

Original article

A STUDY ON ORAL AUTOIMMUNE DISEASES AND THEIR MANAGEMENT IN A TERTIARY HOSPITAL

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ABSTRACT

OBJECTIVE: As many as 22 types of autoimmune diseases affecting oral cavity have been described in literature. This study aims to determine the prevalence, age and gender distribution, and the various treatment options in the management of oral autoimmune conditions seen in a Nigerian tertiary hospital.

METHODS: A retrospective study of all the patients who presented at the Oral Medicine Clinic, Dental Centre, University of Benin Teaching Hospital, Benin City, Nigeria, over a period of 4 years. The medical records, laboratory and histopathology reports of the patients seen within the study period were reviewed. All cases of oral autoimmune conditions were selected and studied.

RESULTS: Of the 404 patients seen during the study period, 57 cases of oral autoimmune disorders were diagnosed giving a prevalence of 14.1%. The male to female ratio was approximately 1:1. The mean age was 37.9 ±17.2 years. Among the 57 oral autoimmune conditions recorded recurrent aphthous ulcer (RAU) accounted for 27 (47.4%) cases, followed by erythema multiforme 12 (21.1%). The 20 to 30 years age group had the highest occurrence of autoimmune conditions 14 (24.6%), made up largely of RAU 11(19.3%) and lichen planus 3 (5.3%). Over 73.7% (n=42) of the patients with autoimmune conditions were treated with corticosteroids (local and systemic), 11 (19.3%) patients were treated with Loratadine, an antihistamine.

CONCLUSION: This study showed a relatively higher prevalence of autoimmune condition presenting in Oral Medicine clinic in this Centre, with the highest occurrence in the 3rd decade of life. Recurrent aphthous ulcers and erythema multiple were the most common forms of oral autoimmune conditions. The treatment administered was mostly corticosteroids and antihistamine.

Keywords: Autoimmune disease, oral lesions, treatment

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INTRODUCTION

Autoimmune diseases are the result of specific immune responses directed against structures of the self.¹ It is defined as the development of immune system reactivity in the form of auto-antibodies and T-cell responses to self-structures. There are many known autoimmune diseases ranging from tissue specific disorders to

systemic disorders.² Autoimmune disorder is an umbrella term for a variety of painful conditions involving a malfunction in the body's complex immune system. In a normal immune response to an infection or invasion of antigenic agents, the immune system causes a temporary inflammation while it kills off the invader cells. In autoimmune disorders, this inflammation

becomes chronic, causing pain and permanent changes or damages the involved tissues.² The mouth is referred to as the mirror that can reflect the overall health of the body, various autoimmune diseases manifests themselves in the oral cavity in their earliest stages, and early diagnosis by a dental examination can be the key for improved outcomes.³

No single theory or mechanism can adequately explain all features or pathogenesis of autoimmune diseases. A complex interplay of many factors like inheritance of susceptible genes; environmental triggers such as infections and tissue damage; activation of self-reactive lymphocytes of immune system and hormonal disturbances lead to the development of autoimmunity.⁴

As many as 22 types of autoimmune diseases affecting oral cavity have been described in literature among which recurrent aphthous stomatitis, lichen planus, pemphigus and pemphigoid, Sjogrens syndrome, rheumatoid arthritis and systemic lupus erythematosus are most commonly encountered by oral physicians. A female predisposition is noted in most of these autoimmune diseases.⁵⁻⁷

Some oral autoimmune conditions have fatal outcome with high morbidity and mortality, and early detection with prompt treatment can avert such fatal outcome.³ Unfortunately, in our environment, there is dearth need of literature on oral autoimmune conditions and their management. Hence, this study aims to determine the prevalence, age and gender distribution, and the various treatment options for the management of oral autoimmune conditions seen in a Nigerian tertiary hospital.

MATERIALS AND METHODS

This was a retrospective study of all patients who presented at the Oral medicine Clinic, Dental Centre, University of Benin Teaching Hospital, Benin City, Nigeria, over a period of 4 years (April 2014 to March 2018). The medical records, laboratory and histopathology reports of the patients seen within the study period were reviewed. All cases of oral autoimmune conditions were selected and studied.

Data on the age, gender, clinical and laboratory diagnosis, and treatment of the oral autoimmune patients were collected, carefully assessed and documented. The data collected was analysed using IBM SPSS Statistics version 21.0. The data was subjected to descriptive analysis in the form of frequencies, percentages, cross-tabulations, mean and standard deviation. Chi square was used to determine association between variables with P-value set at 0.05.

RESULTS

Of the 404 patients seen in Oral Medicine Clinic during the study period, 57 cases of oral autoimmune disorders were diagnosed giving a prevalence value of 14.1%. The sample consisted of 29 (50.9%) male and 28 (49.1%) female patients, with a male to female ratio of approximately 1:1. The age range of the cases was 3 to 76 years with a mean age of 37.9 ± 17.2 years, and the peak age group was 21-30 years (n=14, 24.6%) [Table 1].

Table 1: Relationship between age and gender of the patients with oral autoimmune disease

Age Group (years)	Male (%)	Female (%)	Total (%)
< 10	1 (1.8)	1 (1.8)	2 (3.5)
11-20	5 (8.8)	2 (3.5)	7 (12.3)
21-30	6 (10.5)	8 (14.0)	14 (24.6)
31-40	6 (10.5)	3 (5.3)	9 (15.8)
41-50	5 (8.8)	5 (8.8)	10 (17.5)
51-60	3 (5.3)	5 (8.8)	8 (14.0)
61-70	2 (3.5)	3 (5.3)	5 (8.8)
>70	1 (1.8)	1 (1.8)	2 (3.5)
Total	29 (50.9)	28 (49.1)	57 (100.0)

Among the 57 oral autoimmune conditions recorded (Figure 1), recurrent aphthous ulcer (RAU) accounted for 27(47.4%) cases, followed by erythema multiforme (EM) [n=12, 21.1%]. The least conditions were Sjogren's syndrome (SS) and mucous membrane pemphigoid (MMP) each accounting for a case (n=1, 1.8%) respectively.

RAU occurred more in females 14 (24.6%) than males 13 (22.3%) [Fig 2]. Out of the 12(21.1%) cases of erythema multiforme, 11 (19.3%) cases were seen in males and 1(1.8%) case in female (Fig 3). Lichen planus was mostly found in females 7 (12.3%) as against the males 2 (3.5%) [Fig 4], while the 5(8.8%) cases of allergic stomatitis were found in females. There was a significant association between the oral autoimmune conditions and the gender distribution (P= 0.003) [Table 2].

Table 2: Gender distribution of the autoimmune conditions

Autoimmune Disease	Male (%)	Female (%)	Total (%)
Allergic Stomatitis	-	5 (8.8)	5 (8.8)
Erythema Multiforme	11 (19.3)	1 (1.8)	12 (21.1)
Lichen Planus	2 (3.5)	7 (12.3)	9 (15.8)
Mucous Membrane Pemphigoid	1 (1.8)	-	1 (1.8)
Pemphigus Vulgaris	2 (3.5)	-	2 (3.5)
Recurrent Aphthous Ulcer	13 (22.8)	14 (24.6)	27 (47.4)
Sjogren's Syndrome	-	1 (1.8)	1 (1.8)
Total	29 (50.9)	28 (49.1)	57 (100)

P Value = 0.003

The 20 to 30 age group had the highest occurrence of autoimmune conditions (n=14, 24.6%), made up largely of RAU (n=11, 19.3%) and lichen planus (n=3, 5.3%), and the least occurrence of autoimmune conditions were found at the extremes of age (<10 years and >70 years). Erythema multiforme occurred more around the 2nd decade of life 4 (7.0%), and lichen planus was more in the 3rd and 4th decades of life 5 (8.8%). The association between the autoimmune conditions and age distribution was significant (Table 3).

Over 73.7% (n=42) of the patients with autoimmune conditions were treated with corticosteroids (local and systemic), 11 (19.3%) patients were treated with Loratadine an antihistamine, out of which 8.8% (n=5) had allergic stomatitis, 4 (7.0 %) had lichen planus

and 2 cases (3.5%) of RAU. About 19 (33.3%) patients were placed on antibiotics (Augmentin, Amoxicillin, Metronidazole and Tetracycline mouth rinse) to prevent secondary infections of the immune oral ulcers. Besides, 2 (3.5%) of cases had Levamisole therapy to boost their immunity. Other symptomatic treatment given were analgesia (n=11, 19.3%) and warm saline mouth rinse (n=8, 14.0%) [Table 4].



Fig 2: Minor Recurrent Aphthous ulcers showing areas of oval shaped ulcers with erythematous margins.



Fig 3: Erythema multiforme with haemorrhagic crusted lips and erythematous tongue covered with pseudomembrane.



Fig 4: A case of lichen planus in a female patient affecting the upper gingival and labial mucosa.

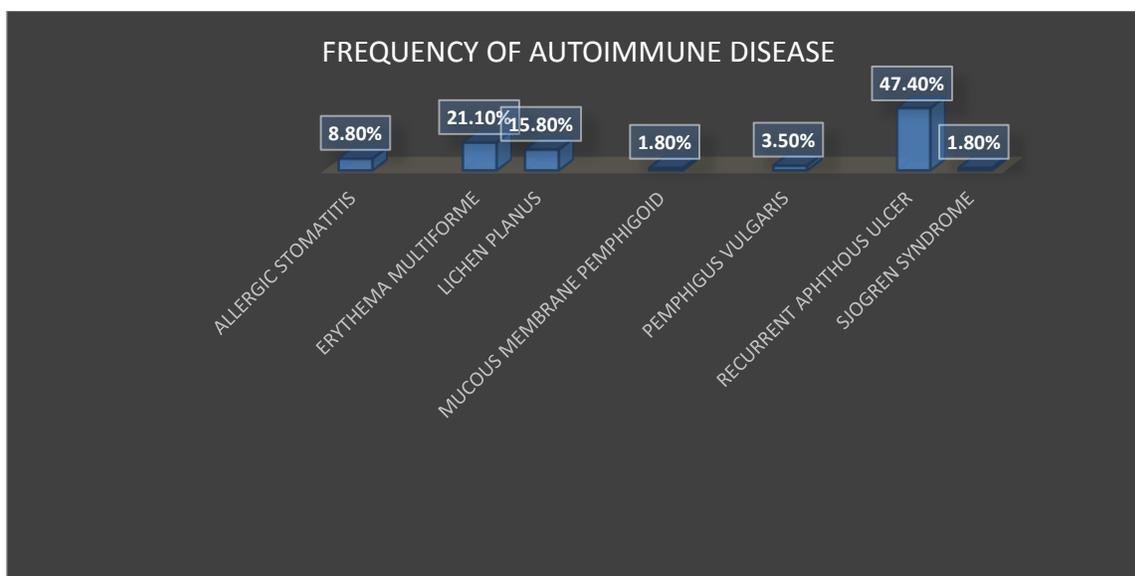


Fig. 1: Frequency of the oral autoimmune diseases in this study

Table 3: Age Distribution of Autoimmune Conditions

Autoimmune Disease	≥10	11-20	21-30	31-40	Age 41-50	Group 51-60	(%) 61-70	>70	Total (%)
Allergic stomatitis	-	-	-	-	1 (1.8)	3 (5.3)	1(1.8)	-	5 (8.8)
Erythema multiforme	1(1.8)	4 (7.0)	-	2(3.5)	3(5.3)	1 (1.8)	-	1(1.8)	12 (15.8)
Lichen planus	1 (1.8)	-	3 (5.3)	2 (3.5)	1 (1.8)	1 (1.8)	-	1(1.8)	9 (15.8)
Mucous membrane pemphigoid	-	-	-	-	-	-	1(1.8)	-	1 (1.8)
Pemphigus vulgaris	-	-	-	2 (3.5)	-	-	-	-	2 (3.5)
Recurrent aphthous ulcer	-	3 (5.3)	11(19.3)	3 (5.3)	4 (7.0)	3 (5.3)	3 (5.3)	-	27 (47.4)
Sjorgren's syndrome	-	-	-	-	1 (1.8)	-	-	-	1 (1.8)
Total	2 (3.5)	7 (12.3)	14(24.6)	9(15.8)	10(17.5)	8 (14.0)	5 (8.8)	2 (3.5)	57 (100)

P value = 0.004

DISCUSSION

Previous study by Omoregie et al⁷ observed a low (0.2%) prevalence of oral autoimmune diseases among 12,179 patients that presented in Oral Medicine and Oral Diagnosis clinics in this Dental Centre. In this present study, a higher prevalence of 14.1% of oral autoimmune was found among 404 patients seen only in the Oral Medicine clinic in the same Centre. This relatively higher prevalence observed may be due to the lower number of patients in this study compared to the patients seen in previous study.

The oral autoimmune diseases in this study consist mainly of recurrent aphthous ulcer, erythema multiforme, lichen planus and allergic stomatitis. Most of the autoimmune conditions seen in this study were predominant in females except for pemphigoid, pemphigus vulgaris, and erythema multiforme which were predominantly seen in males. This is comparable to previous studies, in which female predisposition was noted in most of the autoimmune diseases.^{3, 6, 7}

Recurrent aphthous ulcer which accounted for about 47.7% of the oral autoimmune conditions

was found more in females and predominantly in the third decade of life. This is similar to a prevalence of 47.3%⁸ previously recorded in this centre. RAU presents in the oral mucosa in three major forms namely: herpetiform type, minor and major types. The lesion starts in childhood or adolescence as recurrent small, round or ovoid ulcers with circumscribed margins, erythematous haloes and yellow or grey floor. They are quite painful and the natural course is of eventual remission.^{8,9,10}

Oral EM is a distinct but less well-recognized variant of EM with extensive irregular erythematous ulcerations in the buccal mucosa, labial mucosa, tongue, palate, and lips with blood encrustation.^{11,12} EM frequently occurs in young adolescent males, and a prevalence of 20.8% has been reported.^{7,13,14} This agrees with this study where over 90% of patients diagnosed with EM were males, predominantly in the second decade of life with a prevalence of 21.1%.

Lichen planus is an inflammatory autoimmune type of mucocutaneous disease^{15,16}. The present study reported a prevalence of 15.8%. This is higher than a reported prevalence of 2.6% oral lichen planus in Indian population with more female predilection.¹⁷ According to a previous study,¹⁸ oral lichen planus (OLP), the mucosal counterpart of cutaneous lichen planus, presents frequently in the fourth decade of life and with female predilection. Similarly LP affected patients mostly in the third and fourth decades of life with female predilection in this study.

The present study showed that allergic stomatitis (AS) was found in females predominantly in the sixth decade of life, with a prevalence of 15.8%. This is similar to an earlier study that reported a prevalence of AS to be 16.7%, more in elderly patients with the ratio of female to male as 5:1.⁷

The present study reported a prevalence of 3.5% of Pemphigus vulgaris (PV). PV has been reported to occur worldwide and the incidence varies from 0.5-3.2 cases per 100,000 population.¹⁹ PV is normally associated with oral lesions that generally affect patients aged 40–60 years, manifesting as

extremely painful and persistent oral lesions.^{20,21} Similarly, this study reported two cases of PV seen in male patients in their fourth decade of life.

Mucous membrane pemphigoid (MMP) is an autoimmune blistering disorder that is characterized by subepithelial bullae. This study reported a prevalence of 1.8% seen in a male patient of over 60 years. The true incidence of MMP is unclear. The incidence of MMP was estimated to be 1.3–2.0 per million per year in France and Germany.²²

A case of Sjogren Syndrome (SS) was seen in a female at the fifth decade of life, giving a prevalence of 1.8% in this study. Different studies worldwide reported highly discrepant estimates for the prevalence of primary Sjögren's syndrome (pSS), ranging from 0.01% of the general population to more than 3%.²³ SS is a long-term autoimmune disease that affects the body's moisture-producing glands. Primary symptoms are a dry mouth and dry eyes.²⁴ Since SS is associated with a high prevalence in women, sex hormones, especially oestrogen, are believed to affect humoral and cell-mediated immune responses affecting susceptibility to the syndrome.²⁵

Current therapies for auto immune diseases are not cures but merely palliatives aimed at reducing symptoms, to provide the patient with an acceptable quality of life. These treatments provide nonspecific suppression of the immune response and a protective immune response. The goal of treatment should be to limit the progression, reduce exacerbation and relieve symptoms of disease based on the degree of clinical involvement, the predominant clinical type of lesions, the patient's symptom and age. The most widely accepted and the mainstay of treatment involves the use of corticosteroids. The rationale behind their usage is their ability to modulate inflammation and immune response.³

In this study the main treatment for most of the immune conditions was corticosteroid either given topically or in systemic form in over 70% of cases. Some patients (19.3%) were treated

with loratadine, an antihistamine especially in cases of allergic stomatitis secondary to use of herbal containing toothpaste. The treatment of allergic contact stomatitis involves eliminating the allergenic agent. Antihistamines, topical anaesthetics and topical corticosteroids are the commonly used pharmacological agents.²⁶ Levamisole therapy was given in cases of frequent recurrences of erythema multiforme and recurrent aphthous ulcers to boost patients' immunity. Warm saline mouth gargle was prescribed for most cases of oral autoimmune conditions presenting in form of oral ulcerations for its soothing and cleansing effect. It's of note

that some of these patients are still been followed up because of the recurrent nature of some oral autoimmune diseases.

In conclusion, this study showed a relatively higher prevalence of autoimmune condition presenting in Oral Medicine clinic in this Centre, with the highest occurrence in the 3rd decade of life. Recurrent aphthous ulcers and erythema multiple were the most common forms of oral autoimmune conditions. The treatment administered was mostly corticosteroids and antihistamine.

Conflict of interest: None declared.

Table 4: Treatment Regimen for autoimmune conditions

Autoimmune Condition	Treatment Regimen
Allergic Stomatitis (n=5, 8.8%)	Counselling Withdrawal of the predisposing agent Loratadine 10mg daily Vitamin B complex 1 tablet daily
Lichen planus (n= 9, 15.8%)	Triamcinolone acetonide 0.1% paste applied topically Dexamethasone 2mg tablet dissolved in 5mls of water as oral rinse Clobetasol propionate 0.05% cream (in a severe case) Tabs: Loratadine 10mg daily Prednisolone 0.5mg/kg/body weight and stepped down to 5mg (in recalcitrant cases)
Mucous membrane Pemphigoid (n= 1, 1.8%)	Triamcinolone acetonide paste applied topically twice daily Warm saline mouth bath 6 times daily
Sjogren's Syndrome (n=1, 1.8%)	Carboxymethylcellulose mouth spray 4 times daily Frequent sips of water Oral health education/prevention
Pemphigus vulgaris (n= 2, 3.5%)	Tabs: Prednisolone 1mg/kg/body weight and stepped down to 5mg Azathioprine 50mg daily for a week Triamcinolone acetonide paste for topical application Metronidazole 400mg 8hourly X 5 days Amoxicillin 500mg 8 hourly X 5 days
Erythema multiforme (n= 12, 21.1%)	Withdrawal of the predisposing agent if known Tabs: Prednisolone 0.5-1mg/kg body weight and gradually stepped down to 5mg Triamcinolone dental paste applied topically over the ulcers twice daily Tabs: Paracetamol 1000mg 8 hourly x 3 days Tabs: Acyclovir 400mg 6 hourly x 7 days (in cases of herpes simplex predisposition) Levamisole therapy in patients with frequent recurrences. Warm saline mouth rinse 6 times daily Xylocaine mouth spray 15 minutes before eating
RAU (27, 47.4%)	Triamcinolone acetonide 0.1% paste applied topically twice daily Tetracycline 250mg capsule dissolved in 5mls of water as oral rinse Paracetamol 1000mg 8hourly x 3 days Xylocaine mouth spray/gel 15 minutes before eating Warm saline mouth rinse 6 times daily Prednisolone 0.5-1mg/kg body weight in severe cases. Levamisole therapy in patients with frequent recurrences. Haematinics (folic acid, vitamin B complex, ferrous sulphate) in cases with nutritional deficiency.

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