with habits mucosa	Normal mucosa v/s Lesional mucosa	Normal mucosa with habits v/s Lesional mucosa
Sensitivity	80	75.86	34.48

Specificity	90	90	90
Associated criterion	>1.2745	>1.2745	>1.4071
AUC	0.860	0.890	0.602

The results of the ROC analysis showing the discriminating ability of fractal analysis are presented in this table. In distinguishing the normal mucosa from the lesional mucosa, the cutoff value was 1.2745 to distinguish between the normal mucosa v/s normal mucosa with habits and normal mucosa v/s lesional mucosa. The cutoff value between normal mucosa with habits v/s lesional mucosa was 1.4071.

TABLE 6: Comparison of fractal analysis among normal mucosa, lesional mucosa and oral cancer

Group	Mean	SD	SE	p-value
Normal mucosa	1.10	0.23	0.05	<0.001*
Lesional mucosa	1.37	0.16	0.03	
Oral cancer	1.39	0.05	0.01	

Kruskal Wallis test; * indicates a significant difference at p≤0.05

This table compares the fractal analysis among the three groups. The fractal dimension value in the subjects with normal mucosa was 1.10. The fractal dimension value in the subjects with lesional mucosa was 1.37. The fractal dimension value in the subjects with oral cancer was 1.39. This difference in the fractal dimension values among the three groups was significant.

TABLE 7: Pairwise comparison of fractal analysis among normal mucosa, lesional mucosa and oral cancer

Group	Mean difference	p-value
Normal mucosa vs Normal mucosa with habits	-0.27	<0.001*
Normal mucosa vs Lesional mucosa	-0.29	<0.001*
Normal mucosa with habits vs Lesional mucosa	-0.02	0.814

Post hoc Bonferroni test; * indicates a significant difference at p≤0.05

This table presents the pairwise comparison of the fractal analysis among the three groups. The fractal dimension value in the subjects with normal mucosa group was significantly lower than the other two groups, and the difference in the fractal dimension values of subjects with lesional mucosa and oral cancer was non-significant.

TABLE 8: Diagnostic accuracy of fractal dimension analysis

	Normal mucosa v/s Lesional mucosa	Normal mucosa v/s Oral cancer	Lesional mucosa v/s Oral cancer
Sensitivity	75.86	100.0	100.00
Specificity	90	100.0	44.83
Associated criterion	>1.2745	>1.3349	>1.3377
AUC	0.890	1.000	0.592

The table provides diagnostic accuracy metrics for fractal dimension analysis when distinguishing between different oral tissue types: normal mucosa, lesional mucosa, and oral cancer. In distinguishing the normal mucosa from the lesional mucosa, the cutoff value was 1.2745. Fractal dimension analysis shows good diagnostic accuracy in differentiating normal mucosa from lesional mucosa, with a strong ability to correctly identify both categories. In distinguishing the normal mucosa from the oral cancer, the cutoff value was 1.3349. Fractal dimension analysis appears to be an exceptionally accurate and perfect diagnostic tool for distinguishing normal mucosa from oral cancer, with no errors in classification. In distinguishing the lesional mucosa from the oral cancer, the cutoff value was 1.3377. While fractal dimension analysis is excellent at identifying oral cancer in this comparison (100% sensitivity), its ability to correctly identify lesional mucosa is very poor (44.83% specificity).

DISCUSSION

Fractal analysis has come up as a promising, non-invasive tool for quantifying structural complexity in biological tissues, particularly in oral mucosa. It follows the principle of self-similarity and provides a numeric value (fractal dimension, FD) that denotes the complexity of biological structures [3,5]. The present study explained FD in normal mucosa, mucosa with tobacco intake habits and with no discernible lesions and mucosa with lesions. It also demonstrated a cumulative increase in FD values from normal to pathological states. This observation is in accordance with the parent study, which reported that FD varies with changes in mucosal architecture and keratinization [1].

In the present study, the average FD values were 1.10 for normal mucosa, 1.32 for normal mucosa associated with habits,1.37 for lesional mucosa and 1.39 for malignant mucosa, showing a statistically significant difference in between the categories ($p < 0.001$). This increase in value denotes a gradual disruption in tissue organization and heightened

structural complexity. This hypothesis was further confirmed by Pandey et al. who stated the difference in FD value between pre and post treated lesions and suggested a decrease in complexity/ keratinization of the lesion following treatment, i.e. regression of the lesion.[2]

The pairwise comparison revealed that the FD values of normal mucosa were significantly lower than those of both habit-associated mucosa and lesional mucosa, while no notable difference was found between habit-associated and lesional mucosa. This implies that exposure to tobacco may trigger early microstructural changes, even prior to the appearance of clinically recognizable lesions. Banoczy et al. in their study claimed that leukoplakia was higher in tobacco users and the relationship between the tobacco habit and the anatomical location.[2]

With respect to gender, no statistically significant differences were observed between males and females across all groups. This suggests that FD is primarily influenced by pathological changes rather than gender-related biological variation. However, factors such as sample distribution and image processing parameters may have influenced the FD values.

Similarly, comparison based on tobacco habits (smoking and chewing) showed no statistically significant difference in FD values, indicating that both forms of tobacco exposure contribute similarly to mucosal alterations.

The present study demonstrates a progressive increase in fractal dimension (FD) values from normal mucosa (1.10) to lesional mucosa (1.37) and oral cancer (1.39), indicating a gradual rise in structural complexity of the oral epithelium. The statistically significant difference ($p < 0.001$) among the three groups highlights the ability of fractal analysis to effectively discriminate between normal, premalignant, and malignant tissues. Similar results were obtained from Shenoi et al. and Deepak studies where tissues with higher dysplasia showed higher FD values as compared to tissues with lesser dysplasia. The cutoff value for differentiating normal mucosa from lesional mucosa was 1.2745, while for distinguishing normal mucosa from oral cancer, it was 1.3349. For differentiating lesional mucosa from oral cancer, the cutoff value was 1.3377.

CONCLUSION

The present study demonstrates that fractal dimension (FD) analysis is an effective, non-invasive tool for assessing structural complexity in oral mucosa. The statistically significant difference between normal mucosa and the other two groups highlights the sensitivity of fractal analysis in detecting early mucosal changes. Absence of a significant difference between habit-associated mucosa and lesional mucosa suggests that tobacco exposure itself may induce early microstructural alterations, even before the development of clinically evident lesions. This finding emphasizes the potential role of fractal analysis in early detection and risk assessment among high-risk individuals. Overall, fractal dimension analysis can be considered a reliable, cost-effective, and non-invasive adjunctive diagnostic tool for evaluating oral mucosal changes. With further validation and standardization, it holds promise for incorporation into routine clinical practice for screening, early diagnosis, and monitoring of oral potentially malignant disorders.

LIMITATIONS

Uneven distribution of male and female subjects in the study groups have led to a bias in the gender predilection of the study. The improper distribution of tobacco smoking and smokeless habits has also led to a possible bias in the study results.

INFORMED CONSENT STATEMENT

Informed consent was obtained from all subjects involved in the study.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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