DESQUAMATIVE GINGIVITIS AMONGST PATIENTS WITH AUTOIMMUNE BULLOUS DERMATOSES AT THE KENYATTA NATIONAL HOSPITAL

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DECLARATION

I declare that this thesis is my original work and has not been presented for the award of a degree in any other university.

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SUPERVISORS APPROVAL

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DEDICATION

This work is dedicated to my late father Sammy Henvel Teete; for all the work he put in me but never got to see the results; to my dear mother Truphena Teete, who continues to see the results and yet continues tirelessly to encourage and support.

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DEFINITION OF TERMS

Autoimmune bullous dermatoses; A group of cutaneous diseases characterized by sensitivity to self-antigens with a variety of clinical presentations of vesiculobullous cutaneous eruptions. These conditions include pemphigus vulgaris, pemphigus foliaceous, bullous pemphigoid and lichen planus among others.

Desquamative gingivitis; A gingival condition characterised by intense erythema, sloughing off or ulceration that is associated with autoimmune systemic disease. This condition is non-plaque associated and may be localised to the marginal gingiva, the attached gingiva or both.

Pattern; The clinical presentation of Desquamative gingivitis in terms of anatomical location, that is, either marginal or attached gingiva or clinical appearance ,that is, ulcerative, erythematous or mixed.

LIST OF ACRONYMS

AAP	American Academy of Periodontology
ABDs	Autoimmune Bullous Dermatoses
BP	Bullous Pemphigoid
CSSD	Central Sterilisation Services Department
DG	Desquamative Gingivitis
EBA	Epidermolysis Bulosa Acquisita
FDI	International Dental Federation
GVHD	Graft versus host disease
KNH	Kenyatta National Hospital
LE	Lupus erythematous
LP	Lichen Planus
MMP	Mucous Membrane Pemphigoid
NUG	Necrotising Ulcerative Gingivitis
OLL	Oral lichenoid lesions
OLP	Oral lichen planus
PD	Probing Depth
PF	Pemphigus Foliaceus
PI	Principal Investigator
PNP	Paraneoplastic Pemphigus
PV	Pemphigus Vulgaris

ABSTRACT

Background: Desquamative gingivitis (DG) is a clinical presentation on the gingiva that has been associated with various systemic diseases. An erythematous, ulcerative or a combination of clinical features is noted. This may be limited to the marginal gingiva, extend to the attached gingiva or affect other parts of the oral mucosa. Pain and discomfort from this condition may interfere with practise of oral hygiene thus presenting a long term risk of loss of attachment. The oral related quality of life is affected. Autoimmune bullous dermatoses (ABDs) have especially been associated with DG. ABDs are a group of mucocutenous diseases with a common pathogenic pathway that manifest with vesiculobullous skin eruptions. They include the pemphigus and pemphigoid group of diseases. Although studies in other geographical locations have shown the association between ABDs and DG, no studies have been carried out in Kenya to assess disease association if any.

Objectives: To investigate the occurrence of DG amongst patients with ABDs at the Kenyatta National Hospital.

Study design: A hospital based descriptive cross-sectional study.

Study area: The dermatology outpatient clinic and inpatient ward at the Kenyatta national hospital.

Study population: Patients diagnosed with one of the following ABDs; Pemphigus Vulgaris, Pemphigus Foliaceus, Bullous Pemphigoid and Lichen Planus.

Methods: A total of 94 patients with ABDs of interest were screened, 73 of them met the inclusion criteria. Socio-demographic data were collected by patient interview. The diagnosis of ABDs and type of medication used was recorded from the patients file. DG was diagnosed by clinical examination and the pattern recorded as the type of clinical presentation and anatomic location. The modified Quigley and Hein index was used to assess the oral hygiene. Data was entered, coded and analysed using SPSS 17.0. Relationship between variables was analysed using the chi square.

Results: A total of 73 participants were recruited in the study. 24 (32.9%) were male whereas 49 (67.1%) female. They ranged in age from 12 to 80 years. 47 (64.4%) of them had PV while 7 (9.6%), 10 (13.7%) and 9 (12.3%) had PF, LP and BP respectively. A total of 50 (68.4%) of the participants were on medication with 29 (39.7%) of them taking Prednisone

while 8(13.8%) were on a combined prednisone and Dapsone. 15 (20.55%) of those who participated had DG. 14 (93.9%) of the patients with DG were female and this was statistically significant (x^2 = 5.877 p < 0.05). 13 (86.7%) had extension of DG to the attached gingiva and only 3 (20%) had involvement of other parts of the oral mucosa. The prevalence of DG among the different types of ABDs however was not significant (X^2 = 3.838, p > 0.05).

Conclusion: The prevalence of DG among patients with ABDs was found to be 20.55%. The female gender was significantly more affected with 93.3% of them having DG. Patients suffering from LP had the highest prevalence of DG at 40% in this population. There was no statistically significant relationship between DG and the type of ABDs .A statistically significant number of patients on combined Prednisone and Dapsone appear to have a higher prevalence of DG 53.3% (X^2 = 5.047, p < 0.05) than those on single Prednisone therapy.

Recommendations: Periodontal care is necessary for patients with ABDs due to the high prevalence of DG. A management approach that includes dermatologists and dentists may be necessary. A long term longitudinal study utilizing histological and direct immunofluorescence techniques for the diagnosis of DG is needed and will better establish the associations among the diseases studied.

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Desquamative gingivitis (DG) is a clinical descriptive term that describes a gingival condition characterized by epithelial desquamation, erythema, ulceration and/or the presence of vesiculobullous lesions of the gingiva and other oral tissues. It is not a specific diagnosis but rather a sign of underlying disease. It's characterized by intense erythema or ulceration. Patients may present with pain, dysphagia and peeling of the mucosa1. DG is unrelated to but aggravated by local factors like plaque[2] hence the need to clearly distinguish it from plaque induced gingivitis.

Several diseases have been associated with DG. They include lichen Planus (LP), bullous pemphigoid (BP), pemphigus vulgaris (PV), oral lichenoid lesions (OLL), mucous membrane pemphigoid (MMP), erythema multiforme (EM), graft versus host disease (GVHD), lupus erythematous (LE), Para neoplastic pemphigus (PNP), epidermolysis bullosa acquisita (EBA), linear immunoglobulin A (IgA) disease (LAD), chronic ulcerative stomatitis, plasma cell gingivitis, dermatitis herpetiformis, foreign body gingivitis and psoriasis. Among these diseases the autoimmune bullous dermatoses have shown a higher frequency of associations than most[3]. Patients with DG have worse periodontal status compared to healthy controls due to differences in plaque[4] as well as a poor oral health related quality of life.

Autoimmune Bullous Dermatoses (ABDs) are a spectrum of dermatological conditions characterised by vesiculobullous skin lesions and a common pathogenic pathway[5]. The pathogenesis of these conditions is sensitivity to self-antigens. There are two main categories of these disorders based on the anatomical layer of the skin involved. The first category includes the intraepithelial group which may be referred to as "pemphigus" and includes; Pemphigus Foliaceus (PF), PV, Immunoglobulin A (IgA) pemphigus and PNP. This group is generally characterised by sensitivity to antigens located on the desmosomes between keratinocytes found in the epithelium. Hence microscopically, these diseases present with intraepithelial clefting and tend to heal without scar formation. The second category consists of the sub-epithelial diseases that generally constitute sensitivity to self-antigens found at the basement membrane, that is, the dermo-epidermal junction. This category is generally referred to as "pemphigoid" and includes Bullous pemphigoid (BP), Pemphigoid gestationis

(PG), Linear IgA bullous dermatoses, EBA, Bullous lupus erythematosus (BLE), Cicatricial pemphigoid (CP) and LP[6]. A prevalence of 11.8% of DG among patients with ABDs has been found in a Greek population[7] whereas up to 88% of patients with DG have been shown to have one form or another of ABDs among the Northern Europeans[3].

The aim of this study, therefore, was to investigate the occurrence of DG among patients with ABDs at the Kenyatta National Hospital (KNH). The information from this study could be used by clinicians and policy makers to improve on the management of DG in patients with ABDs.

1.2 Literature review

1.2.1 Historical background of Desquamative gingivitis

The term DG was coined by Prinz in 1932 to describe a peculiar condition characterized by intense erythema, desquamation and ulceration of the free gingival margin and extending to the attached gingiva[8]. In 1960 McCarthy and colleagues suggested that DG was not a specific entity but a gingival response associated with a variety of conditions[9]. This was further concluded by Glickman and colleagues in 1964[10]. Belding in 1968 proposed a mechanism whereby hormones influence DG[11] but this has largely been discounted.

1.2.2 Epidemiology of Desquamative gingivitis

Markopoulos while studying a Greek population in 1996 found 11.8% of patients with autoimmune bullous dermatoses had DG in varying clinical presentations[7]. An evaluation of 125 patients found that 88% of patients with DG had one form of an ABDs[3]. In a cohort of 187 patients diagnosed with DG, 70.5% of them were found to have had oral lichen planus (OLP), 14% with MMP while 13% had PV. Other studies have shown 88%[12] to 98%[13] of DG to have been due to one form or another of an ABDs. This varying prevalence can be explained by the different spectrum of ABDs in different studies and population variations. The methods used to diagnose DG, that is, clinical examination or histopathological techniques may also influence this variation.

1.2.3 Pathogenesis of Desquamative gingivitis

The pathogenesis of DG closely resembles the underlying systemic disorder. Intraepithelial lesions generally associated with the "pemphigus" diseases whereas sub-epithelial lesions are associated with the "pemphigoid" diseases. Antibodies produced against self-antigens like Desmoglein 3, BP 180 and other intraepithelial and basement membrane proteins constitute the main mechanism[14]. Irrespective of the underlying mechanism the clinical presentation is somewhat similar. Figure 1 shows the major proteins responsible for epithelial integrity that may be targeted by antibodies[15].
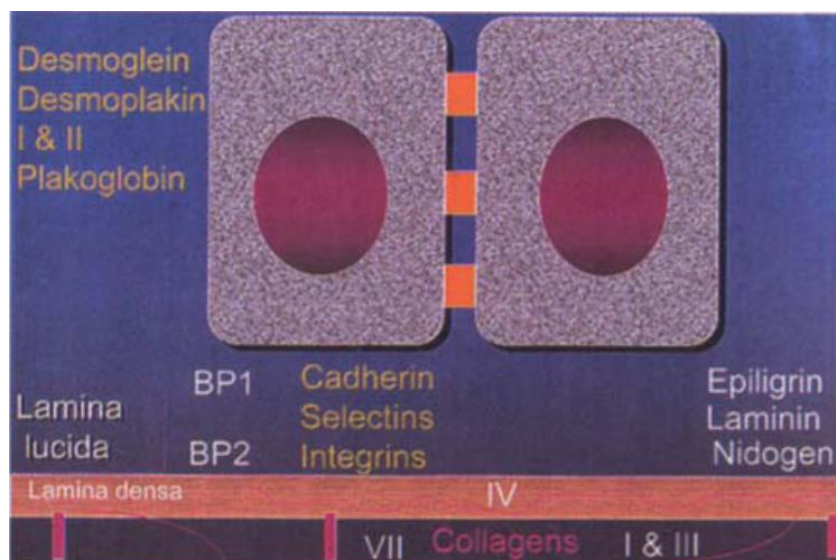
Figure 1: Major proteins responsible for epithelial integrity[15]

1.2.4 Clinical presentation and diagnosis of Desquamative gingivitis

Oral clinical features of DG may include areas of erythema and erosion to ulceration. Intact vesicles and bullae may also be found[16]. Soreness and pain associated with blistering have also been described[2]. Incisional biopsy that includes the lesion and peri-lesional tissues for histology and immunofluorescence (IF) is the recommended way to make a diagnosis. The diagnosis arrived at should also point at the underlying condition[3]. Using 239 consecutive archival cases of gingival biopsy with a clinical diagnosis of DG Suresh and others (2012) concluded that the definitive diagnosis of DG was most accurately achieved when Hematoxylin and Eosin stain (H&E stain) along with two biopsies for direct IF studies were submitted for testing[17].

1.2.5 Effect of DG on periodontal status and oral health related quality of life

Studies on the periodontal status of patients with LP[18], MMP[19] and PV[4] have not shown any evidence that DG can cause loss of attachment and alveolar bone destruction. However, the wide range of oral and gingival symptoms associated with DG can significantly compromise a patient's ability to maintain good oral hygiene. This presents a potential risk factor for long-term periodontal health[20]. In a pilot study of 12 patients Lo Russo et al (2010) have shown a significant difference when comparing the clinical parameters of probing depth and attachment loss between DG affected sites and those not affected[21]. In a study of 29 patients using the Community Periodontal Index of Treatment Needs (CPTIN) it was shown that

periodontal status is worse in PV patients. The authors further concluded that PV might contribute to the development and / or progression of periodontitis[22]. Improvement of the mean score for oral health related quality of life has been demonstrated in a case report[23]. In this case Saito et al (2009) demonstrated improved oral health related quality of life after management of a 77 year old patient diagnosed with DG.

1.2.6 Treatment of Desquamative gingivitis

The most widely used therapy for DG is corticosteroids which can be used topically or systemically[8] Scully and Laskaris (1998) have suggested guidelines for the management of DG including improving the oral hygiene; minimizing irritation of the lesions, using specific therapies for the underlying disease where available, and often suppressing the inflammatory reaction with local or systemic immunosuppressants, notably corticosteroids[15].

1.2.7 Systemic conditions associated with DG

A number of systemic conditions have been associated with DG. These include LP, BP, PV, oral lichenoid lesions (OLL), MMP, erythema multiforme (EM), graft versus host disease (GVHD), LE, PNP, EBA, LAD, chronic ulcerative stomatitis, plasma cell gingivitis, dermatitis herpetiformis, foreign body gingivitis and psoriasis[3] . Among these the ABD group is well studied and characterised.

1.2.8 Autoimmune Bullous Dermatoses

Autoimmune Bullous Dermatoses have been reported worldwide although the prevalence varies in different populations. By far, the intraepithelial group is far more common accounting for 63.7% of cases in a Hong Kong study[24], 70% of the cases in an American study[25] and 68% of the cases in a United Kingdom study[26]. Within the pemphigus group, PV accounts for most of the cases. The pemphigoid group has a lower prevalence across different populations[27]. ABDs have a variety of mucocutaneous manifestations as well as oral leasions[28].

The American Academy of Periodontology (AAP) is of the position that the oral mucosa may be affected by a variety of mucocutaneous diseases. These erosive gingival lesions associated with vesiculobullous diseases such as lichen planus, bullous pemphigoid, and pemphigus vulgaris have been collectively referred to as Desquamative gingivitis[29].

CHAPTER TWO

2.0 STATEMENT OF THE RESEARCH PROBLEM, STUDY JUSTIFICATION AND OBJECTIVES

2.1 Statement of the Research Problem

Desquamative gingivitis is a painful oral condition that may reduce oral health related quality of life as well as increase plaque accumulation through interference with oral hygiene practice. This plaque accumulation may lead to a long-term increased risk of plaque induced periodontal diseases. Identification of systemic conditions related to DG is of importance to clinicians in the management of this condition. While DG is associated with ABDs the frequency, gender distribution modifying factors and exact pathogenesis of this association remains unknown.

2.2 Study justification

There is scanty information on DG among patients with ABDs in Kenya and indeed Africa. DG being a relatively rare condition and one that cuts across different specialisations of healthcare has received very little attention. Studies in other set ups have shown a relationship between ABDs and DG. However this relationship if any has not been studied in our setup. This lack of even basic data on DG means that policy and protocols cannot be formulated on the management of such patients. This study, therefore, was aimed at studying the relationship, if any, between DG and ABDs at the Kenyatta National Hospital. The findings and conclusions from this study could be used by clinicians and policy makers to improve on the management of DG in patients with ABDs. These findings could also be used to sensitize medical practitioners in the identification of the condition for better management.

2.3 Objectives.

2.3.1 Broad objective

The broad objective of this study was to investigate the occurrence of DG amongst patients with ABDs at the Kenyatta National Hospital.

2.3.2 Specific objectives

The following specific objectives were developed for this study:

1. To determine the types of ABDs amongst patients at the KNH

2. To determine the prevalence of DG amongst patients with ABDs at the KNH

3. To determine the pattern of DG in patients with ABDs at the KNH

4. To determine if there is any association between DG and the type of ABDs amongst patients with ABDs at the KNH.

2.4 Hypothesis

2.4.1 Null hypothesis
There is no relationship between DG and the type of ABDs amongst patients with ABDs at the KNH

2.4.2 Alternate Hypothesis
There is a relationship between DG and type of ABDs amongst patients with ABDs at the KNH

2.5 Variables

Table 1: Study Variables

VARIABLE	MEASUREMENT
SOCIO-DEMOGRAPHIC	
Age	Number of years
Sex	Male or female
INDEPENDENT	

Autoimmune Bullous dermatoses:	Type of ABD;
	    a) Lichen Planus,
	    b) Pemphigus Vulgaris
	    c) pemphigus Foliaceus
	    d) Bullous Pemphigoid

DEPENDENT	

Desquamative gingivitis	1. Presence or absence.
	2. Clinical presentation;
	    a) Erythematous
	    b) Ulcerative
	    c) Mixed
	3. Anatomical location;
	    a) Marginal gingiva
	    b) Attached gingiva
	    c) Other part of oral mucosa

CONFOUNDER	
Oral hygiene	Plaque score

CHAPTER THREE

3.0 MATERIAL AND METHODS

3.1 Study area

The study was carried out in the dermatology outpatient clinic as well as the dermatology ward at the Kenyatta National Hospital (KNH). KNH is the country's largest referral hospital located in the capital city, Nairobi. Though situated in a metropolitan city, it serves both urban and rural populations from most of the surrounding and far flung counties in Kenya as well as the east and central African region. It also serves a large spectre of socio-economically endowed patients. The dermatological service at the KNH consists of the outpatient clinic run twice weekly and the ward. Patients are attended to by both consultants and registers'/postgraduate students in internal medicine.

3.2 Study Design

The current study was a descriptive cross-sectional hospital based study. The participants in this study were each examined once except those who participated in calibration. Information gathered was then recorded in a clinical form and later coded and analysed.

3.3 Study population

The study population consisted of patients diagnosed with one of the following ABDs; pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid and lichen planus attending either the dermatology outpatient clinic or ward at the KNH during the study period, that is, from February to April 2013. The spectrum of ABDs in this study was chosen to represent the pemphigus group; PV and PF and the pemphigoid group LP and BP. The laboratory facilities and expertise at the KNH enable complete and full diagnosis of these conditions.

3.4 Sampling

3.4.1 Sample size determination

The prevalence of DG among patients with ABDs has been reported to be 11.8% by Markopoulos (1996) in a Greek population[7]. Using Fischers formula for prevalence in cross sectional studies enumerated below for sample size of more than 10000

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n = sample size,

Z = statistic for a level of confidence i.e. 1.96 for 95% confidence

P = expected prevalence or proportion of patients with ABDs with DG

d = precision of 5%

The minimum sample size calculated is:

n = $\dfrac{1.96^2 \text{ X } 0.118 (1 - 0.118)}{0.05 \text{ X } 0.05}$

= 160

 The number of patients with ABDs seen in KNH within twelve weeks is below 10000, the formula below for a population below 10,000 is used

nf = $\dfrac{n}{1 + n/N}$

Where: N is expected population

nf is sample size in a finite population

nf = $\dfrac{160}{1 + 160/120}$ = 69

The minimum calculated sample size for this study was 69

3.4.2 Sample selection

Convenient sampling was used where all the patients attending the dermatology outpatient clinic or currently admitted in the ward who fit the inclusion criteria were recruited. Patients with a chart diagnosis of an ABDs specifically, PV, LP, PF or BP had their information collected and ascertained using a checklist. Then the patients were briefed about the study

and their consent sought. Thereafter, further interview and examination of the patients who agreed to participate was conducted. All patients with the aforementioned conditions and fulfilled the study inclusion criteria had an equal chance of participating in the study so long as they attended the dermatology outpatient clinic or inpatient ward during the study period.

3.4.3 Inclusion criteria

All patients with the ABDs of interest whose information had been ascertained by a checklist had to fulfil the following criteria to participate in the study

1.   A confirmed chart diagnosis of an ABDs of interest.

2.   A written and signed consent to participate in the study.

3.   Individuals below 18 years of age who assented to the study and whose parents or authorised guardians consented to the study.

3.4.4 Exclusion criteria

Patients with a diagnosis of an ABDs of interest were excluded under the following conditions

1.   Patients who had undergone sulphonamide therapy in the past three months because this class of drugs is associated with mucosal changes that make it difficult to diagnose DG.

2.   Patients with a history of radiotherapy due to the presence of radiation mucositis that will make it difficult to diagnose DG.

3.   Patients using partial denture prostheses

4.   Patients who had undergone periodontal therapy in the past six months

3.4.5   Participant recruitment

During the period of this study 94 patients with one of the following ABDs; PV, PF, BP and LP attended the dermatology outpatient clinic and ward at the KNH and were screened. Out of these 94 patients 21 were excluded while 73 qualified for inclusion according to the criteria set. Figure 2 shows different reasons for exclusion of the participants who fell within the sample. Figure 3 and 4 are examples of the cutaneous appearance of patients recruited in the study.
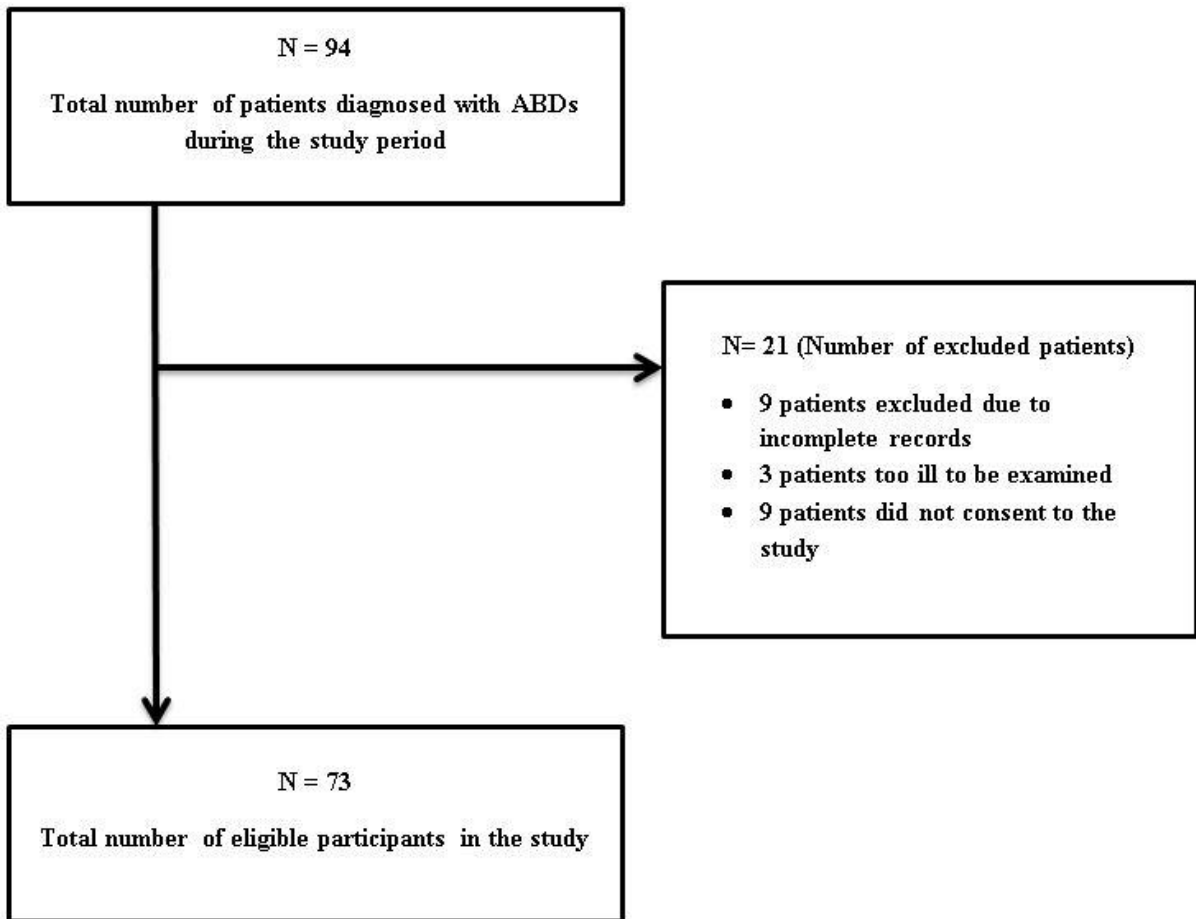
Figure 2: Participants recruitment consort diagram

Figure 3: Pemphigus Foliaceus, healing lesions on the back.

Figure 4: Pemphigus Vulgaris, affected flexor surfaces of the upper limb.

3.5 Data Collection Instruments and Techniques

Data was collected using various tools and techniques described as follows:

3.5.1 Data collection tools

A clinical examination form (Appendix I) was developed and used to record socio-demographic data, the participants' diagnosis, the presence or absence of DG and the plaque score. The plaque score was assessed using the Quigley Hein Index - (Modified by Turesky et al, 1970) index (Appendix II). A disclosing tablet (Produits dentaires Vevey, Switzerland) was used to improve plaque visibility.

3.5.2 Preliminary phase

A preliminary visit was made to the selected study site, which is the dermatology outpatient clinic and inpatient ward at the KNH in order to work out logistics and to familiarise with the staff, rules and procedures.

3.5.3 Calibration

Data collection was done by the Principal investigator (PI) who was calibrated by one of the supervisors (a Periodontologist); Kappa values were calculated for plaque score (0.9) showing an almost perfect agreement. For intra-examiner variability, repeated examinations of every tenth patient to adjust for intra - examiner errors was done

3.5.4 Actual data collection phase

Socio-Demographic data on age and gender were collected through patient interview by the PI.

Clinical examination

The recruited patients were examined in a designated examination room in the outpatient clinic and in the procedure room in the wards while lying supine on an examination couch. The examination was done under natural light. Sterile Hu- Friedy (Marquis) periodontal probes and mouth mirrors were used in the examination. The findings were dictated to an assistant who recorded on the clinical examination form.

Plaque measurement

Plaque levels were assessed using the Turesky modification of plaque index by Quigley and Hein (1970) (appendix II). Disclosing tablets (Produits dentaires Vevey, Switzerland) were used to assess the plaque levels and to increase the sensitivity of detection and visual quantification of plaque. The plaque levels on the buccal and lingual surfaces of the 'Ramfjord' index teeth, that is, 16, 21, 24, 36, 41 and 44 (FDI nomenclature) was assessed and dictated to an assistant for recording in the clinical examination form.

Medication use

The type of medication the patient was on was obtained from the patient files and treatment sheets and recorded in the clinical examination form.

Infection control

Disposable face masks, cups and gloves were used. A set of autoclaved instruments (a periodontal probe and a dental mirror) was used for each patient

3.5.5 Definition of Desquamative gingivitis

The erosive, erythematous or ulcerative gingival lesions associated with vesiculobullous diseases such as lichen planus, mucous membrane pemphigoid, and pemphigus vulgaris have been collectively referred to as Desquamative gingivitis[29]. Figure 5 and 6 below illustrates examples of patients diagnosed with DG

Figure 5: DG, erythematous presentation on the marginal gingiva

Figure 6: DG, ulcerative presentation on the marginal and attached gingiva.

3.6 Data Analysis and Presentation

The data collected were entered into a computer using the Statistical Package for Social Sciences (SPSS version 17.0 SPSS Inc, Chicago, Illinois, USA). Data cleaning was done by checking frequencies and re- entering missing data. Data were analysed using the same SPSS version 17.0. Descriptive and inferential statistics were used. Descriptive statistics were measures of central tendencies and dispersions for continuous variables (age and plaque scores). The Chi-square statistic was used to determine the association between key categorical variables. Significance levels were accepted at p equals to or less than 0.05.   The data were presented in the form of tables and figures.

3.7 Main outcome measures

The main outcome measures among the study populations, that is, patients diagnosed with ABDs and attending the dermatology outpatient clinic and ward during the study period were:

1.   The age and gender of patients.

2.   Type of Autoimmune Bullous Dermatoses.

3.   The types of medications given to these patients.

4.   Frequency of DG among these patients.

5.   Gender and age distribution of DG among these patients.

6.   Pattern of DG (clinical presentation and anatomical location) in this group of patients.

7.   Plaque levels among these group of patients.

3.8 Ethical considerations

Ethical approval was obtained from the Kenyatta National hospital and University of Nairobi Ethics and Research committee (Appendix III), approval number P558/10/2012. Permission for data collection was granted by the head of department dermatology at the KNH. The purpose of the study and expected benefits were clearly explained to the participants.   Only participants who gave an informed written consent were recruited. Voluntary participation, confidentiality and the withdrawal privilege were observed at all times during the study. Only the participants' file numbers were recorded in the data forms to ensure confidentiality. The entire examination was carried out maintaining universal infection control standard precautions, and those requiring dental treatment were referred accordingly.

Study benefits

The patients received free dental check-ups and were informed of their dental health status and advised accordingly. The results obtained from the study will provide baseline data for the development of viable management protocols to help prevent or minimise oral afflictions of patients with ABDs. This study will benefit other researchers in the field of periodontology.

Disclosure

The cost of this study was met by the PI for academic purposes. The instruments used were obtained and sterilised from the School of Dental Sciences University of Nairobi.

CHAPTER FOUR

4.0 RESULTS

4.1 Socio-Demographic characteristics of the participants

Out of the 73 participants with Autoimmune Bullous Dermatoses (ABDs) examined 24 (32.9%) were males and 49 (67.1%) females giving a gender ratio 1:2.04. The participants' ranged in age from 12 to 80 years with a mean age of 45.1 years whereas 38 (52.1%) were in the 40 to 49 age group. Twenty five (34.25%) of the participants were inpatients. Table 2 shows the socio-demographic characteristics of the participants' enrolled in the study.

Table 2: Socio-Demographic characteristics of the participants

Variable		Proportion n (%)
Gender	Male	24 (32.9%)
	Female	49 (67.1%)
Total		**73 (100%)**
Age group	10-19	2 (67.1%)
	20-29	3 (4.1%)
	30-39	11 (15.1%)
	40-49	38 (52.1%)
	50-59	13 (17.8%)
	60-69	4 (5.5%)
	70-79	1 (1.4%)
	80-89	1 (1.4%)
Total		**73 (100%)**

4.2 Autoimmune Bullous Dermatoses

Pemphigus Vulgaris was the most prevalent ABDs with 47 (64.4%) of the participants having been diagnosed with this condition, Pemphigus Foliaceus was diagnosed in 7(9.6%) of the participants hence the least prevalent. Lichen Planus and Bullous Pemphigoid each was diagnosed on 10(13.7%) and 9(12.3%) patients respectively. Figure 7 illustrates the prevalence of different ABDs among the participants.
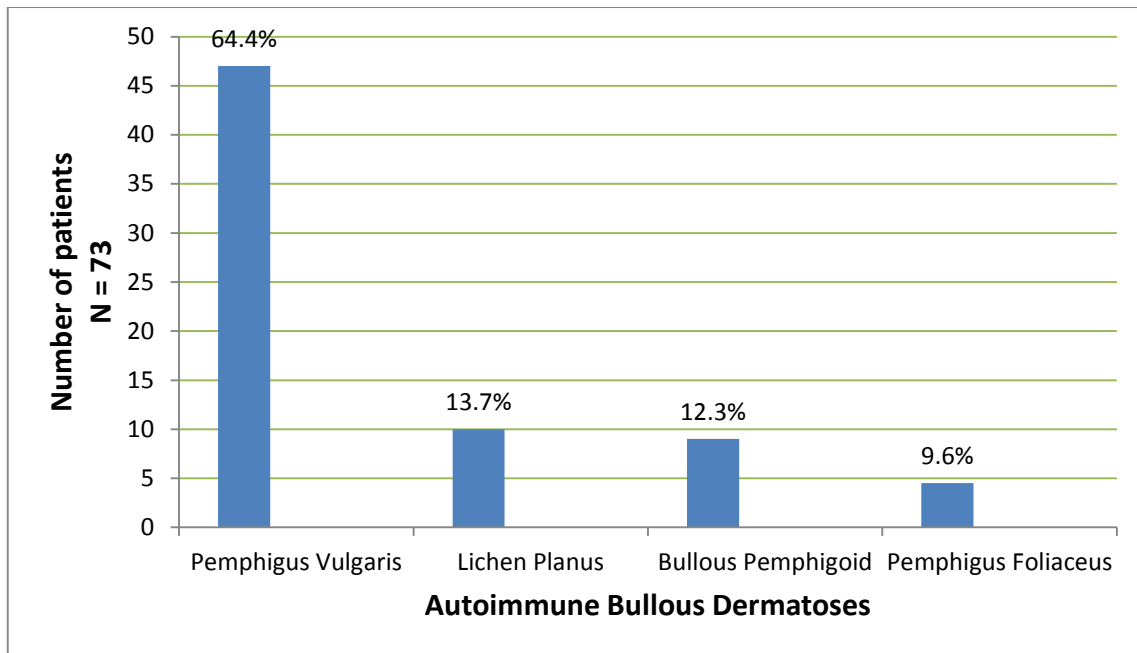
Figure 7: Prevalence of different Autoimmune Bullous Dermatoses

Majority of the patients with ABDs were in the fourth and fifth decades of life as shown in table 3. Twenty one (53.8%) of patients with PV were in the fifth decade of life representing the single largest group of participants within an age group. However the age was not statistically significant among the different ABDs ($X^2 = 5.852$, P > 0.05)

Table 3: Distribution of different types of ABDs in different age groups

Age group (Years)	Bullous pemphigoid n (%)	Pemphigus Vulgaris n (%)	Lichen Planus n (%)	Pemphigus Foliaceus n (%)
10-19	-	2(5.1%)	-	-
20-29	-	2(5.1%)	1(10%)	-
30-39	3(30%)	5(12.8%)	2(20%)	1(7.1%)
40-49	4(40%)	21(53.8%)	6(60%)	7(50%)
50-59	2(20%)	6(15.4%)	1(10%)	4(28.6%)
60-69	1(10%)	2(5.1%)	-	2(14.3%)
70-79	-	-	-	-
80-89	-	1(2.6%)	-	-
Total	**10**	**39**	**10**	**14**

The majority of female 29(59.2%) and male 10 (41.7%) patients had PV. Figure 8 shows the gender distribution of the different ABDs. Among the males 4(16.7%), 2(8.3%) and 8 (33.3%) had BP, LP and PF respectively. Six (12.2%), 8(16.3%) and 6(12.2%) of the females had BP, LP and PF respectively. PF was the only type of ABDs with a higher prevalence in the male gender than the females. There was no statistical significance in the gender distribution of the various ABDs (X^2=5.642, P > 0.05)
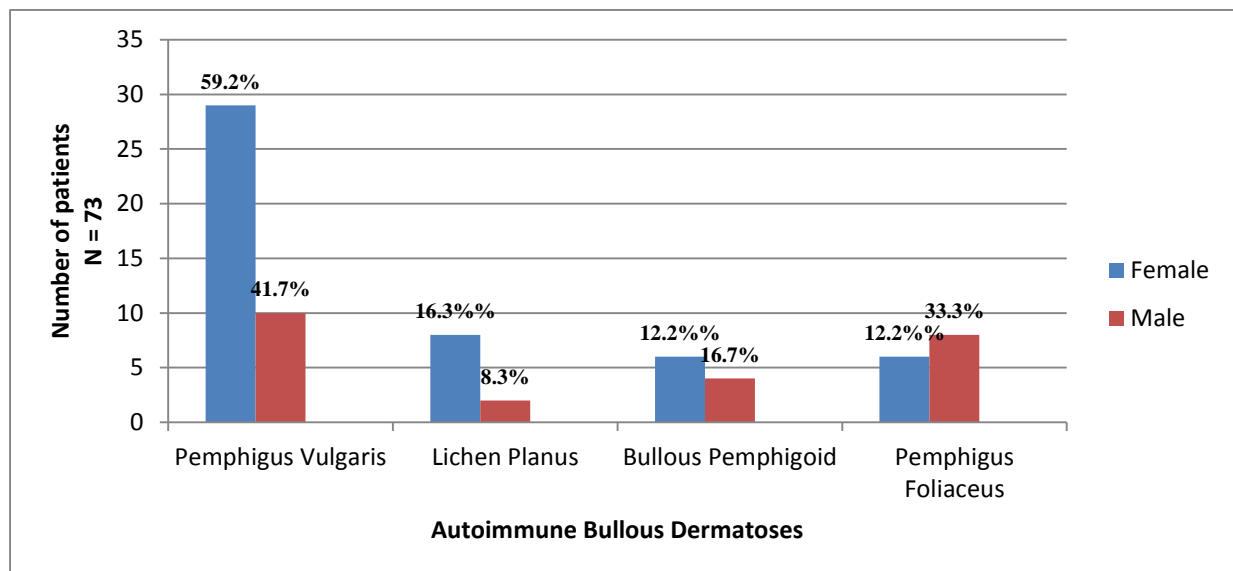
Figure 8: Gender distribution among different autoimmune bullous dermatoses

4.3 Type of medication

Fifty (68.4%) of the study participants were on one or combination therapy for ABDs, among whom the majority 29 (39.7%) were on prednisone therapy. 8 (13.8%) of the patients were on combined prednisone and dapsone, 2 (3.4%) were on hydrocortisone combined with dapsone. None of the patients was on single dapsone therapy.

Table 4: Type of medication taken among the different ABDs

Medication	BP	PV	LP	PF	Total
No medication	4 (30%)	8 (21.1%)	2 (20%)	9 (64.3%)	23(30.6%)
Prednisone	2 (20%)	17(44.7%)	5 (50%)	5 (35.7%)	29(40.3%)
Hydrocortisone	-	3 (7.9%)	-	-	3(4.2%)
Prednisone/dapsone	5 (50%)	9 (23.7%)	2 (20%)	-	16(22.2%)
Hydrocortisone/dapsone	-	1 (2.6%)	1 (10%)	-	2 (2.8%)
Total	10	38		14	73

4.4 Desquamative gingivitis

The prevalence of DG among patients with ABDs was 20.55%, that is, 15 out of the 73 participants were found to have one form or the other DG.

All the participants with DG had involvement of the marginal gingiva. In 13 (86.67%) the condition extended to the attached gingiva while only 3 (20%) had involvement of other parts of the oral mucosa other than the gingiva. Out of the 15 patients diagnosed with DG, 6 (40%) had erythematous clinical presentation, 3 (20%) had the ulcerative presentation whereas 6 (40%) had a mixed clinical presentation.

4.4.1 Desquamative gingivitis and age

Participants with DG ranged in age from 21 to 71 years with a mean age of 43.93 years and standard deviation of 11.81 . However majority, 7 (46.7%) of these participants were in the 40-49 (5th decade) and the 50 to 59 (6th decade) age groups. The third and fourth decade of life had 2 (13.3%) of the patients each whereas the eighth decade had only one participant with DG. None of the participants with DG were in the second, seventh or ninth decade of life. There was no statistical significance in the distribution of DG among the different age groups (X^2 =9.779, P > 0.05). Among the six participants with erythematous DG, a majority 3 (50%) were in the 40 to 49 age group. A majority of the six participants with mixed DG, that is, 3 (50%) were also in the 40 to 49 age group. However the was no statistical significance in the distribution of the different clinical presentation types among the various age groups (X^2 = 4.226, P > 0.05). Table 5 below summarises the distribution of different types of DG among the different age groups.

Table 5: Clinical presentation of DG amongst various age groups.

Age group	Erythematous	Ulcerative	Mixed	Total
20 – 29	1 (16.7)	-	1 (16.7)	**2 (13.3%)**
30 – 39	-	1 (33.3%)	1 (16.7)	**2 (13.3%)**
40 – 49	3 (50%)	1 (33.3%)	3 (50%)	**7 (46.7%)**
50 - 59	1 (16.7)	1 (33.3%)	1 (16.7)	**3 (20%)**
70 - 79	1 (16.7)	-	-	**1 (6.7%)**
Total	**6**	**3**	**6**	**15 (100%)**

4.4.2 Desquamative gingivitis and gender

Fifteen participants were diagnosed with DG, among these 14 (93.9%) were females. This was statistically significant ($X^2 = 5.877$, P < 0.05). Six (42.9%) of the female participants had a mixed clinical presentation of DG, 5 (35.7%) had an erythematous presentation while only 3 (21.4%) had ulcerative presentation. The single male participant with DG had an erythematous clinical presentation. Table 6 summarises the clinical presentation of DG among the male and female participants.

Table 6: Clinical presentation of DG among male and females

Gender	Erythematous n (%)	Ulcerative n (%)	Mixed n (%)	Total N (%)
Male	1 (100%)	-	-	**1 (6.1%)**
Female	5 (35.7%)	3(21.4%)	6 (42.9%)	**14 (93.9%)**
Total	**6**	**3**	**6**	**15 (100%)**

4.4.3 Desquamative Gingivitis and type of medication

Majority 25 (43.1%) of patients without DG were on single therapy Prednisone therapy unlike patients with DG where 8 (53.3%) were on combined Prednisone and Dapsone therapy. This was statistically significant ($X^2 = 5.047$, P < 0.05). Table 7 shows a summary of the type of medication in presence or absence of DG.

Table 7: Type of medication and presence of Desquamative gingivitis

Medication	DG present	DG absent	Total
No medication	3 (20%)	20 (34.5%)	**23 (31.5%)**
Prednisone	4 (26.7%)	25 (43.1%)	**29 (39.7%)**
Hydrocortisone	-	3 (5.2%)	**3 (4.1%)**
Prednisone and Dapsone	8 (53.3%)	8 (13.8%)	**16 (21.9%)**
Hydrocortisone and Dapsone	-	2 (3.4%)	**2 (2.7%)**
Total	**15**	**58**	**73**

4.4.4 Desquamative gingivitis and plaque score

The mean plaque score among patients with DG was found to be 3.00 while that of patients without DG was 2.48. This was statistically significant ($X^2 = 4.357$, $p < 0.05$). Table 8 shows the mean plaque score and presence or absence of DG.

The mean plaque score of patients with a clinical presentation of erythematous DG was 2.96, ulcerative 3.11 and that of mixed clinical presentation was 2.98. This was found not to have been statistically significant. Figure 10 illustrates the mean plaque levels in patients with various clinical presentations of DG.
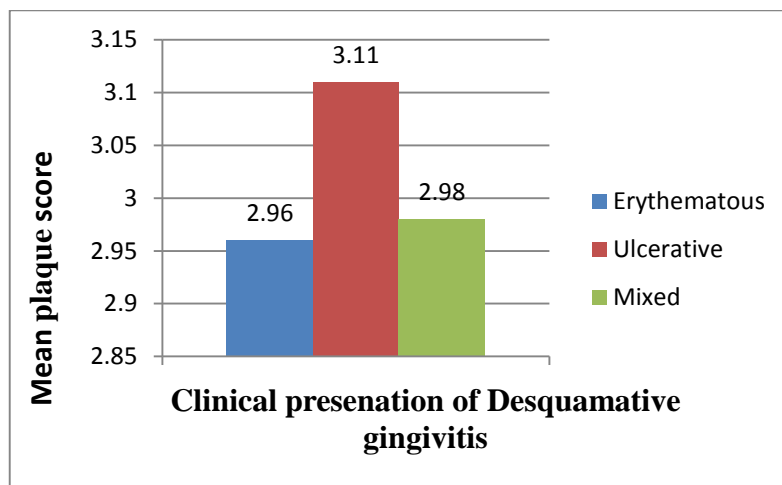
Figure 9: Mean plaque score and clinical presentation of DG

4.4.5 Desquamative gingivitis and type of autoimmune bullous dermatoses

The highest prevalence of DG was found among patients with LP 4 (40%); patients with a diagnosis of PF had the lowest occurrence of DG 2 (14.3%). The prevalence of DG in BP and PV was 30% and 15.4% respectively. The prevalence of DG in the different types of ABDs however was not statistically significant ($X^2 = 3.838$, $P > 0.05$). Table 9 shows the type of ABDs and presence or absence of DG.

Table 8: Type of ABDs and presence or absence of DG

ABDs	DG Present	DG Absent	Total
Lichen planus	4 (40%)	6 (60%)	**10**
Bullous Pemphigoid	3 (30%)	7 (70%)	**10**
Pemphigus Vulgaris	6 (15.4%)	33 (84.6%)	**39**
Pemphigus Foliaceus	2 (14.3%)	12 (85.7%)	**14**
Total	**15**	**58**	**73**

CHAPTER FIVE

5.0 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Socio-Demographic characteristics of the study population

Significantly more women (67.1%) than men participated in the study. This unequal gender ratio (male to female 1: 2.04) could be a reflection of the higher prevalence of Autoimmune Bullous Dermatoses (ABDs) among the female gender. A female preponderance to ABDs with a ratio of 2:1 has been demonstrated before[30, 31]. Therefore the current study compares well despite the population differences. Several reasons have been proposed to explain this gender disparity, however hormonal influence has received more attention[32]. It is possible that in the current study the health seeking behaviour of women influenced this outcome in that females are more likely to seek medical attention compared to their male counterparts. In this study most of the participants were in the 40 to 49 year age group (52.1%). This is in contrast to Markopoulous (1996) who showed that most of the participants were in the 60 to 69 age group in a Greek population[7]. This difference can be explained by the different population hence different racial and genetic characteristics[5]. Furthermore the spectrum of ABDs studied by Markopoulos (1996) although having been almost similar to the current study did not include patients with PF.

5.1.2 Autoimmune bullous dermatoses

This study found out that 64.4% of the participants had a diagnosis of pemphigus vulgaris making it the most prevalent among the ABDs studied. This differs with other studies [33, 34] mostly done in Western Europe that show BP predominated. A study among 112 patients with various forms of pemphigus in South Africa found that 80% of the black patients had PF. That study concluded that among people of black origin, PF is the most prevalent form of pemphigus whereas amongst people of Asian origin PV was the most prevalent [35]. However in a study involving a total of 1402 patients diagnosed with ABDs over a 10 year period in Iran[36], PV was the most common ABDs (81.2%), followed by bullous pemphigoid (BP) (11.6%). This difference in prevalence of different types of ABDs is explained both by racial and genetic variations in the study populations[37].

5.1.3 Desquamative gingivitis

In the current study, 20.5% of the patients with ABDs had DG. This differs from the 11.8% reported previously[7]. This could be explained by the racial and genetic differences given that the present study was conducted among Africans whereas the previous study was conducted among people of Greek origin. Further only three ABDs were studied by Markoupoulos et al (1996), that is, BP, PV and LP. The current study looked at PF in addition to the aforementioned. Other studies have found prevalence as high as 88% and 98% [12, 13]. However these studies used different spectra of ABDs. Lo Russo (2009) found that 88% of patients with DG had one form or another of ABDs [3]. This study by Lo Russo (2009) differs from the current study in that the population studied was that of persons presenting with DG, the current study used a population of participants diagnosed with ABDs of interest and then assessed the presentation of DG in them.

5.1.4 Desquamative gingivitis and gender

This study found out that 93.3% of the participants diagnosed with DG were female, a statistically significant finding ($X^2 = 5.877$, $p < 0.05$). In a study of 125 patients over three years it was found that 84% were female [3]. In a cohort of 187 patients diagnosed with DG 67.4% were female [2]. The current study is similar in the sense that it shows a high female preponderance, however the prevalence was much higher than previously published. This could be explained by the obvious difference in the population studied. It was also noted that ABDs are more common in the female gender hence one expects a higher proportion of the affected to be female.

5.1.5 Pattern of Desquamative gingivitis

In the current study 40% of the participants with DG had the erythematous clinical presentation, 20% ulcerative and 40% had a mixed clinical presentation. While studying a cohort of 187 patients Leao et al (2008) found that only 5% had ulceration with 92% having erythema [2]. This variation to the current study can be explained by the methodology given that Leao and colleagues assessed their participants retrospectively, that is, they used records of patients they had treated before and had been followed up. The current study being cross sectional only looked at participants at one point in time.

The Leao (2008) study showed that 72% of patients had localised DG while 28% had generalised DG, however the current study did not collect data on disease distribution rather anatomical location of the lesions was assessed. The current study has demonstrated that all

participants diagnosed with DG had the marginal gingiva affected. In 86.6% of the patients the lesions extended to the attached gingiva whereas only in 20% was there extension to other oral sites other than the gingiva. Other studies have shown that only 22% of the patients had the condition affecting the gingiva only, with 78% of the patients having areas other than the gingiva affected [3]. This wide variation is explained by the choice of ABDs studied by Lo Russo et al which included Oral lichen planus which has a particular predilection for the oral cavity [14]. Leao et al (2008) found 20.4% had involvement of other sites other than the gingiva a finding that is similar to the current study [2].

Different studies have assessed the pattern, that is, clinical presentation, anatomical location, distribution and severity of DG differently this makes difficult to make direct comparisons [38]. However the current study only looked at the clinical presentation and anatomical location. Severity was not assessed due to lack of an appropriate index that is reproducible and familiar to the principal investigator. Further the study populations consisted of patients at different stages of treatment of the ABDs such that an assessment of severity would have been futile.

5.1.6 Desquamative gingivitis and medication type

This study has demonstrated a statistically significant relationship between the type of medication when compared to presence and absence of Desquamative gingivitis ($X^2 = 5.047$, $P < 0.05$). It appears that patients with DG would mostly have been taking a combined therapy of Prednisone and Dapsone (53.3%) compared to patients without DG for whom 43.1% were on Prednisone mono-therapy. Given that in the current study an assessment of the severity of ABDs was not carried out due to the varying stages of ABDs management and lack of an appropriate index. The explanation for this difference can only be speculative. It therefore appears that either the combination therapy is given to patients with severe ABDs who have oral symptoms or Dapsone may have properties that induced DG.

5.1.7 Desquamative gingivitis and plaque score

There was a statistically significant difference in the mean plaque score among patients with DG (3.00) and those without DG (2.48) ($X^2 = 4.357$, $p < 0.05$). However, there was no statistically significant difference in the mean plaque scores among the different clinical presentation of DG. Various authors have pointed out that DG may lead to accumulation of plaque due to interference with oral hygiene practise [4, 18, 19, 20, 22]. This may, in turn be an independent risk factor for periodontal destruction. However given the current study was cross sectional the relationship between DG and plaque cannot be fully examined to ascertain

which of the two variables came first. A longitudinal study design with baseline plaque scores and follows up of such a group of patients over a period of time would be best placed to address this matter.

5.1.8 Desquamative gingivitis and type of autoimmune bullous dermatoses

In the current study the highest prevalence of DG, 40% was found among patients with LP, whereas PF had the lowest prevalence of DG at 14.3%. Indeed the pemphigoid class of ABDs studied, including LP and BP showed a higher prevalence of DG, that is, 40% and 30% respectively than the pemphigus class of ABDs constituting, PV and PF that had 15.4% and 14.3% respectively. This general trend of higher prevalence in the pemphigoid group has been observed before [2, 3, and 15]. Despite this general trend, the prevalence of DG in patients with LP was found to have been 75% in an Italian population[3] and 70.5% in a Northern European population [2]. This higher prevalence in these studies compared to the current one can be attributed to the fact that these studies used Oral lichen planus, a particular variant of LP that has a higher incidence of oral symptoms [14]. This study however did not find a statistically significant relationship between the presence of DG and the type of ABDs (X^2 = 3.838, p > 0.05) and therefore failed to reject the null hypothesis.

In a study that used an almost similar spectrum of ABDs as the current study, Markopoulos (1996) showed that the prevalence of DG was 41.6% in patients with BP and 9.1% in patients with PV. These findings although different are closer to those of the current study, that is, 30% and 15.4% respectively. This difference can be explained by use of different methodology in diagnosis of DG. Whereas this study used clinical characteristics to diagnose DG, Markopoulos et al used clinical characteristics, as well as histopathologic and immunohistochemical methods. This increases the sensitivity of diagnosis. Racial differences in the studied populations could also contribute to this.

5.2 Conclusion

Based on the findings of this study, it was concluded that:

1. There was no relationship between DG and the type of ABDs.
2. The prevalence of DG among patients with ABDs is 20.55%.
3. The female gender is significantly more affected with 93.3% of them having DG.
4. Patients suffering from LP have the highest prevalence of DG at 40% in this population.

5. The mean plaque score is higher in patients with DG (3.00) than patients without (2.48).

6. Pemphigus Vulgaris is the most prevalent form of ABDs in the population under study affecting 64.4% of the participants.

7. A statistically significant number of patients on combined Prednisone and Dapsone appear to have a higher prevalence of DG (53.3%) than those on prednisone single therapy.

5.3 Limitations

The diagnosis of DG might have been slightly overestimated given that this study used only clinical parameters to arrive at a diagnosis of DG rather than histological or direct immunofluorescence techniques.

The duration in which the participants had Desquamative gingivitis could not be established so that it was difficult to assess the effect of medication and time on the presentation.

5.4 Recommendations

Based on the findings of this study and within its limits the following is recommended:

1. Periodontal care is necessary for patients with ABDs due to the high prevalence of DG.

2. A management protocol that includes dermatologists and dentists may be necessary.

3. A long term longitudinal study utilizing histological and direct immunofluorescence techniques could better establish the associations between ABDs and DG.

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APPENDIX I CLINICAL EXAMINATION FORM

CLINICAL EXAMINATION FORM

Form Number _____ Checklist Number _____

1. Age………………………………………………………………….

2. Gender   male   ⬛   female   ⬛

3. Medications ……………………………………………………

4. Autoimmune bullous dermatoses ………………...

5. Desquamative gingivitis

a) Presence   yes ⬛   no   ⬛

b) Anatomical location of DG

       Marginal gingiva …………………………………………

       Attached gingiva …………………………………………

       Oral mucosa …………………………………………………

       Diffuse………………………………………………………………

c) Type of DG

      Erythematous ……………Ulcerative ……………..mixed…………….

6. Plaque scores

Tooth	Buccal/lingual	tooth	Buccal/lingual	tooth	Buccal/lingual
16		11		26	
46		31		36	

Total………………………… Average……………………………………

APPENDIX II INDICES

Quigley Hein Index - (Modified by Turesky et al, 1970). The Plaque Index System as scored after use of disclosing tablet.

Scores	Criteria
0	No plaque
1	Separate flecks of plaque at the cervical margin of the tooth.
2	A thin continuous band of plaque (up to one mm) at the cervical margin of the tooth.
3	A band of plaque wider than one mm but covering less than one-third of the crown of the tooth.
4	Plaque covering at least one-third but less than two-thirds of the crown of the tooth.
5	Plaque covering two-thirds or more of the crown of the tooth

APPENDIX III ETHICAL APPROVAL LETTER

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21st February 2013

Dr. Alumera Hudson
Dept. of Periodontology/Community and Preventive Dentistry
School of Dental Sciences
University of Nairobi

Dear Dr. Alumera

RESEARCH PROPOSAL: DESQUAMATIVE GINGIVITIS AMONG PATIENTS WITH AUTOIMMUNE BULLOUS DERMATOSES AT THE KENYATTA NATIONALHOSPITAL (P558/10/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above revised proposal. The approval periods are 21st February 2013 to 20th February 2014.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN**

Yours sincerely

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

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