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Chronic inflammatory lesions of the jaws and orofacial tissues

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Original Article

Abstract

BACKGROUND: Chronic inflammation is a persistent inflammation characterized by tissue repair which may occur around the jaws due to varying causes. This study aims to review its clinico-pathologic features.

METHODS: The study location was the Oral Pathology Laboratory, University College Hospital (UCH), Ibadan, Nigeria. Archival records were examined and all entries made as histopathological diagnosis of a chronic inflammatory lesion were identified and included in the study. The clinical data regarding age, gender, site of lesion, clinical diagnosis, and histopathological diagnosis were extracted from the histopathology reports of the patients. Data were presented using summary statistics and analysed with the SPSS software. Chi-square test was used to test the association between age, gender, and histopathological diagnosis. Statistical significance was set at $P < 0.050$.

RESULTS: Orofacial lesions diagnosed as chronic inflammatory lesions were 95, constituting 4.6% of 2046 diagnoses made. They occurred mostly in the 21-40 years age group recording 34 (35.8%) of cases. The mean age of men was 36.6 ± 19.0 years, while for women was 49.0 ± 21.5 [t = -2.82, degree of freedom (df) = 95, P = 0.006]. Women were more affected while the mandible was the most commonly affected site, making up 43.2% of cases. Non-specific chronic inflammation was the most frequently diagnosed lesion constituting 32.6% of cases followed by chronic osteomyelitis constituting 30.5%.

CONCLUSION: Summarily, chronic inflammatory lesions are rarely seen around the jaws and orofacial region. Larger studies on these rare lesions are advocated to further assess their prevalence globally.

KEYWORDS: Chronic Disease, Inflammation, Jaw, Face

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Introduction

Chronic inflammation is a prolonged and persistent inflammation characterized by tissue repair, often as a continuation of an acute form or a prolonged low-grade form.[1] It is a localized protective response caused by injury or which serves to destroy, dilute, or wall off both the injurious agent that is not easily digested and the injured tissue. The inflammatory response can be provoked by prolonged exposure to physical (e.g., trauma, ultraviolet radiation), chemical (e.g., acid, oxidizing agents), and biological agents including infectious agents such as bacteria (e.g., Staphylococcus spp., Streptococcus spp.), viruses (e.g., paramyxovirus), and other pathogenic microorganisms (e.g., protozoan).[1,2] Chronic inflammatory lesions of the jaws and orofacial tissues vary and may be caused by the spread of odontogenic (e.g., apical abscess) and non-odontogenic (e.g., carbuncles) infections, overlying soft tissue traumatic injury as well as infected extraction sockets and open fracture lines.[3] Similarly, other sources include hematogenous spread (e.g., from infected intravascular catheters and

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distant foci of infection), systemic infections and diseases [e.g., human immunodeficiency virus (HIV), diabetes mellitus (DM)], autoimmune diseases [e.g., synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome (SAPHO syndrome)], primary chronic granulomatous diseases (CGDs), and some diseases of unknown aetiology (e.g., sarcoidosis).[2,3]

Chronic inflammation is characterized by infiltration with mononuclear cells (macrophages, lymphocytes, and plasma cells), tissue destruction (induced by the persistent offending agent or by the inflammatory cells), and attempts at healing by connective tissue replacement of damaged tissue, all occurring simultaneously with angiogenesis.[1] Macrophages are recruited and activated by the action of lymphokines to phagocytose certain microorganisms as well as to process antigens, allowing them to be neutralized by lymphocytes. Likewise, they secrete monokines that attract other cells and cause tissue destruction.[1] T-lymphocytes are the predominant cells in chronic inflammation activated by monokines and at times, directly by antigens. Activated lymphocytes in turn destroy antigens or render them harmless while secreting lymphokines that stimulate macrophages.[1] Other mediators in the chronic inflammatory process include B-lymphocytes that aid in the manufacturing and secretion of antibodies against specific antigen.[1] Moreover, eosinophils contain granules with major basic proteins for destroying parasites and are seen in parasitic infestations, hypersensitivity reactions, and some autoimmune conditions.[1] Furthermore, lymphokines and monokines recruit fibroblasts to the site of chronic inflammation to produce collagen, which may become excessive if cause of inflammation is persistent, leading to fibrosis.[1]

Moreover, a type of chronic inflammation is granulomatous inflammation which is composed of aggregates of the mononuclear phagocyte system and characterized by well demarcated focal lesions described as granulomas with a background of reparative tissue.[4,5] Distinguishing feature is the presence of activated macrophages which have an epithelioid appearance diagnostic of chronic granulomatous inflammation, with or without giant cells.[4,5]

Furthermore, previous studies have examined the occurrence of different chronic inflammatory conditions in the orofacial region either as a series or as case reports on interesting findings.[6-9] Gaetti-Jardim Jr et al. discussed their management of patients with jaw chronic osteomyelitis in Brazil, emphasizing the role of anaerobic organisms in its aetiology as well as its susceptibility to b-lactams and clindamycin.[6] Similarly, Adekeye and Cornah reviewed 141 cases of chronic osteomyelitis of the jaws in a Nigerian population, noting a preference for the maxilla in the first decade of life.[7] Moreover, Sezer et al. reported four cases of actinomycotic tuberculosis (TB) occurring in three women and a man in Turkey, equally affecting the maxilla and mandible,[8] while Rattan and Rai also highlighted the management of extra pulmonary TB in a few Indian patients.[9]

Conversely, there is a dearth of studies appraising the occurrence of all chronic inflammatory diseases in the jaws and orofacial region. Thus, this study aims to review the clinico-pathologic features of chronic inflammatory lesions diagnosed at the Oral Pathology Laboratory, University College Hospital (UCH), Ibadan, Nigeria.

Materials and Methods

The study location was the Oral Pathology Laboratory, UCH, Ibadan. The archival records were examined and all entries made as histopathological diagnosis of a chronic inflammatory lesion involving either the jaws or orofacial tissues from January 1990 to December 2016 were identified and included in the study. Only cases with complete and

adequate records were included while cases with incomplete records were excluded. The clinical data regarding age, gender, site of lesion, clinical diagnosis, and histopathological diagnosis were extracted from the histopathology reports of the patients using a data collection form. Cases were further sub-classified into two groups namely those with specific diagnoses signifying certain disease entities occurring in known sites and those with vague non-specific diagnosis which were not related to particular disease entities or sites. Data were presented using summary statistics and analysed with the SPSS software (version 21, IBM Corporation, Armonk, NY, USA). Chi-square test was used to test the association between age, gender, and histopathological diagnosis. Statistical significance was set at $P < 0.050$.

Results

Over the study period, 95 orofacial lesions were diagnosed as chronic inflammatory lesions, constituting 4.6% of 2046 histopathology diagnoses. The age group of 21-40 years had the highest occurrence with 35.8% of cases, while mean age of 43.6 ± 21.3 years was obtained. The mean age of men was 36.6 ± 19.0 years, while for women it was 49.0 ± 21.5. There was a statistically significant difference between these mean ages. [t = -2.82, degree of freedom (df) = 95, P = 0.006]. Moreover, there was a female preponderance of 1.3 in this study. The most commonly affected site was the mandible making up 43.2% of cases and majority of the cases constituting 80 (84.2%) had no underlying systemic disease (Table 1).

The most frequent histological diagnosis was non-specific chronic inflammation constituting 31 (32.6%) followed by chronic osteomyelitis 29 (30.5%), while chronic sialadenitis, foreign body granulomas, and chronic sinusitis all recorded 6.3% of cases. Moreover, the most common clinical findings in these lesions were swellings in 49.5% of cases, followed by swellings with pus discharge in 31 (32.6%), and ulcerations in 9 cases (9.5%) (Table 2).

Table 1. Characteristics of patients by socio-demographics, site of lesion, and co-existing disease

	Frequency	Percentage
Age group (year)		
≤ 20	15	15.7
21-40	34	35.8
41-60	21	22.1
61-80	22	23.2
≥ 81	3	3.2
Gender		
Men	41	43.2
Women	54	56.8
Site of lesions		
Mandible	41	43.2
Nose	2	2.1
Maxilla	8	8.4
Submandibular glands	7	7.4
Palate	7	7.4
Tongue	5	5.2
Antrum	7	7.4
Others*	18	18.9
Co-existing disease		
Nil	80	84.2
DM	2	2.1
Hypertension + DM	2	2.1
Hypertension	3	3.2
Asthma	3	3.2
Others**	5	5.2

* Floor of mouth- 2, lips- 3, labial mucosa- 2, face- 3, parotid gland- 2, cervico-mandibular- 1, neck- 2, cheek- 1, buccal mucosa- 2

** Sickle cell disease- 1, hypertension + hyperthyroidism- 1, peptic ulcer- 1, human immunodeficiency virus (HIV)- 1, hypertension + leukemia- 1

DM: Diabetes mellitus

Following sub-classification, lesions were grouped as follows: the specific group consisted of chronic osteomyelitis, TB lymphadenitis, actinomycosis, eosinophilic granuloma, Wegener's granulomatosis, chronic sinusitis, mucormycosis, chronic sialadenitis, Kimura's disease, sarcoidosis, and Garre's osteomyelitis; while foreign body granulomas, chronic inflammations, and chronic granulomatous inflammations were

considered to be non-specific. More women constituting 34 (61.8%) were found in the specific histodiagnosis group; however, the non-specific diagnoses were equally distributed between both genders (Table 3).

Table 2. Distribution of patients by histological diagnosis and clinical findings

	Frequency	Percentage
Histological diagnosis		
Chronic osteomyelitis	29	30.5
Chronic sialadenitis	6	6.3
Foreign body granuloma	6	6.3
TB lymphadenitis	4	4.2
Wegener's granulomatosis	2	2.1
Non-specific chronic inflammation	31	32.6
Chronic granulomatous inflammation	3	3.2
Chronic sinusitis	6	6.3
Others*	8	8.5
Clinical findings		
Swelling	47	49.5
Swelling + pus discharge	31	32.6
Ulceration	9	9.5
Pus discharge	2	2.1
Others**	6	6.3

* Garre's osteomyelitis- 1, Eosinophilic granuloma- 1, Sarcoidosis- 1, Kimura's disease- 1, Mucormycosis- 2, Actinomycosis- 2
** Pain- 1, swelling + pus discharge + facial nerve palsy- 1, swelling + ulceration- 1, swelling + fever- 1, ulceration + pus discharge- 1, oro-antral fistula + pus discharge- 1
TB: Tuberculosis

Moreover, both specific and non-specific diagnoses recorded the highest frequency in the 21-40 years age group, but this was not statistically significant (Fisher's exact test = 6.00*, P = 0.190) (Table 3).

Figures 1-3 show the histopathology findings of this study.

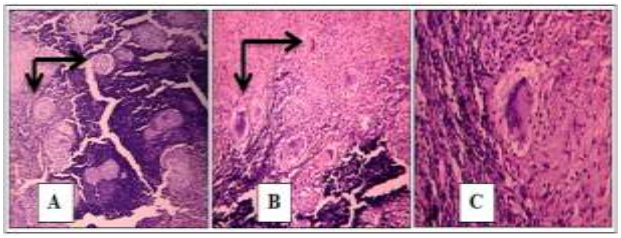

Figure 1. Tuberculous lymphadenitis showing A- numerous necrotizing granulomas [Hematoxylin and eosin (H&E) staining, ×40]; B- multinucleated giant cells (H&E, ×40); C- Langhans' type multinucleated giant cells (H&E, ×100)

Discussion

All chronic inflammatory lesions of the jaws and orofacial tissues are scarcely reported conjointly. They exist separately mostly as case reports and series, due to their varied aetiopathogenesis.[6-9]

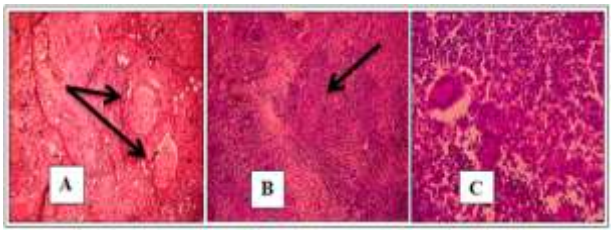

Figure 2. Sarcoidosis showing A- necrotizing granulomas [Hematoxylin and eosin (H&E) staining, ×40]; B- multinucleated giant cells (H&E, ×40); C- Langhans' type multinucleated giant cells (H&E, ×100)

Table 3. Association between patients' histodiagnoses and age/gender

	Specific (n = 55) [n (%)]	Non-specific (n = 40) [n (%)]	χ^2	Df	P
Gender			1.32	1	0.250
Men	21 (38.2)	20 (50.0)			
Women	34 (61.8)	20 (50.0)			
Age group (year)			6.00*		0.190
≤ 20	9 (16.4)	6 (15.0)			
21-40	19 (34.5)	15 (37.5)			
41-60	11 (20.0)	10 (25.0)			
61-80	16 (29.1)	6 (15.0)			
≥ 81	-	3 (7.5)			

* Fisher's exact test
Df: Degree of freedom

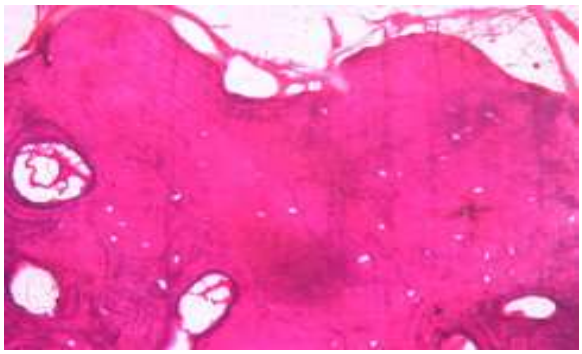

Figure 3. Chronic Osteomyelitis showing necrotic bone with empty lacunae [Hematoxylin and eosin (H&E) staining, ×40]

In this study, these lesions occurred most in the 21-40 years age group compared to other age groups.

This finding is contrary to common belief that old and elderly patients are more susceptible to oral diseases,[10] considering the various factors that may interfere with oral health status in elderly patients.[10,11] Moreover, other demographic and clinical parameters such as gender of patients as well as site of chronic inflammatory lesions were assessed in this study. There was a slight female predilection, while the mandible was the most prevalent site of occurrence. These outcomes were however not statistically significant. The female gender has been reported to express higher levels of immunoreactivity in comparison to men, which affords them increased resistance to many types of infections but increases their susceptibility to autoimmune diseases.[12] Moreover, women have a more active humoral and cell-mediated immunity,[13] thus making them more susceptible to chronic inflammatory conditions, probably due to increased sensitivity to aetiological agents of chronic inflammation.

The most commonly diagnosed disease in this study was non-specific chronic inflammation accounting for 31 (32.6%) of all chronic inflammatory lesions seen. The microscopic features of the lesions were typified by chronic inflammatory cell infiltration, angiogenesis, and fibrosis not specific of any defined lesion. Considering the various functions of the oral cavity and the presence of a large population of microorganisms, non-specific chronic inflammation as seen in the present study is not unexpected due to the numerous sources of chronic irritation that may exist intraorally.[14,15]

In this study, chronic osteomyelitis was the next most prevalent lesion to non-specific chronic inflammation. Osteomyelitis of the jaws are chronic lesions characterized by inflammation of the jaw bones and their marrow spaces.[3] It may manifest either as suppurative or non-suppurative form,[16] often as a result of polymicrobial infection including alpha haemolytic Streptococci, Staphylococcus aureus, Bacteroides, and Fusobacterium species.[3,6] Moreover, it may occur due to less virulent organisms or following failure of resolution of the acute infective phase due to inadequate treatment.[3,6] Clinical features of chronic osteomyelitis include a dull aching pain with slightly indurated swelling of the affected jaw and presence of an intra-oral or extra-oral discharging sinus.[3] Typically, in the chronic focal sclerosing type, the mandibular first molar is commonly the source of infection and it radiographically appears as a well-circumscribed radio-opaque mass of sclerotic bone around the affected molar tooth,[17] 50% of cases are seen in patients under 30 years of age.[18] In the chronic diffuse sclerosing type, older age group is commonly affected. They exhibit a mixed radiolucent/radiopaque appearance on radiograph.[19] Another distinct form of chronic osteomyelitis is Garre's osteomyelitis, typically seen in children and young adults. Radiographically, it is characterized by concentric layers of calcification described as the "onion skin" appearance of the affected part of the mandibleon radiograph.[20] Diagnosis of gnathic

osteomyelitis is often by clinical findings. However, histology of gnathic osteomyelitis is used to supplement and can be used in combination with clinical and radiological findings.[21] Secondary chronic osteomyelitis with suppuration may resemble acute osteomyelitis showing large amounts of polymorphonuclear leukocytes, macrophages, and plasma cells, along with a variable degree of marrow fibrosis, necrotic bone, and reactive bone formation; while secondary chronic osteomyelitis with a more chronic course would have a lymphocytic infiltrate instead.[3]

Previous studies have reported the prevalence of jaw osteomyelitis in various populations.[7,22,23] Prasad et al. reported 84 cases of osteomyelitis of the head and neck over a 10-year period, diagnosed based on clinical and radiological findings.[22] Similarly, Daramola and Ajagbe had earlier reported 34 cases of chronic osteomyelitis,[24] while Adekeye and Cornah reviewed 141 cases based on clinical features.[7] In addition, Singh conducted a prospective study of 21 cases of chronic suppurative osteomyelitis.[23] In this study, chronic osteomyelitis constituted 30.5% of chronic inflammatory lesions of the jaws and 1.4% of all biopsies over the study period, which is less than what was obtained in other studies.[7,22,23] This may be due to the use of only cases that had histological diagnosis of chronic osteomyelitis in obtaining data as employed in this study, while most studies largely utilized clinical records.[6,7,22-24]

Additionally, chronic inflammation within and around the jaws may include chronic granulomatous lesions such as those caused by specific infections involving bacteria such as mycobacteria, syphilis, and actinomycosis. Fungal infections such as histoplasmosis and aspergillosis species as well as parasitic infections such as leishmaniasis may likewise be seen.[3,4,8,9,25,26] This study recorded 4 (4.2%) cases of TB lymphadenitis. TB is a chronic infectious disease caused by the tubercle bacillus bacteria, mycobacterium TB.[27,28] Transmission occurs by droplet infection from airborne particles of an infected person with the primary site of implantation being the lungs.[27,28] Orofacial TB is a rare presentation of extrapulmonary TB[29] which could be primary, commonly seen in children as well as adolescents or the secondary form seen more in middle-aged and elderly patients.[30] Various forms of presentation of orofacial TB exist including TB lymphadenitis which is the most common type of extrapulmonary TB seen,[31] constituting all the four cases seen in this study. Other forms are TB ulcers which are the most common oral TB presentation,[30] TB gingivitis, TB periapical granuloma, TB osteomyelitis, and rarely TB of the temporomandibular joint (TMJ).[32] Histopathology of TB is that of a necrotizing granulomatous lesion consisting of central areas of caseating granulomas with associated peripheral rims of epitheloid histiocytes and giant cells of the Langhans' type. Exterior to these are outer rims of lymphocytes and plasma cells.[2,29]

Actinomycosis is a rare suppurative and granulomatous chronic infectious disease caused by Actinomyces spp., an anaerobic gram-positive bacterium.[33,34] This study recorded 2 (2.1%) cases of actinimycosis seen in a 14-year-old boy and a 67-year-old woman occurring as gingival and mandibular swelling, respectively. Actinomyces spp. exists as commensal in the human respiratory and digestive tracts, invading deeper tissues via mucosal lesions.[33,34] Most common predisposing factors are of odontogenic origin involving the perimandibular regions usually following trauma or surgery. Other sites, including the tongue, sinuses, middle ear, larynx, and thyroid gland may be affected.[35,36] Rarely, the TMJ could also be involved.[37] Cervicofacial actinomycosis is the most common form constituting 50% of all cases seen.[33,34] Characteristically, it is seen as a

gradual progressive painless indurated swelling with draining sinus tracts on the skin or oral mucosa, occasionally discharging thick yellow exudate with distinctive sulfur granules.[34,38] Definitive diagnosis is by culturing bacteria from the lesion, macroscopic demonstration of the classic sulfur granules in tissue specimens, and histologic examination revealing granulomatous inflammation with a central zone of necrosis which contains multiple basophilic granules that signify lobulated micro-colonies of filamentous actinomyces.[34,38]

Common to all granulomatous lesions are the presence of granulomas on histopathology.[2,4,39] This feature is seen in other chronic inflammatory lesions with orofacial manifestations including sarcoidosis, Crohn's disease, and orofacial granulomatosis.[4,40] Foreign bodies, chemicals, and drugs may also provoke a chronic granulomatous inflammation in the orofacial region.[4,39] Sarcoidosis is a rare idiopathic multi-systemic non-caseating granulomatous disease.[41] Pulmonary involvement occurs in nearly 90% of cases, while 25% occur in skin and 10%–15% affects the head and neck region.[42] Oral sarcoidosis is rarely seen, while accompanying chronic multi-system sarcoidosis may seldom occur in the acute stage.[41,42] The oral lesions may be solitary, multiple, or part of a widespread disease. In some instances, oral involvement occurs first, or could be the only manifestation of the disease.[43] The case of sarcoidosis seen in this study was diagnosed in a 38-year-old man, presenting as part of a multi-system disease involving the lungs, skin, and tongue.

Accounts of oral sarcoidosis recorded in literature are case reports and series.[43,44] However, Suresh and Radfar reviewed 68 cases of oral sarcoidosis and reported a female predilection, slight racial preference for Caucasians, and a median age of 37 years.[41] Moreover, oral soft tissues were more commonly affected than the jaw bones with the buccal mucosa and gingivae being most affected.[41] The most common mode of clinical presentation was localized swellings, while ulcerations, gingivitis, gingival hyperplasia, and gingival recession were the less commonly seen presentations.[41] Histological appearance of the lesion shows typical sarcoid granulomas with non-caseating necrosis.[2,43,44]

Conclusion

This study presented a review of the clinico-pathologic features of chronic inflammatory lesions of the jaws and orofacial tissues. While the cases obtainable over the study period may constitute a majority of these lesions, the use of histopathology records as engaged in this study excluded lesions where diagnoses were based on clinical and radiological parameters. Summarily, chronic inflammatory lesions of 'non-plaque origin' are rarely seen around the jaws and orofacial region. They are slightly more common in women and in the 21-40 years age group. The mandible was the most commonly affected site, while non-specific chronic inflammation and chronic osteomyelitis were the most frequently seen lesions. Larger studies on these rare lesions are advocated to further assess their prevalence globally.

Conflict of Interests

Authors have no conflict of interests.

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References

1. Kumar V, Abbas AK, Aster JC. Robbins and Cotran pathologic basis of disease. Philadelphia, PA: Elsevier/Saunders; 2015. p. 30-48.
2. Shah KK, Pritt BS, Alexander MP. Histopathologic review of granulomatous inflammation. J Clin Tuberc Other Mycobact Dis 2017; 7: 1-12.
3. Baltensperger M, Eyrich GK. Osteomyelitis of the

Jaws. Berlin, Germany: Springer Science & Business Media; 2008. p. 5-56.
4. James DG. A clinicopathological classification of granulomatous disorders. Postgrad Med J 2000; 76(898): 457-65.
5. Zumla A, James DG. Granulomatous infections: Etiology and classification. Clin Infect Dis 1996; 23(1): 146-58.
6. Gaetti-Jardim E Jr, Ciesielski FI, Possagno R, Castro AL, Marqueti AC, -Jardim EC. Chronic osteomyelitis of the maxilla and mandible: Microbiological and clinical aspects. Int J Odontostomatol 2010; 4(2): 197-202.
7. Adekeye EO, Cornah J. Osteomyelitis of the jaws: A review of 141 cases. Br J Oral Maxillofac Surg 1985; 23(1): 24-35.
8. Sezer B, Akdeniz BG, Gunbay S, Hilmioglu-Polat S, Basdemir G. Actinomycosis osteomyelitis of the jaws: Report of four cases and a review of the literature. J Dent Sci 2017; 12(3): 301-7.
9. Rattan V, Rai S. Tuberculosis of the oral cavity and associated structures: The PGIMER Experience. J Postgrad Med Edu Res 2013; 47(4): 214-7.
10. Saunders MJ, Yeh CK. Oral health in elderly people. In: Chernoff R, Editor. Geriatric nutrition. burlington, MA: Jones & Bartlett Publishers; 2013. p. 165-210.
11. Razak PA, Richard KM, Thankachan RP, Hafiz KA, Kumar KN, Sameer KM. Geriatric oral health: A review article. J Int Oral Health 2014; 6(6): 110-6.
12. Cannon JG, St Pierre BA. Gender differences in host defense mechanisms. J Psychiatr Res 1997; 31(1): 99-113.
13. Spitzer JA. Gender differences in some host defense mechanisms. Lupus 1999; 8(5): 380-3.
14. Regezi JA, Sciubba JJ, Jordan RC. Oral pathology: Clinical pathologic correlations. Philadelphia, PA: Saunders Elsevier; 2008.
15. Neville BW. Oral & maxillofacial pathology. Philadelphia, PA: W.B. Saunders; 2002.
16. Topizan RG, Goldberg MH. Osteomyelitis of the Jaws. In: Topazian RG, Goldberg MH, Editors. Oral and maxillofacial infections. Philadelphia, PA: Saunders; 1994. p. 251-88.
17. Rajendran R, Sivapathasundharam B. Shafer'S textbook of oral pathology. Delhi, India: Elsevier India; 2009. p. 438-47.
18. Eliasson S, Halvarsson C, Ljungheimer C. Periapical condensing osteitis and endodontic treatment. Oral Surg Oral Med Oral Pathol 1984; 57(2): 195-9.
19. Yeoh SC, MacMahon S, Schifter M. Chronic suppurative osteomyelitis of the mandible: Case report. Aust Dent J 2005; 50(3): 200-3.
20. Suma R, Vinay C, Shashikanth MC, Subba Reddy VV. Garre's sclerosing osteomyelitis. J Indian Soc Pedod Prev Dent 2007; 25(Suppl): S30-S33.
21. Baltensperger M, Gratz K, Bruder E, Lebeda R, Makek M, Eyrich G. Is primary chronic osteomyelitis a uniform disease? Proposal of a classification based on a retrospective analysis of patients treated in the past 30 years. J Craniomaxillofac Surg 2004; 32(1): 43-50.
22. Prasad KC, Prasad SC, Mouli N, Agarwal S. Osteomyelitis in the head and neck. Acta Otolaryngol 2007; 127(2): 194-205.
23. Singh G. Chronic Suppurative Osteomyelitis of the Mandible: A Study of 21 Cases. OHDM 2014; 13(4): 971-4.
24. Daramola JO, Ajagbe HA. Chronic osteomyelitis of the mandible in adults: A clinical study of 34 cases. Br J Oral Surg 1982; 20(1): 58-62.
25. Kapoor S, Gandhi S, Gandhi N, Singh I. Oral manifestations of tuberculosis. CHRISMED J Health Res 2014; 1(1): 11-4.
26. Montone KT. Infectious diseases of the head and neck: A review. Am J Clin Pathol 2007; 128(1): 35-67.
27. Serafino Wania RL. Tuberculosis 2: Pathophysiology and microbiology of pulmonary tuberculosis. South Sudan Medical Journal 2013; 6(1): 10-3.
28. More CB, Patel HJ, Asrani M, Thakkar K, Das S, Piparia V. Oral lesions of tuberculosis-an overview. Journal of Orofacial & Health Sciences 2011; 2(2): 41-4.
29. Jain P, Jain I. Oral manifestations of tuberculosis: Step towards early diagnosis. J Clin Diagn Res 2014; 8(12): ZE18-ZE21.
30. Nagalakshmi V, Nagabhushana D, Aara A. Primary tuberculous lymphadenitis: A case report. Clin Cosmet Investig Dent 2010; 2: 21-5.
31. Fontanilla JM, Barnes A, von Reyn CF. Current diagnosis and management of peripheral tuberculous lymphadenitis. Clin Infect Dis 2011; 53(6): 555-62.
32. Andrade NN, Mhatre TS. Orofacial tuberculosis--a 16-year experience with 46 cases. J Oral Maxillofac Surg 2012; 70(1): e12-e22.
33. Lancella A, Abbate G, Foscolo AM, Dosdegani R. Two unusual presentations of cervicofacial actinomycosis and review of the literature. Acta Otorhinolaryngol Ital 2008; 28(2): 89-93.
34. Volante M, Contucci AM, Fantoni M, Ricci R, Galli J. Cervicofacial actinomycosis: Still a difficult differential diagnosis. Acta Otorhinolaryngol Ital 2005; 25(2): 116-9.
35. Atespare A, Keskin G, Ercin C, Keskin S, Camcioglu A. Actinomycosis of the tongue: A diagnostic dilemma. J Laryngol Otol 2006; 120(8): 681-3.
36. Vorasubin N, Wu AW, Day C, Suh JD. Invasive

sinonasal actinomycosis: Case report and literature review. Laryngoscope 2013; 123(2): 334-8.
37. Bochev V, Angelova I, Tsankov N. Cervicofacial actinomycosis-report of two cases. Acta Dermatovenerol Alp Pannonica Adriat 2003; 12(3): 105-8.
38. Valour F, Senechal A, Dupieux C, Karsenty J, Lustig S, Breton P, et al. Actinomycosis: Etiology, clinical features, diagnosis, treatment, and management. Infect Drug Resist 2014; 7: 183-97.
39. Silveira VA, de Carmo ED, Colombo CE, Cavalcante AS, Carvalho YR. Intraosseous foreign-body granuloma in the mandible subsequent to a 20-year-old work-related accident. Med Oral Patol Oral Cir Bucal 2008; 13(10): E657-E660.
40. Nwawka OK, Nadgir R, Fujita A, Sakai O. Granulomatous disease in the head and neck: Developing a differential diagnosis. Radiographics 2014; 34(5): 1240-56.
41. Suresh L, Radfar L. Oral sarcoidosis: A review of literature. Oral Dis 2005; 11(3): 138-45.
42. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med 1997; 336(17): 1224-34.
43. Bouaziz A, Le Scanff J, Chapelon-Abric C, Varron L, Khenifer S, Gleizal A, et al. Oral involvement in sarcoidosis: Report of 12 cases. QJM 2012; 105(8): 755-67.
44. Kolokotronis AE, Belazi MA, Haidemenos G, Zaraboukas TK, Antoniades DZ. Sarcoidosis: Oral and perioral manifestations. Hippokratia 2009; 13(2): 119-21.