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Correlation of Clinically Desquamative Gingivitis and Histopathology at a Private College Hospital in Chennai, India - A Retrospective Study

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Abstract

Desquamative gingivitis is an elucidating term used to demonstrate epithelial desquamation erythema, erosions and vesiculobullous lesions. It is a clinical manifestation that can be caused by several systemic disorders. Detection and differentiation between conditions that manifest desquamative gingivitis has been a continuing problem. Accurate clinical, histologic and serologic investigations are often required to differentiate among desquamative gingivitis disorder. This study focuses on understanding the correlation between clinically desquamative gingivitis and the histopathological reports. A retrospective cross-sectional study was conducted using the patient records from the department of periodontics and oral pathology, Saveetha Dental College from June 2019- April 2020 and patients who underwent treatment for desquamative gingivitis were selected by nonprobability sampling Microsoft Excel® 2016 (Microsoft office 10) data spreadsheet was used to collect data and later exported to SPSS® statistical package for social sciences for Windows (version 20.0, SPSS Inc, Chicago IU, USA). From the data analyzed it is observed that the overall incidence of desquamative gingivitis was higher in females (60%) predominantly in the age group of (51-60) years (50%). The most predominant histopathology report diagnosed Oral lichen Planus (70%). The correlation between clinical diagnosis and histopathology reports was statistically significant with $p<0.05$. Within the limits of the study, a significant number of patients with desquamative gingivitis had a female predilection predominantly in the age group of 50-60 years. The most common histopathology report of clinically desquamative gingivitis was Oral Lichen Planus. As clinically suggestive desquamative gingivitis may be an initial symptom of a systemic disease, the need for biopsy as a diagnostic tool should be made mandatory.

Keywords: *Oral Lichen Planus, Pemphigus Vulgaris, Mucous Membrane Pemphigoid, Linear IgA disease, Desquamative Gingivit*is

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Introduction

Desquamative Gingivitis is a descriptive clinical term for desquamation, erosion, vesicles, and bullae that involve the free and attached gingiva. [1] The term "desquamative gingivitis" was first described by Tomes and Tomes in 1894, but it was Prinz in 1932, who established [2] that it was a descriptive term used to define the presence of the erythema, desquamation, erosions and blistering of the marginal and attached gingiva.[3] In 1960, Mc Kathy and Co were the first to suggest that

desquamative gingivitis is not an entity but a gingiva response to a variety of systemic disturbances of varied etiologies. [4] Furthermore, in 1964, Glickman and Jerome demonstrated that this alteration of the gingiva was secondary to other systemic conditions.[5] It is usually associated with autoimmune blistering disorders like pemphigus Vulgaris, pemphigoid, and oral lichen planus and other systemic disorders. [4,6]

The pathogenic mechanism of desquamative gingivitis involves the separation of epithelium from the underlying connective tissue by a disease that can cause either a subepithelial or an intraepithelial vesicles [6–8]. Desquamation can also be triggered by intentional local factors (Nikolsky sign) or intentional factors like masticatory forces, poor restoration, and calculus[9,10] and habits like smoking and tobacco chewing. [11]Cicatricial pemphigoid (CP) is an autoimmune vesiculobullous disease which targets various components of the basements membrane such as BP 180 and laminin 332 resulting in the formation of subepithelial vesicles.[12,13]

Pemphigus Vulgaris is an autoimmune disease which shows its initial symptoms of desquamative gingivitis.[14] In this disease, antibodies are directed against desmosomal proteins (desmoglein 1 and 3) of the cells in a spinous layer which leads to the formation of intraepithelial blisters.[15,16] Lichen planus is an autoimmune disease that manifests desquamative gingivitis. In lichen planus, subepithelial separation is induced due to the destruction of the basal cell layer of the epithelium resulting in loss of adhesion in connective tissue.[17] lichen planus is associated with oxidative stress in saliva as the levels of various biomarkers were seen to be altered in the disease [18,19]. However, these markers are of no help in the Oral Tongue Squamous Cell Carcinoma.[20] high degree of Reactive Oxygen Species (ROS) release leads to heightened oxidative damage to gingival tissue, periodontal ligament, and alveolar bone. [21] Oral leukoplakia which is a potentially malignant disorder and oral lichen planus have different etiopathology but their clinical representation can be very similar. [22–24] Ankyloglossia otherwise called tongue-tie restricts the cleansing activity due to limited movement of the tongue leading to gingivitis and other varied periodontal diseases. [25]

Establishing the correct diagnosis of the underlying disease is of paramount importance in order to provide proper treatment.[26] The appearance and location of lesions must alert the clinician and proper photographs must be taken for future references.[27,28]. Hence, the aim of the study is to find the correlation between clinically diagnosed desquamative gingivitis and histopathology diagnosis.

Materials and Methods

Study Design And Setting

This pilot retrospective study examined the records of 86,000 patients from June 2019- April 2020 undergoing treatment at Saveetha Dental College and Hospital, Chennai in the department of periodontics. Ethical approval was obtained from the institutional ethics committee. The study population included patients who underwent treatment for desquamative gingivitis at the Outpatient Department of Saveetha Dental College.

Data were collected from the hospital's patient database records which were used to identify n= 86,000 patients from which n=10 patients who were diagnosed for desquamative gingivitis and underwent treatment for the condition.

Relevant data like patient's age, gender was recorded. Patient:s age groups were divided as (20-30) years,(30-40) years, (40-50) years, (51-60) years, and (61-70) years. Repeated patient records and incomplete data were excluded. Data were reviewed by an external reviewer. Data were recorded in Microsoft Excel® 2016 (Microsoft office 10) and later exported to SPSS® statistical package for social sciences for windows versions, 20.0, SPSS Inc, Chicago IU, USA), and subjected to statistical analysis. A Chi-square test was done and $p < 0.05$ was considered significant.

Results and Discussion

The final dataset consisted of n= 10 patients of Indian origin who underwent treatment for desquamative gingivitis.

The prevalence of desquamative gingivitis based on age was found to be higher in the (51-60 years) age group (50%) followed by (31-40 years) age group (20%), following which (20-30 years), (40-50 years) and (61-70

years) showed (10%) each. (figure 1) and was found to be higher in females (60%) than males (40%) (figure 2). The prevalence of desquamative gingivitis as a clinical diagnosis was about (50%) while oral lichen planus was about (40%) and vesiculobullous lesions were about (10%) (figure 3) The most prevalent histopathology report of the clinically suggestive desquamative gingivitis was Oral Lichen Planus (70%) followed by 'Not Available' (20%) and Vesiculo Bullous Lesion (10%) (figure 4). Biopsy was subjected for (30%) of the patients and the rest of the (70%) were ill-advised. (figure 5) About 30% of the biopsies were done after initiating treatment for the differential diagnosis. (figure 6) The correlation of clinical diagnosis of desquamative gingivitis and histopathology reports was found to be significant with $p< 0.05$ (figure 7).

The data for this retrospective study was based on the residents of Chennai seeking treatment at Saveetha Dental College and Hospitals.

Desquamative gingivitis is a group of non-plaque induced gingival disorders according to the current classification of periodontal diseases and conditions. It appears very early during its clinical course. Most cases of oral lichen planus, Mucous Membrane Pemphigoid and Pemphigus Vulgaris initially present as gingival lesions.[29,30]

In the current study, the prevalence of desquamative gingivitis on the basis of age was observed to be higher (50%) in the 51-60 years age group when compared with other age groups. Few studies stated that Desquamative gingivitis generally has a peak during the fourth and sixth decade of life. They had also reported that Desquamative Gingivitis cases were rarely associated with children and adolescents.[31–34]. In a similar study by Suresh L et al, the median age of the patients was 58 years. [35] A study by Leao et al, stated that the reason behind this could be related to hormonal changes that occur during menopause, which occurs generally in the 5th decade of life.[7] Another study by Yih et al stated that it occurs due to the lack of oestrogen and progesterone which occurs at menopause. [36] All the previously literature is in concordance with our results.

The current study showed that females(60%) had a higher predilection with Desquamative Gingivitis than males. There is a female predilection for all the diseases which clinically represents Desquamative Gingivitis except for pemphigus and linear IgA disease. [35,37] In a study by Suresh L et al, there was a female predilection to diseases like Oral Lichen Planus and Mucous Membrane Pemphigoid which are associated with Desquamative Gingivitis.[35] These findings could be because of hormonal changes that occur during menopause in women. [7]

A few studies state that desquamative gingivitis is a clinical symptom that may represent an underlying disease. [37,38]. In the current study, 50% of the diagnosis which was made based on the clinical appearance was Desquamative gingivitis. When the disease is confined to the gingiva, the diagnosis becomes difficult. Clinical presentation of the generalized symptoms makes the definitive diagnosis of Desquamative gingivitis more difficult. The clinical symptoms of Desquamative Gingivitis is polymorphous and the presence of plaque and calculus complicates the diagnosis. Many diseases like Oral Lichen Planus [17,39] and other vesiculobullous diseases such as Mucous Membrane Pemphigoid [40,41], Pemphigus Vulgaris[30,42], etc. present as desquamative gingivitis so diagnosis from the clinical symptom becomes difficult.

This current study found a higher prevalence (70%) of Oral lichen planus based on the histopathology reports of the clinically suggestive desquamative gingivitis. A few similar studies were done by Suresh L et al and Lo Russo et al stated that the clinical diagnosis of Oral Lichen Planus was the most common disease presenting with Desquamative Gingivitis. [35,38]. The frequency of desquamative gingivitis in patients with lichen planus is lower than in cicatricial pemphigoid and pemphigus Vulgaris. However, due to the significantly higher prevalence of lichen planus compared to cicatricial pemphigoid and pemphigus Vulgaris, desquamative gingivitis is most commonly attributed to lichen planus. [38,43] According to a few different studies, Mucous membrane pemphigoid was responsible for (35%-48%) of the cases of desquamative gingivitis whereas Oral Lichen Planus and Pemphigus Vulgaris accounted for about (24%-45%) and (3%-5%) respectively. [30,41] In the current study, the possible reason for the higher prevalence of oral lichen Planus may be because of its epidemiology, which occurs in 1 to 2% of the population. [38]

In the current study, there was an unusual contradiction in histopathology in which a particular case was diagnosed and treated for both Oral Lichen Planus and Pemphigus Vulgaris. This may be due to the nonavailability of Immunofluorescence in which case the reporting pathologist for the second time could have probably considered bullous lichen planus in lieu of the previous report and clinical presentation. In a study by Bernt A et al, 14 patients with desquamative gingivitis were first subjected to histopathological and immunofluorescence studies before treatment with tetracycline was started.[44] In a study by Roger et al, 41 patients with desquamative gingivitis were treated. Biopsies were done initially and the tissue was subjected to light and direct immunofluorescence microscopy. Based on the histopathological findings the present disease was established and treatment started thereafter with topical corticosteroids and systemic dapsone. [29] In all previous clinical studies, treatment was started after conducting histopathological and immunofluorescence studies.

In our study,70% of patients were not advised for biopsy probably due to comorbid factors such as Uncontrolled Diabetes, Anticoagulant Therapy, Compromised general health, Chronic Kidney Disease, Hypertension, and various other ailments which could have probably delayed the clinician to advice incisional biopsy. Literature suggests that patients should be carefully evaluated prior to biopsy if they have comorbid conditions to avoid unnecessary complications.[45]In order to relieve the symptoms the treating physician could have empirically started the patient on medication.

Desquamative gingivitis can mimic plaque related gingival inflammation, as painful symptoms impair maintenance of oral hygiene and cause accumulation of dental plaque.[46–48] this can cause a delay in diagnosis as clinicians might confuse with plaque-induced gingivitis and which potentially increases the risk of morbidity and the risk of life-threatening complications.[49,50] However, typical and distinctive oral and skin lesions presenting in a specific location can present as a valuable aid in the differential diagnosis.[38] It is known that desquamative gingivitis is a clinically descriptive term and not an actual disease and also knowing the fact that it may be a manifestation of severe systemic disease and that only histopathology will help us in finding the definitive diagnosis. This shows an increasing need to mandate biopsy as the disease goes undiagnosed or misdiagnosed without subjecting the patient for biopsy and also without the histopathology reports. Making a definitive diagnosis by differentiating these disorders from one another is important because the treatment, management, and prognosis differ among the disorders.

Upon conducting histopathological studies characteristic features are seen in different pathological states. Acantholytic keratinocytes (Tzanck cells) are seen in Pemphigus Vulgaris, subepithelial or intraepithelial vesiculation and necrotic keratinocytes in Erythema Multiforme, basal cells liquefaction degeneration and lymphocytic band-like sub basilar infiltrate in Oral Lichen Planus and Keratinocyte vacuolization with lamina propria edema in Lupus Erythematosus. [51] These findings direct the diagnosis and treatment planning of the affected individual in an efficient manner.

The limitation of the study includes geographic limitations as the study was conducted only among the South Indian population predominantly. The study included small sample size and hence the results obtained cannot be generalized.

The future scope of the study will be better and will yield accurate results if different ethnic populations are considered along with a larger study population.

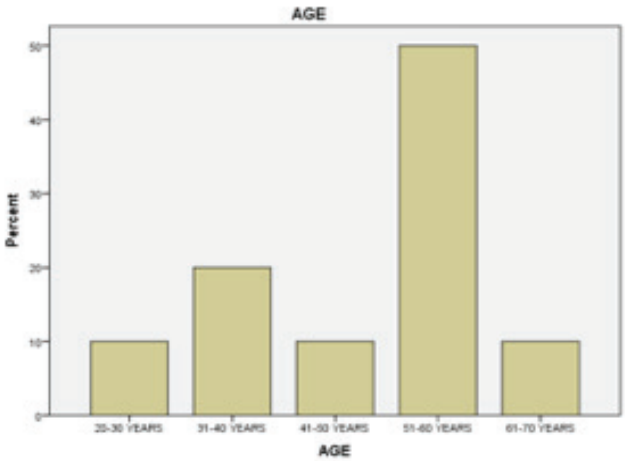

Figure 1: This bar graph represents the percentage of desquamative gingivitis based on age. Age is distributed as 20-30 years, 31-40 years, 41-50 years, 51-60 years on the x-axis. From the graph, it is evident that desquamative gingivitis is more prevalent in the 51-60 years age group.

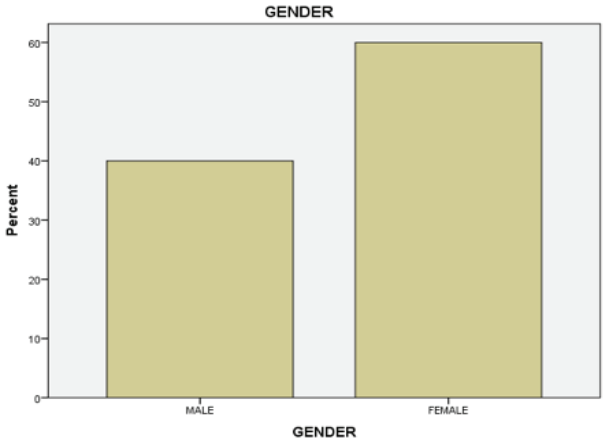

Figure 2: This bar graph represents the percentage of desquamative gingivitis based on gender. Parameters were Males and females and were represented on the x-axis. From the graph, it is evident that desquamative gingivitis is more prevalent in females than males.

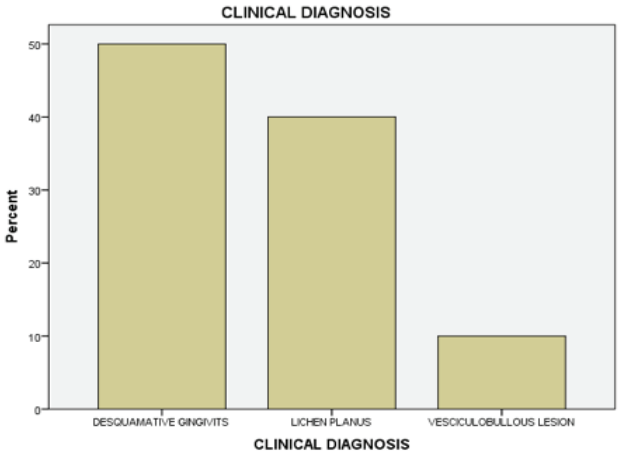

Figure 3: This bar graph represents the percentage of clinical diagnosis of desquamative gingivitis where the parameters like Desquamative gingivitis, lichen planus and Vesiculobullous lesion are represented on the x-axis. From the graph it is evident that desquamative gingivitis was the most prevalent clinical diagnosis. Wow

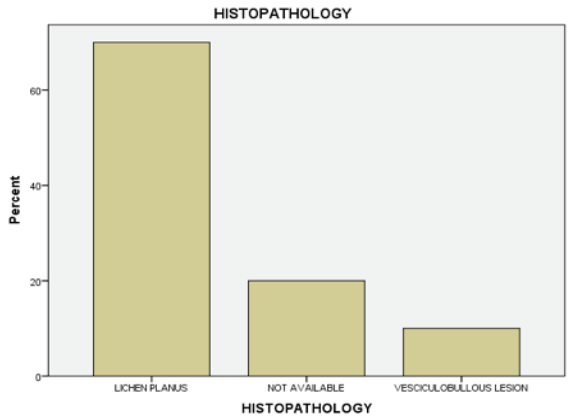

Figure 4: This bar graph represents percentage of Histopathology diagnosis of Desquamative gingivitis where Parameters like lichen planus, Vesiculobullous lesion, and not available are represented on the x-axis, From the graph, it is evident that lichen planus is the most prevalent histopathology diagnosis of desquamative gingivitis.

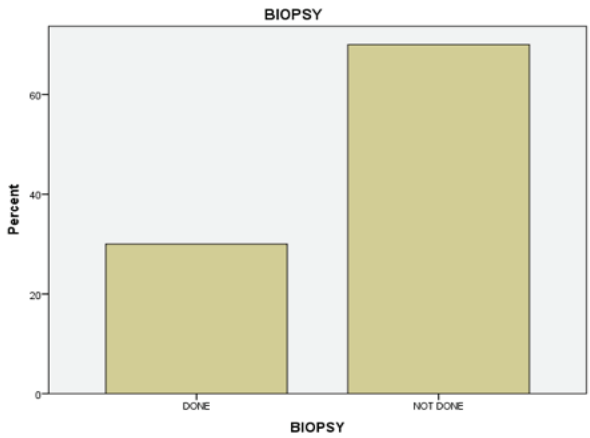

Figure 5: This bar graph represents the percentage of Biopsy status in Desquamative gingivitis where Parameters were 'done' or 'not done' were represented on the x-axis. From the graph it is evident that not done was the most prevalent status of biopsy.

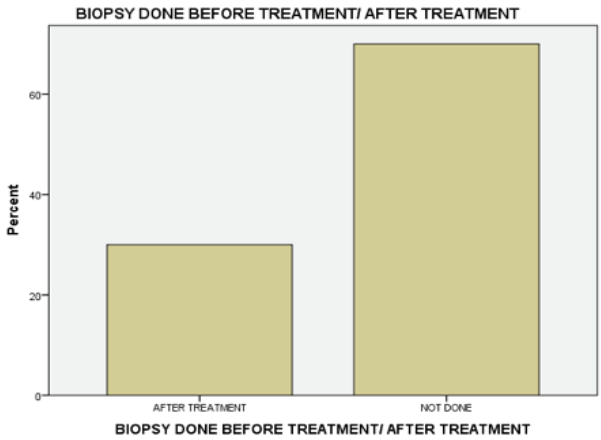

Figure 6: This bar graph represents the percentage of Biopsy status whether it was done before or after desquamative gingivitis where the parameters included 'after treatment' and 'not done' on the x-axis. From the graph, it is evident that most of the biopsies were not done.

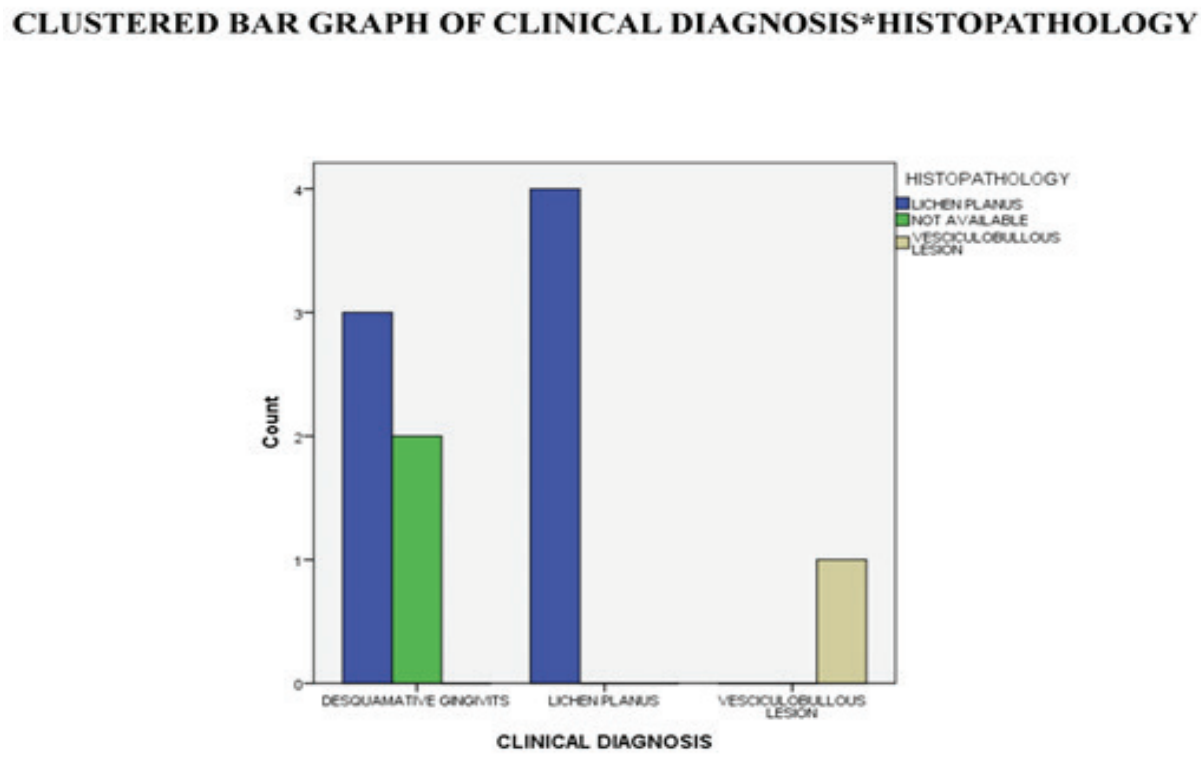

Figure 7: This bar graph depicts the association between the clinical diagnosis and histopathology reports of the study population. Different clinical diagnosis are represented in various colours on the X axis, Blue represents Lichen Planus, green represents data not available and brown represents Vesiculobullous Lesions. Y axis represents the histopathology reports of the study population on a scale from 0 to 4. There is a significant association between the clinical diagnosis and histopathology reports. (Pearson chi square test; p value =0.015, statistically significant)

Conclusion

Within the limits of the present study, it is observed that desquamative gingivitis was more prevalent in females and predominantly in the age group of 51-60 years. The most prevalent histopathology diagnosis was oral lichen planus. Also, there was a positive correlation between clinical diagnosis and histopathology reports with $p<0.05$. This study helps us to understand the importance of biopsy as a diagnostic tool and histopathology results in diagnosing clinically significant desquamative gingivitis. It is known that desquamative gingivitis is a clinically descriptive term and not an actual disease and also knowing the fact that it may be a manifestation of severe systemic disease and that only histopathology will help us in finding the definitive diagnosis hence, a biopsy must be made mandatory. Also, patient education and motivation in biopsy must be considered a high priority whilst determining the treatment plan for Clinically suggestive Desquamative Gingivitis.

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Conflict of Interest: None declared.

Ethical Clearance: It is taken from "Saveetha Institute Human Ethical Committee" (Ethical Approval Number- SDC/SIHEC/2020/DIASDATA/0619-0320)

References

1. Endo H, D. T. Diagnosis and Management of Desquamative Gingivitis [Internet]. Gingival Diseases - Their Aetiology, Prevention and Treatment. 2011. Available from: http://dx.doi.org/10.5772/22864
2. Guiglia R, Di Liberto C, Pizzo G, Picone L, Lo Muzio L, Gallo PD, et al. A combined treatment regimen for desquamative gingivitis in patients with oral lichen planus [Internet]. Vol. 36, Journal of Oral Pathology & Medicine. 2007. p. 110–6. Available from: http://dx.doi.org/10.1111/j.1600-0714.2007.00478.x
3. Gagari E, Damoulis PD. Desquamative gingivitis as a manifestation of chronic mucocutaneous disease [Internet]. Vol. 9, JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2011. p. 184–7. Available from: http://dx.doi.org/10.1111/j.1610-0387.2010.07543.x
4. Hasan S. Desquamative gingivitis - A clinical sign in mucous membrane pemphigoid: Report of a case and review of literature. J Pharm Bioallied Sci. 2014 Apr;6(2):122–6.
5. Glickman I, Smulow JB. Chronic Desquamative Gingivitis — Its Nature and Treatment [Internet]. Vol. 35, Journal of Periodontology. 1964. p. 397–405. Available from: http://dx.doi.org/10.1902/jop.1964.35.5.397
6. Suresh L, Kumar V. Significance of IgG4 in the diagnosis of mucous membrane pemphigoid. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007 Sep;104(3):359–62.
7. Leao JC, Ingafou M, Khan A, Scully C, Porter S. Desquamative gingivitis: retrospective analysis of disease associations of a large cohort. Oral Dis. 2008 Sep;14(6):556–60.
8. Laskaris G, Demetriou N, Angelopoulos A. Immunofluorescent studies in desquamative gingivitis [Internet]. Vol. 10, Journal of Oral PathologyandMedicine.1981.p.398–407.Available from: http://dx.doi.org/10.1111/j.1600-0714.1981.tb01291.x
9. Swathy S, Gheena S, Varsha SL. Prevalence of pulp stones in patients with history of cardiac diseases [Internet]. Vol. 8, Research Journal of Pharmacy and Technology. 2015. p. 1625. Available from: http://dx.doi.org/10.5958/0974-360x.2015.00291.7
10. Kumar A, Sherlin HJ, Ramani P, Natesan A, Premkumar P. Expression of CD 68, CD 45 and human leukocyte antigen-DR in central and peripheral giant cell granuloma, giant cell tumor of long bones, and tuberculous granuloma: An immunohistochemical study. Indian J Dent Res. 2015 May;26(3):295–303.
11. Gupta V, Ramani P. Histologic and immunohistochemical evaluation of mirror image biopsies in oral squamous cell carcinoma. J Oral Biol Craniofac Res. 2016 Sep;6(3):194–7.
12. Gregory M. A SEVERE CASE OF MUCOUS MEMBRANE PEMPHIGOID COMPLICATED BY STEROID INDUCED PSYCOSIS [Internet]. Available from: http://dx.doi.org/10.26226/morressier.578e3b4ed462b802923823c7
13. Jayaraj G, Sherlin HJ, Ramani P, Premkumar P, Anuja N. Cytomegalovirus and Mucoepidermoid carcinoma: A possible causal relationship? A pilot study. J Oral Maxillofac Pathol. 2015 Sep;19(3):319–24.
14. Mignogna MD, Lo Muzio L, Bucci E. Clinical features of gingival pemphigus vulgaris [Internet]. Vol. 28, Journal of Clinical Periodontology. 2001. p. 489–93. Available from: http://dx.doi.org/10.1034/j.1600-051x.2001.028005489.x
15. Cura MJ, Torre AC, Cueto Sarmiento KY, Bollea Garlatti ML, Riganti J, Puga MC, et al. Pemphigus Vulgaris: A Retrospective Cohort Study of Clinical Features, Treatments, and Outcomes. Actas Dermosifiliogr [Internet]. 2020 May 25; Available from: http://dx.doi.org/10.1016/j.ad.2019.10.004
16. O'Regan E, Bane A, Flint S, Timon C, Toner M. Linear IgA Disease Presenting as Desquamative Gingivitis [Internet]. Vol. 130, Archives of Otolaryngology–Head & Neck Surgery. 2004. p. 469. Available from: http://dx.doi.org/10.1001/archotol.130.4.469
17. Zakrzewska JM. Re: Mollaoglu N. Oral lichen planus: a review. Br J Oral Maxillofac Surg 2000; 38: 370-377. Br J Oral Maxillofac Surg. 2001 Oct;39(5):407.
18. Hema Shree K, Ramani P, Sherlin H, Sukumaran

G, Jeyaraj G, Don KR, et al. Saliva as a Diagnostic Tool in Oral Squamous Cell Carcinoma - a Systematic Review with Meta Analysis. Pathol Oncol Res. 2019 Apr;25(2):447–53.

19. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Oral Pathol Med. 2019 Apr;48(4):299–306.
20. Thangaraj SV, Shyamsundar V, Krishnamurthy A, Ramani P, Ganesan K, Muthuswami M, et al. Molecular Portrait of Oral Tongue Squamous Cell Carcinoma Shown by Integrative Meta-Analysis of Expression Profiles with Validations. PLoS One. 2016 Jun 9;11(6):e0156582.
21. Gheena S, Ezhilarasan D. Syringic acid triggers reactive oxygen species–mediated cytotoxicity in HepG2 cells [Internet]. Vol. 38, Human & Experimental Toxicology. 2019. p. 694–702. Available from: http://dx.doi.org/10.1177/0960327119839173
22. Viveka TS, Shyamsundar V, Krishnamurthy A, Ramani P, Ramshankar V. p53 Expression Helps Identify High Risk Oral Tongue Premalignant Lesions and Correlates with Patterns of Invasive Tumour Front and Tumour Depth in Oral Tongue Squamous Cell Carcinoma Cases [Internet]. Vol. 17, Asian Pacific Journal of Cancer Prevention. 2016. p. 189–95. Available from: http://dx.doi.org/10.7314/apjcp.2016.17.1.189
23. Jayaraj G, Sherlin HJ, Ramani P, Premkumar P, Natesan A. Stromal myofibroblasts in oral squamous cell carcinoma and potentially malignant disorders. Indian J Cancer. 2015 Jan;52(1):87–92.
24. Sridharan G, Ramani P, Patankar S. Serum metabolomics in oral leukoplakia and oral squamous cell carcinoma. J Cancer Res Ther. 2017 Jul;13(3):556–61.
25. Jangid K, Alexander A, Jayakumar N, Varghese S, Ramani P. Ankyloglossia with cleft lip: A rare case report [Internet]. Vol. 19, Journal of Indian Society of Periodontology. 2015. p. 690. Available from: http://dx.doi.org/10.4103/0972-124x.162207
26. Jayaraj G, Ramani P, Herald J. Sherlin, Premkumar P, Anuja N. Inter-observer agreement in grading oral epithelial dysplasia – A systematic review [Internet]. Vol. 27, Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2015. p. 112–6. Available from: http://dx.doi.org/10.1016/j.ajoms.2014.01.006
27. Sivaramakrishnan SM, Ramani P. Study on the Prevalence of Eruption Status of Third Molars in South Indian Population [Internet]. Vol. 07, Biology and Medicine. 2015. Available from: http://dx.doi.org/10.4172/0974-8369.1000245
28. Hannah R, Ramani P, Herald. J. Sherlin, Ranjith G, Ramasubramanian A, Jayaraj G, et al. Awareness about the use, Ethics and Scope of Dental Photography among Undergraduate Dental Students Dentist Behind the lens [Internet]. Vol. 11, Research Journal of Pharmacy and Technology. 2018. p. 1012. Available from: http://dx.doi.org/10.5958/0974-360x.2018.00189.0
29. Rogers RS 3rd, Sheridan PJ, Nightingale SH. Desquamative gingivitis: clinical, histopathologic, immunopathologic, and therapeutic observations. J Am Acad Dermatol. 1982 Dec;7(6):729–35.
30. Vaillant L, Chauchaix-Barthes S, Hüttenberger B, Arbeille B, Machet M, Jan V, et al. Chronic desquamative gingivitis syndrome: retrospective analysis of 33 cases. In: Annales de dermatologie et de venereologie. 2000. p. 381–7.
31. Ariyawardana A, Tilakaratne WM, Dissanayake M, Vitanaarachchi N, Basnayake LK, Sitheeque MAM, et al. Oral pemphigus vulgaris in children and adolescents: a review of the literature and a case report. Int J Paediatr Dent. 2005 Jul;15(4):287–93.
32. Sklavounou A, Laskaris G. Childhood cicatricial pemphigoid with exclusive gingival involvement. Int J Oral Maxillofac Surg. 1990 Aug;19(4):197–9.
33. Laeijendecker R, Van Joost T, Tank B, Oranje AP, Neumann HAM. Oral lichen planus in childhood. Pediatr Dermatol. 2005 Jul;22(4):299–304.
34. Roche C, Field EA. Benign mucous membrane pemphigoid presenting as desquamative gingivitis in a 14□year□old child. Int J Paediatr Dent [Internet]. 1997; Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-263X.1997.tb00270.x
35. Suresh L, Neiders ME. Definitive and differential diagnosis of desquamative gingivitis through direct immunofluorescence studies. J Periodontol. 2012 Oct;83(10):1270–8.

36. Yih WY, Maier T, Kratochvil FJ, Zieper MB. Analysis of desquamative gingivitis using direct immunofluorescence in conjunction with histology. J Periodontol. 1998 Jun;69(6):678–85.
37. Scully C, Laskaris G. Mucocutaneous disorders. Periodontol 2000. 1998 Oct;18:81–94.
38. Russo LL, Lo Russo L, Fedele S, Guiglia R, Ciavarella D, Lo Muzio L, et al. Diagnostic Pathways and Clinical Significance of Desquamative Gingivitis [Internet]. Vol. 79, Journal of Periodontology. 2008. p. 4–24. Available from: http://dx.doi.org/10.1902/jop.2008.070231
39. Eisen D, Carrozzo M, Bagan Sebastian J-V, Thongprasom K. Number V Oral lichen planus: clinical features and management. Oral Dis. 2005 Nov;11(6):338–49.
40. Scully C, Carrozzo M, Gandolfo S, Puiatti P, Monteil R. Update on mucous membrane pemphigoid: a heterogeneous immune-mediated subepithelial blistering entity. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999 Jul;88(1):56–68.
41. Nisengard RJ, Neiders M. Desquamative lesions of the gingiva. J Periodontol. 1981 Sep;52(9):500–10.
42. Yih WY, Richardson L, Kratochvil FJ, Avera SP, Zieper MB. Expression of estrogen receptors in desquamative gingivitis. J Periodontol. 2000 Mar;71(3):482–7.
43. Sklavounou A, Laskaris G. Frequency of desquamative gingivitis in skin diseases [Internet]. Vol. 56, Oral Surgery, Oral Medicine, Oral Pathology. 1983. p. 141–4. Available from: http://dx.doi.org/10.1016/0030-4220(83)90278-5
44. Rønbeck BA, Lind PO, Thrane PS. Desquamative gingivitis: preliminary observations with tetracycline treatment. Oral Surg Oral Med Oral Pathol. 1990 Jun;69(6):694–7.
45. Vyas T. Biopsy of Oral Lesion-A Review Article. Journal of Advanced Medical and Dental Sciences Research [Internet]. 2018;6(1). Available from: http://jamdsr.com/uploadfiles/8biopsyvol6isue1pp27-35.20180112073218.pdf
46. Tricamo MB, Rees TD, Hallmon WW, Wright JM, Cueva MA, Plemons JM. Periodontal status in patients with gingival mucous membrane pemphigoid. J Periodontol. 2006 Mar;77(3):398–405.
47. Mignogna MD, Lo Russo L, Fedele S. Gingival involvement of oral lichen planus in a series of 700 patients [Internet]. Vol. 32, Journal of Clinical Periodontology. 2005. p. 1029–33. Available from: http://dx.doi.org/10.1111/j.1600-051x.2004.00761.x
48. Holmstrup P, Schiøtz AW, Westergaard J. Effect of dental plaque control on gingival lichen planus. Oral Surg Oral Med Oral Pathol. 1990 May;69(5):585–90.
49. Yeh SW, Ahmed B, Sami N, Razzaque Ahmed A. Blistering disorders: diagnosis and treatment. Dermatol Ther. 2003;16(3):214–23.
50. Gravitis K, Daley TD, Lochhead MA. Management of patients with foreign body gingivitis: report of 2 cases with histologic findings. J Can Dent Assoc. 2005 Feb;71(2):105–9.
51. Lo Russo L, Fierro G, Guiglia R, Compilato D, Testa NF, Lo Muzio L, et al. Epidemiology of desquamative gingivitis: evaluation of 125 patients and review of the literature. Int J Dermatol. 2009 Oct;48(10):1049–52.