JABET
Journal of Advanced Biotechnology and Experimental Therapeutics

ORIGINAL ARTICLE

J Adv Biotechnol Exp Ther. 2025 Jan; 8(1): 182-191
eISSN: 2616-4760, https://doi.org/10.5455/jabet.2025.15
Published by www.bsmiab.org

Role of CD117 and mast cells in periodontal diseases: Histological and immunohistochemical study

Fatin L. Khaphi[1], Hanaa Ali Hussein[1,*], Oula Fouad Hameed[1], Huda jassem jebur[1], Zahra Kadhum Saeed[1]

[1]University of Basrah, College of Dentistry, Basrah city 61001, Iraq

***Corresponding author**
Hanaa Ali Hussein, PhD
University of Basrah, College of Dentistry, Basrah city 61001, Iraq
Email: hanaazahraa85@gmail.com

Academic editor
Md. Abdul Hannan, PhD
Bangladesh Agricultural University, Bangladesh

Article info
Received: 02 September 2024
Accepted: 08 January 2025
Published: 27 January 2025

Keywords
Chronic periodontitis, CD117, Mast cells, Plaque periodontitis

ABSTRACT

Mast cells are mobile secretory cells with a variety of biological tasks such as phagocytosis, processing of antigens, cytokine production, and the release of both newly formed and preexisting physiological mediators. This study aimed to investigate and establish the relationship between mast cells and various stages of periodontal diseases. A total of 36 soft tissue samples, 12 each of normal healthy periodontal, dental plaque periodontitis, and chronic periodontitis were selected. Samples were collected from patients with periodontal surgery in chronic periodontitis and plaque periodontitis. Samples were stained with 1% toluidine blue (TB), immunohistochemistry for CD117 expression, and observed under a light microscope for the presence of mast cells. All data were analyzed using SPSS. The mast cells were found to be highest in the chronic periodontitis group, followed by the dental plaque periodontitis group, as compared to the healthy periodontal group. The quantitative study of mast cells using TB staining showed statistically significant differences among the three groups. However, the results showed no statistically significant difference in the expression levels of CD117 in the plaque periodontitis and healthy periodontal group but showed a statistically significant difference between chronic periodontitis and healthy periodontal group. Thus, an increase in mast cells in human periodontal diseases suggests that these cells are crucial for developing chronic periodontitis.

INTRODUCTION

Periodontitis is one of the most common chronic gum diseases, caused by bacterial infection and irritation of the supporting structures and tissues around the teeth [1]. The symptoms of this disease include the gradual accumulation of dental plaque, which triggers an immune response and, ultimately, results in the destruction of the gums and the supporting bone tissues that hold the tooth. Halitosis is a symptom of periodontitis, which can also lead to other symptoms such as gum recession, bleeding gums, loss or shifting teeth, and, eventually dental loss [1]. Inflammatory periodontal disease has been linked primarily to bacterial plaque as the etiological factor. However, in recent years, several studies have highlighted the function of the immune system, suggesting that bacterial antigens set off an immunopathological reaction and that the final course of the disease process depends on the host's response [2, 3].

In varying amounts, mast cells can be found in the periodontal tissues in healthy and inflamed gingival sites. When these cells are stimulated or active, mediators produced from mast cells are released through degranulation from the secretory granules [4]. Mast cells originating in the bone marrow are immune cells residing in various tissues. They are characterized by their large, coarse, spherical appearance, prominent nuclei, and different cellular components like microvilli and ribosomes [5]. Mast cells are involved in several processes, including host defense, tissue damage healing, allergic inflammation, and vascular regulation. In addition, controlling mast cell activity is essential for the treatment of many inflammatory diseases because of their substantial

role in tissue damage and the spread of inflammatory responses [6]. A variety of inflammatory cytokines secreted by mast cells can be detrimental to periodontal tissue. Mast cells have been linked to periodontal disease in numerous studies [5]. Mediators are kept in secretory granules found in mast cells. As mast cells degranulate, mediators will be released. The periodontal tissue is destroyed as a result of these mediators. The results of a study indicate a connection between the severity of periodontal disease and the extent of mast cell degranulation [6, 7].

CD117 is a tyrosine kinase protein type-3 (c-kit) that functions as a receptor for the SCF (stem cell factor), which binds to the SCF to control cell proliferation, differentiation, chemotaxis, and apoptosis [8]. Immunoglobulin E (IgE) has a high-affinity receptor called FcεRI. This receptor is crucial for the degranulation of mast cells. When SCF binds to the CD117 receptor, it increases FcεRI collection on the surface of the mast cells, which causes the mast cells to degranulation [9]. CD117 can be beneficial for the identification of normal and tumor mast cells. Both normal mast cells and mast cell malignancies express CD117, and both have notable levels of CD117 expression [10]. Fukuda *et al.* [11] noted that humoral and natural mast cells expressed CD117. Therefore, this study aimed to quantify mast cells in healthy and periodontic groups and determine the correlation between these groups. Also, this study measures the CD117 expression level in the mast cells present in periodontal diseases.

MATERIALS AND METHODS

Study design

This study was performed in the Department of Periodontics in Dentistry College, University of Basrah, Iraq. The patients included in this study had no disease history, had not taken any drugs that would have affected periodontal tissues in the preceding two months, were not smokers, and did not have any special hormonal situations, such as pregnancy. Written informed consent was obtained, and the patient was informed of the treatment protocol before treatment implementation. The Institutional Ethical Committee Review Board in Dentistry College, University of Basrah, granted ethical approval (Ref.no BDC-1-02-23-9-1).

Sample collection and preparation of periodontal tissues

In this study, 36 cases were reported, including 12 instances of dental plaque periodontitis, 12 instances of progressive loss of periodontium in Chronic Periodontitis, and 12 cases of the clinically healthy periodontal group as a control. The classification rules for periodontal diseases and disorders set by the American Academy of Periodontology were followed [12].

Twelve periodontal healthy tissue samples were obtained from the extraction of teeth, usually premolars, for orthodontic therapy with no BOP (bleeding on probing). Twelve tissues with plaque periodontitis (PD (probing depth) < 3 mm and CAL (clinical attachment loss) < 1 mm with BOP). Twelve tissue samples with moderate-to-advanced chronic periodontitis (using BOP to PD and CAL more than 4 mm) as shown in Figure 1.

The tissue sample was collected from patients with periodontal surgery in a minor surgical operating room returning to the surgery unit. Some of the samples were taken from patients who required periodontal surgery as part of their periodontal treatment to remove the operculum over the third molar. Other patients donated a small piece of tissue after extraction. The surgery was performed by a single periodontist using an

identical technique. Informed consent was obtained from the patients for the collection, preservation, and analysis of gingival tissues for the present study.

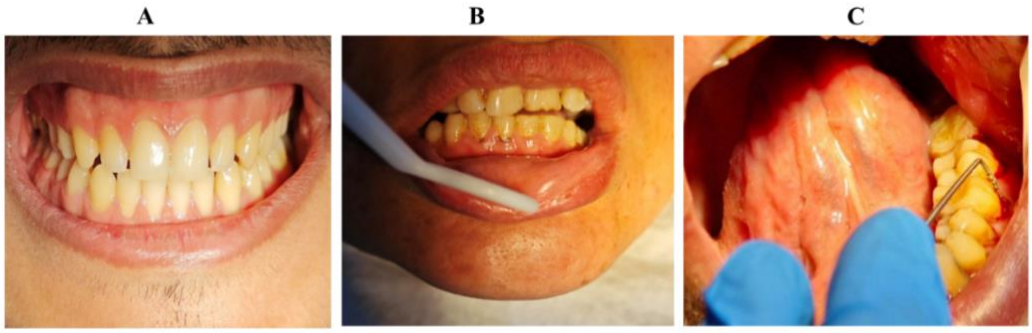

Figure 1. Images of clinical cases (A) healthy periodontal group, (B) plaque periodontitis, and (C) chronic periodontitis group.

Biopsies

Biopsies were obtained using a scalpel blade number 11 for excisional biopsy and were approximately 3x2 mm in size, taken from appropriate sites immediately after diagnosis. The specimens were promptly fixed in formalin (10%, Sigma–Aldrich Chemicals, St Louis, MO, USA) for further processing, followed by dehydration, clearing, and embedding in paraffin (Sigma–Aldrich Chemicals, St Louis, MO, USA) as described previously [4].

Histological and staining procedure

Following standard tissue preparation, 5 µm thick tissue slices were acquired, deparaffinized, and rehydrated in distilled water (D.W.) before being stained with 1% Toluidine Blue (TB, Sigma–Aldrich Chemicals, St Louis, MO, USA) stain following the manufacturer's instructions. After carefully blotting the sections, they were dehydrated using progressively higher grades of ethanol, absolute alcohol, and xylene (Sigma–Aldrich Chemicals, St Louis, MO, USA). They were then mounted in DPX (Dibutylphthalate Polystyrene Xylene, Sigma–Aldrich Chemicals, St Louis, MO, USA) and examined under a light microscope. Mast cells were recognized by deep blue-purple staining [13].

Quantitative analysis of mast cell using TB staining

The number of mast cells (positively stained) was counted in 10 successive high-power (objective ×64; tube factor ×1; eyepiece ×12.5; ×800) microscopic fields. It has been done to count the mast cells in the inflammatory cell infiltration of periodontally healthy tissue areas and diseased tissue. The mean ± SD of mast cell observations stained with TB was presented per millimeter. Additionally, a comparison of the number of mast cells/mm^2 in the groups with healthy and diseased periodontal tissues was done. After that, the mean value of mast cells was expressed. Data were statistically analyzed using SPSS (Statistical-Package for the Social-Sciences, version 18) for an ANOVA and a Student's t-test. *P* values below 0.05 were regarded as statistically significant.

Immunohistochemistry staining

The samples (gingival tissue) were initially sliced into 3 μm sections and prepared for Immunohistochemistry (IHC) staining. Following this, the tissues were deparaffinized in xylene and then hydrated with alcohol (80%, 90%, and 100%) for 30 min. The retrieval stage was carried out with a Tris-buffered saline (TBS, Sigma–Aldrich Chemicals, St Louis, MO, USA) solution (pH = 7.6). Next, running water was used to indirectly cool the jar that held the samples. After treating the microscopic slide with 10% H_2O_2 (Junsei Chemical Co. Ltd., Tokyo, Japan) for 10 min, it was rinsed for 5 min under running water. Following this, the slide was incubated with blocking serum for 5 min and then shaken to remove excess serum. The first antibody, CD117 (Bio Genex, The Hague, the Netherlands), was applied for 50 min, and then the slide was rinsed with a TBS solution. Subsequently, a secondary antibody was used for 1 h, followed by another rinse with a TBS solution. Finally, the slide was treated with diammonium phosphate solution for 10 min and then washed with D.W. After using hematoxylin (Sisco Research Laboratories Pvt. Ltd., India) for 5 min, D.W. was utilized once again to wash. The slide was submerged in xylol for 2 min after being submerged in alcohol 100 for 1 min. Finally, a cytologic adhesive was used to mount the slides. To guarantee stain accuracy, positive control samples, such as tissue blocks from the stomach, were also supplied.

After labeling with IHC, we counted the number of mast cells in 10 high-power fields at the highest density area (hot spot) using a Nikon optical microscope (Tokyo, Japan) at ×400 magnification. We determined the mast cell count for each field. We then selected the ten fields with the highest concentration of mast cells and noted the average mast cell count for each group.

Statistical analysis

Data statistical analysis was done using SPSS. The independent t-test was employed to compare the expression level of CD117 between the three study groups, taking into account the normal distribution of scores and percentages. It was determined that the obtained $P < 0.05$ was statistically significant.

RESULTS

Quantitative analysis and statistical evaluation of mast cells stained with TB

The presence of mast cells was observed in all study groups, including the healthy periodontal group, plaque periodontitis group, and chronic periodontitis group. Mast cells were quantitatively analyzed by counting their total number, and a qualitative analysis was conducted by counting the intact and degranulated mast cells in TB-stained sections. The mean total of mast cells (Table 1) compared the mast cell quantification values between the periodontitis and periodontal health groups (Figure 2A). The mean mast cell value was found to be 2.450 ± 0.375, 5.97 ± 0.499, and 11.35 ± 0.403 mast cells/ mm^2 in the healthy periodontal group, plaque periodontitis, and chronic periodontitis group, respectively. At $P \leq 0.05$, there is a statistically significant difference among the healthy periodontal, plaque periodontitis, and chronic periodontitis groups. This result indicated a slightly significant difference between the plaque periodontitis group and the periodontally healthy group, but there is a highly significant difference between the healthy and chronic periodontitis groups.

The tissue sections were stained with TB to identify mast cells. The mast cells appeared granular and deep blue-purple against a blue ortho-chromatic background (Figure 3A-C). In the healthy periodontal group, only a few mast cells with undegranulation were observed (Figure 3A). In the plaque periodontitis group, more mast cells with degranulation were observed (Figure 3B). In the chronic periodontitis group, numerous mast cells with significant degranulation were observed (Figure 3C).

Table 1. Mean total number of mast cells among study groups.

Group	N	Mean	SD*	Medium	Min	Max	F- value	*P value**
Healthy periodontal (N=12)	12	2.450	0.375	2.55	1.8	2.9	1.530	0.05
Plaque Periodontitis (N=12)	12	5.79	0.499	5.9	5.2	6.8		
Chronic Periodontitis (N=12)	12	11.35	0.403	11.45	10.7	11.8		

* P ≤ 0.05: statistically significant, SD: Standard deviation

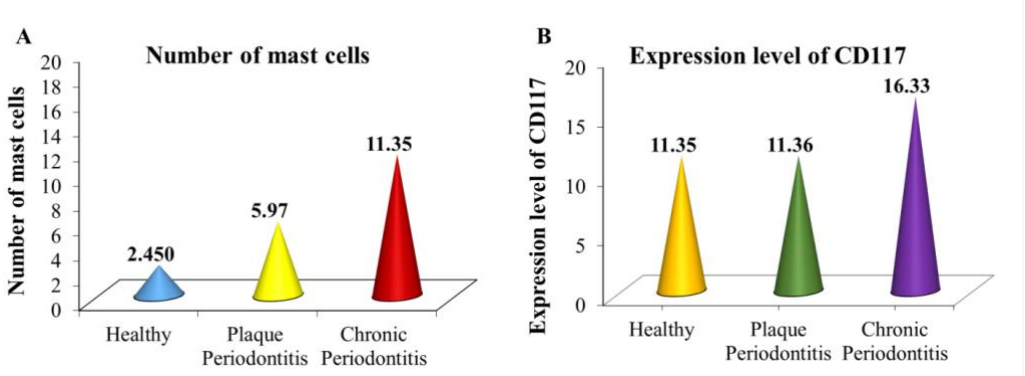

Figure 2. (A) Comparison of mean mast cell quantification among the study groups; and (B) The level of CD 117 expression among the study groups.

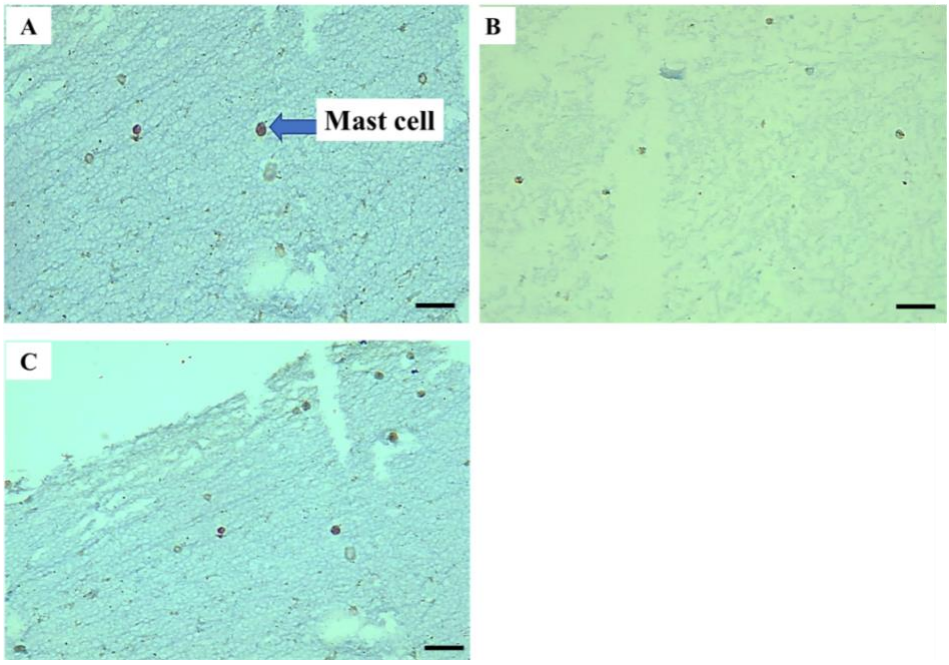

Figure 3. Histological section of mast cells in: (A) healthy periodontal group, (B) plaque periodontitis group, and (C) chronic periodontitis group. TB stain, X 400.

IHC outcomes

The average number of mast cells in each study group was recorded after counting the mast cells in each field and selecting the highest count of mast cells (Figure 4A-C). The immuno-reactivity of the CD117 in mast cells in periapical granulomas and periapical cysts. The mean CD117 expression level in the healthy, plaque periodontitis and chronic periodontitis was 11.35± 0.430, 11.36± 0.462, and 16.33±0.353 mast cells/mm², respectively (Table 2 and Figure 2B). The results showed a statistically significant difference between healthy and chronic periodontitis groups, with no statistically significant difference between healthy and plaque periodontitis groups at $P < 0.05$.

Table 2. CD117 expression levels in the healthy periodontal group, plaque periodontitis, and chronic periodontitis.

Group	Mean± SD	F value	df	Groups	T test	*p* value
Healthy periodontal	11.35±0.430			Healthy vs Plague	-0.05	0.961
		1.831	9	Healthy vs Chronic	**	
Plaque Periodontitis	11.36±0.462				*-28.31	***2.23×10^{-16}
Chronic Periodontitis	16.33±0.353			Plague vs Chronic	*-27.03	*5.03×10^{-16}

* P ≤ 0.05: statistically significant, SD: Standard deviation, df: Degrees of freedom, T: test statistic

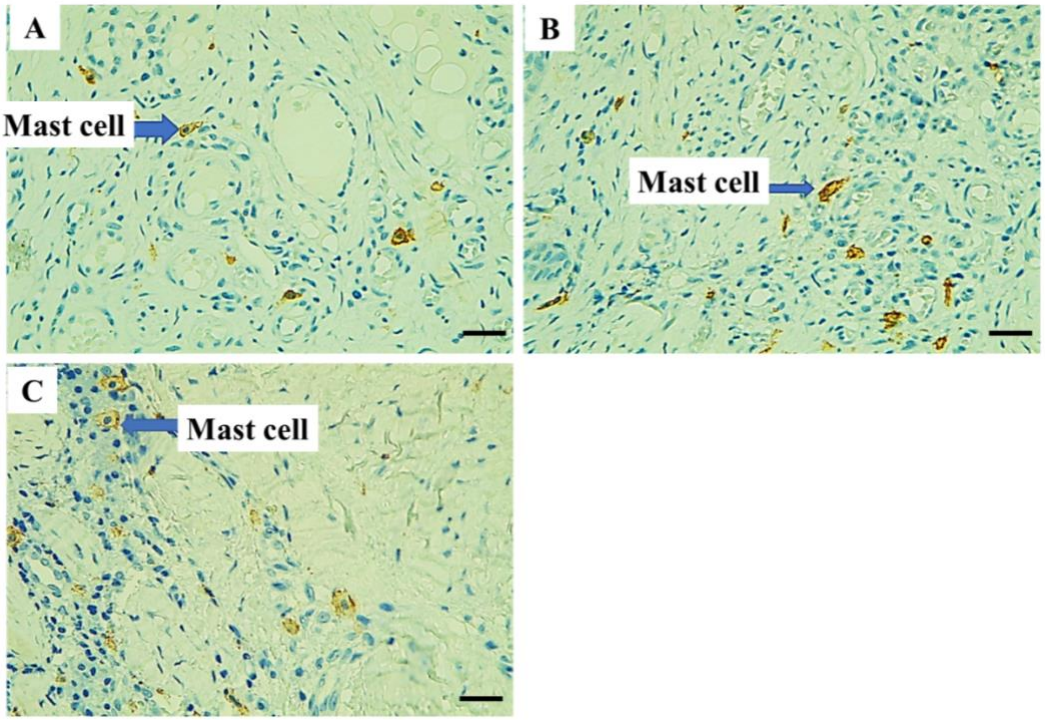

Figure 4. The mast cells contained in: (A) healthy periodontal group, (B) plaque periodontitis group, and (C) chronic periodontitis group (IHC, X400).

DISCUSSION

Gingival tissue has the highest number of mast cells; their density does not seem to be influenced by systemic drugs (antivirals). However, it is sensitive to physical factors such as metal ions or laser radiation (low-intensity) [14, 15]. Thus, mast cells are adaptable, adjusting their functions based on the surrounding micro-environment instead of systemic pharmacological treatments [16]. After partially differentiating in the bone marrow from pluripotent hematopoietic cells, they travel through the

bloodstream to complete their differentiation in specific microenvironments within peripheral mucosal or connective tissues [14, 15]. Mast cells are dispersed sub- and intraepithelial, as well as throughout the gingival connective tissue, frequently close to endothelial cells. Mast cells are seen in greater quantity in gingiva which is both inflammatory and healing [17]. Mast cells can be thin and elongated like fibroblasts, or they can be round, oval, or spindle-shaped with plenty of cytoplasm. The nuclei of mast cells are spherical to oval in shape, and the cytoplasm is heavily packed with granules that are bright red. They can be stained using either TB dye or Giemsa stain. Each mast cell typically contains between 80 and 300 granules, densely packed with biologically active mediators such as proteases, histamine, growth factors, and cytokines [18].

Mast cells may undergo explosive de-granulation and then reassemble their granules, or they may release individual granules when activated in a process called 'piecemeal degranulation [12, 18]. After the process of degranulation, large numbers of mast cell mediators are released into the extracellular environment, affecting the endothelial cells [19, 20]. In this study, we found the possibility of rapidly increased numbers of mast cells at sites of tissues with chronic periodontal infections, indicating high cellular activity at these sites. This finding agreed with studies reported by Lagdive *et al.* [4], Agrawal *et al.* [21], Fattahi *et al.* [22], and Batista *et al.* [23]. Additionally, a slightly significant increase in plaque periodontitis tissue compared to the healthy periodontal group may be attributed to either a higher rate of degranulation or migration of mast cells [24]. Migratory potential is directly related to the mast cell growth factor. This factor is not modified by degranulation of the mast cell, and this explains the accumulation of large numbers of mast cells close to or in the epithelial tissue in inflamed conditions as reported by Walsh *et al.* [25] and Korkmaz *et al.* [26]. The findings of this study indicate that mast cell counts might be linked to periodontitis. Numerous authors have demonstrated that periodontitis causes an increase in mast cell density [27], while others reported that periodontal inflammation causes a decrease in mast cell density [28]. These conflicting findings may be attributed to the dynamic nature of the periodontal disease, characterized by varying growth and activity stages, or due to various levels of inflammation in the analyzed specimens. However, mast cells contribute to inflammation and host defense in gingival tissues, regardless of mast cell density in periodontitis [7]. This discovery serves as our basis for demonstrating the involvement of mast cells in the chronic breakdown of periodontal tissue. There are reinforcing factors, and histamine is one of them; it is a biological and biochemical factor that works on the tissue barrier, deteriorates it, brings about edema, and aids cellular infiltration [29]. Furthermore, mast cells are acknowledged to comprise the majority of the body's histamine. In addition, mast cells express the strongest levels of matrix metalloproteinases (MMPs) 1, 2, 8, 9, and 13. MMPs play a crucial role in degrading the main components in the extracellular matrix [30-32]. Future research should concentrate on the regulatory mechanisms that influence mast cell behavior in gingival tissues, including their interactions with physical and chemical stimuli, to clarify their potential as therapeutic targets in managing periodontal disease.

Latent collagenase can partake in tissue destruction in periodontitis, which can be activated by tryptase besides that tryptase can break down the third component of collagen. Furthermore, it has been indicated that tryptase activity is confined to mast cell granules. Mast cells appear to be competent in introducing antigens to T cells. The activation of T-cells leads to activating mast cells through cytokine release and degranulation [33]. This study established that the number of mast cells will be increased in inflamed areas as compared to healthy periodontal. This suggests significant changes in the localization and migration of mast cells during the development of periodontal disease, which may need to be more strictly considered

[28]. However, still up for debate whether mast cells have a role in the destructive events and defensive mechanism as responder and effector cells in severe inflammation, or as potential functional populations in periodontal lesions [17].

For CD117 marker expression levels in the mast cells, the results showed study no significant variance between the healthy and the plaque periodontitis with a significant variance between the healthy and chronic periodontitis groups. This is incompatible with the results of the study by Gemmell *et al.* [34], Mazreah *et al.* [10], Vahabi *et al.* [35], and Huang *et al.* [7]. There are contradictory findings in other studies for example, some studies have found that mast cells play a key role in the development of periodontitis, and other studies have shown no significant difference between chronic periodontitis and healthy periodontitis [30, 32]. This finding may be attributed to variations in tissue processing, sample handling, methodological approaches, and population heterogeneity. Additionally, hypoxic stress and cytokine profiles (IL-1 and TNF-α) play a crucial role in modulating mast cell behavior, especially the expression of CD117 levels. Consequently, mast cells interact with other immune and stromal cells, adapting their functions to the local tissue environment and affecting on expression level of CD117 in chronic periodontitis [36]. These findings highlight the need for further research to clarify the regulatory mechanisms underlying CD117 expression in chronic periodontitis. Such studies could enhance our understanding of its role in disease pathogenesis and its potential as a therapeutic target. Researching biologics or pharmacological agents that can modulate mast cell activity is necessary, especially those targeting CD117 or other mast cell receptors that help regulate their proliferation and activation.

Malcolm *et al.* [37] found a direct link between the decline in periodontal tissue deterioration and the decrease in mast cell count. Additionally, Agrawal *et al.* [21] investigated the correlation between the various stages of periodontal disease and the presence of mast cells. This suggests the role of these cells in the development and degradation of periodontal disease. However, further research with larger sample sizes and novel techniques is required to find suitable therapies to overcome the development of periodontal disease, understand its mechanism, and its correlation with mast cells. Moreover, the current study encountered challenges in selecting the most effective method for counting mast cells and securing a substantial number of samples and difficulty in encouraging non-cooperative patients to participate.

CONCLUSIONS

The study confirmed the correlation between the presence of a high number of mast cells with periodontal disease compared to the healthy periodontal group. Chronic periodontitis sites showed increased mast cell numbers compared to healthy and plaque periodontitis sites. The results also suggest a significant variance in the expression level of CD117 between the healthy and chronic periodontitis groups with no significant variance between healthy and plaque periodontitis. Further research is required to better understand the immunological dynamics and cellular interactions of the disease to provide a better understanding of how periodontitis develops and potential treatment approaches. To obtain more definitive and trustworthy results, cell DNA analysis and assessment of particular mediators released from mast cells should be carried out in further research.

ACKNOWLEDGMENTS

Not applicable.

AUTHOR CONTRIBUTIONS

FLK and HAH designed the outlines, drafted the manuscript, and wrote the initial draft of the manuscript. OFH and FLK performed the experiments and analyzed the data. HJJ and ZKS reviewed the manuscript. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

REFERENCES

[1] Ray RR. Periodontitis: An oral disease with severe consequences. Applied biochemistry and biotechnology. 2023;195:17-32.
[2] Eltas A, Uslu MÖ. Evaluation of oral health-related quality-of-life in patients with generalized aggressive periodontitis. Acta Odontologica Scandinavica. 2013;71:547-52.
[3] Lazar V, Ditu L-M, et al. Impact of dental plaque biofilms in periodontal disease: Management and future therapy. Periodontitis: A Useful Reference; Arjunan, P, Ed; InTech Open: London, UK. 2017:11-42.
[4] Lagdive SS, Lagdive SB, et al. Correlation of mast cells in periodontal diseases. Journal of Indian Society of Periodontology. 2013;17:63-7.
[5] Savita S, Ambica RK, et al. Quantification of mast cells in periodontal diseases: A comparative study. Journal of Pharmaceutical and Biomedical Sciences. 2015;5:919-23.
[6] Dileepan KN, Raveendran VV, et al. Mast cell-mediated immune regulation in health and disease. Frontiers in Medicine. 2023;10:1213320.
[7] Huang S, Lu F, et al. Mast cell degranulation in human periodontitis. Journal of Periodontology. 2013;84:248-55.
[8] Mitchell SG, Bunting ST, et al. A variant c-kit mutation, d816h, fundamental to the sequential development of an ovarian mixed germ cell tumor and systemic mastocytosis with chronic myelomonocytic leukemia. Pediatric blood & cancer. 2017;64:e26282.
[9] Yamazaki S, Nakano N, et al. The transcription factor ehf is involved in tgf-β–induced suppression of fcεri and c-kit expression and fcεri-mediated activation in mast cells. The Journal of Immunology. 2015;195:3427-35.
[10] Mazreah SA, Shahsavari M, et al. Immunohistochemical evaluation of cd117 in mast cell of aggressive periodontitis. Journal of Indian Society of Periodontology. 2020;24:216-20.
[11] Fukuda T, Kamishima T, et al. Expression of the c-kit gene product in normal and neoplastic mast cells but not in neoplastic basophil/mast cell precursors from chronic myelogenous leukaemia. The Journal of pathology. 1995;177:139-46.
[12] Armitage GC. Development of a classification system for periodontal diseases and conditions. Annals of periodontology. 1999;4:1-6.
[13] de Campos Vidal B, Mello MLS. Toluidine blue staining for cell and tissue biology applications. Acta histochemica. 2019;121:101-12.
[14] Paul J, D'lima JP, et al. Histological evaluation of epithelial thickness, microvasculature and number of mast cells in the gingiva of smokers and non-smokers with chronic periodonti-tis. Journal of Clinical and Diagnostic Research. 2017;11:18-21.
[15] Subramani T, Rathnavelu V, et al. Influence of mast cells in drug-induced gingival overgrowth. Mediators of inflammation. 2013;2013:275172.
[16] Frisancho-Kiss S. Fine-tuning mast cells is essential for the maintenance and regulation of the systemic and immune homeostasis. Journal of Integrative Medicine. 2021;10:60-74.
[17] Steinsvoll S, Helgeland K, et al. Mast cells–a role in periodontal diseases? Journal of clinical periodontology. 2004;31:413-9.
[18] Elieh Ali Komi D, Wöhrl S, et al. Mast cell biology at molecular level: A comprehensive review. Clinical reviews in allergy & immunology. 2020;58:342-65.
[19] Moon T, St Laurent C, et al. Advances in mast cell biology: New understanding of heterogeneity and function. Mucosal immunology. 2010;3:111-28.

[20] Paivandy A. Induction of mast cell apoptosis via granule permeabilization: A novel approach to target mast cells: Acta Universitatis Upsaliensis; 2020.
[21] Agrawal R, Gupta J, et al. Correlation of mast cells in different stages of human periodontal diseases: Pilot study. Journal of Oral and Maxillofacial Pathology. 2016;20:91-5.
[22] Fattahi S, Sadighi M, et al. Comparison of mast cell counts between the patients with moderate and severe periodontitis. Journal of Advanced Periodontology & Implant Dentistry. 2019;11:34.
[23] Batista A, Rodini CdO, et al. Quantification of mast cells in different stages of human periodontal disease. Oral diseases. 2005;11:249-54.
[24] Yang B-G, Kim A-R, et al. Degranulation of mast cells as a target for drug development. Cells. 2023;12:1506.
[25] Walsh LJ. Mast cells and oral inflammation. Critical reviews in oral biology & medicine. 2003;14:188-98.
[26] Korkmaz Y, Plomann M, et al. Dental pulp inflammation initiates the occurrence of mast cells expressing the α1 and β1 subunits of soluble guanylyl cyclase. International journal of molecular sciences. 2023;24:901.
[27] Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. Journal of periodontology. 2007;78:1387-99.
[28] Beyens M, Toscano A, et al. Diagnostic significance of tryptase for suspected mast cell disorders. Diagnostics. 2023;13:3662.
[29] Thangam EB, Jemima EA, et al. The role of histamine and histamine receptors in mast cell-mediated allergy and inflammation: The hunt for new therapeutic targets. Frontiers in immunology. 2018;9:1873.
[30] Muluk NB, Arikan O, et al. Expressions of mmp2, mmp9, and timp-1 in the inflammatory cells of nasal polyps: Granulocytes, monocytes, and mast cells. European Review for Medical & Pharmacological Sciences. 2023;27.
[31] Naesse E, Schreurs O, et al. Matrix metalloproteinases and their inhibitors in gingival mast cells in persons with and without human immunodeficiency virus infection. Journal of periodontal research. 2003;38:575-82.
[32] Wang G, Fan W-T, et al. Expression of matrix metalloproteinase-8 and matrix metalloproteinase-13 in mast cells of human periapical lesions. International Journal of Clinical and Experimental Pathology. 2018;11:2530.
[33] Cairns JA, Walls AF. Mast cell tryptase stimulates the synthesis of type i collagen in human lung fibroblasts. The Journal of clinical investigation. 1997;99:1313-21.
[34] Gemmell E, Carter C, et al. Mast cells in human periodontal disease. Journal of dental research. 2004;83:384-7.
[35] Vahabi S, Rezazadeh F, et al. Relationship between mast cell counts and different types of periodontitis. Journal of Advanced Periodontology & Implant Dentistry. 2010;2:56-60.
[36] Neurath N, Kesting M. Cytokines in gingivitis and periodontitis: From pathogenesis to therapeutic targets. Frontiers in Immunology. 2024;15:1435054.
[37] Malcolm J, Millington O, et al. Mast cells contribute to porphyromonas gingivalis–induced bone loss. Journal of dental research. 2016;95:704-10.