A descriptive analysis of oral lichen planus from tertiary diagnostic centres in the Western Cape.

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Abstract

Epidemiological studies on *oral lichen planus* are few. Those that have been conducted have been in developed nations such as North America and Europe as well as Asia and the Middle East. Few African studies report on the demographics of the affected patients. This study reported on the demographics of patients who had been diagnosed with *oral lichen planus* in a subset of the South African population, within the Western Cape, with an emphasis of the ethnic origin of the affected patients.

The study aimed to analyse cases of *oral lichen planus* with regard to patient ethnicity, age, sex and the intra-oral location of lesions from archival pathology reports of confirmed cases of *oral lichen planus*, as diagnosed at tertiary diagnostic centres within the Western Cape. A retrospective descriptive analysis of all confirmed diagnoses of *oral lichen planus* from archived oral pathology reports was conducted. The inclusion criteria were determined by the histological diagnosis as outlined by Eisenberg, 2000 and Sugerman *et al*, (2002). Two hundred and forty-nine confirmed cases met the inclusion criteria and data recorded from those oral pathology reports included the ethnic origin of the patient, gender, age and the intra-oral location of the lesion. The occurrence rate in African individuals was considerably lower than for the other ethnic groups, as only 2 African males were affected, and no African females. The overwhelming majority of patients were White females. The overall female to male ratio was 3:1. The ethnic distribution within this sample was different to the expectation considering the population distribution of both South Africa and the Western Cape. The age distribution of the sample showed that females were older at the age of onset than males. The buccal mucosa was the favoured intra-oral location of *oral lichen planus*, a high percentage (85%) of gingival involvement was evident among the females.

Declaration

I, Anthea Jeftha, declare that the work contained in this research report is my own original work. I have not previously submitted this research report to any university for a degree or examination.

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A Jeftha

_____ Day of _____ of 2009

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Chapter One

Introduction and Literature Review

1.1 Introduction

Lichen planus is a systemic disease that follows a chronic course. The exact aetiology remains unknown but an immune mediated pathogenesis has been implicated. *Oral lichen planus* is a common form of this disease and can occur in isolation or it may include the skin, genitalia and lesions involving the scalp and hair follicles.

Epidemiological studies on *oral lichen planus* are few. Those that have been conducted have been in developed nations such as North America and Europe as well as Asia and the Middle East. Few African studies report on the demographics of the affected patients.

Factors such as patient demographics and trends of diseases are essential to investigate. Findings of such studies may be useful in determining additional patient based criteria that can assist in obtaining a definitive diagnosis and subsequently aid in the management protocols of the specific disease in question. This process is as essential for *oral lichen planus* as for other diseases. *Oral lichen planus* can have clinical similarities with other diseases of the oral mucosa. Similarities can also be seen histologically that may further complicate the process of defining the diagnosis. *Oral lichen planus* may not be commonly associated with frank morbidity, but severe discomfort can be experienced in some clinical variants. This disease has been described as “difficult to manage”

(Camacho-Alonso *et al*, 2007). Furthermore, there is an ongoing debate about its malignant potential (Sugerman & Savage; 2002; Scully and Carrozzo; 2008).
These factors support the relevance of further investigation of *oral lichen planus*.

This study will report the demographics of patients who have been diagnosed with *oral lichen planus* in a subset of the South African population, within the Western Cape. The description of the ethnic groups in South Africa was as described by Statistics South Africa, namely; “African” was used to describe Black individuals, “Coloured” was used to describe individuals of mixed ethnic origin, “Indian” was used to describe patients whose ethnic origin was of the Indian/Asian continent, the latter however excluded persons of Chinese decent and “White” described those persons of European origin. The ethnic distribution reported from within the literature will report on the terminology used by the respective authors and hence not follow the guidelines outlined above.

1.2 Aim

This study aimed to analyse cases of *oral lichen planus* with regard to patient ethnicity, age, sex and the intra-oral location of lesions from archival pathology reports of confirmed cases of *oral lichen planus*, as diagnosed at tertiary diagnostic centres within the Western Cape.

1.3 Objectives

1. To report the ethnic distribution of patients diagnosed with *oral lichen planus*
2. To report the distribution of the affected patients by sex
3. To report the age distribution of the diagnosed patients
4. To report the intra-oral distribution of *oral lichen planus*,

1.4 Literature Review

1.4.1 Literature search

The literature was sought by using keywords such as, “epidemiology + *oral lichen planus”* or “lichen planus” on its own and repeating the search by adding “South Africa” to the keywords. A limit of 10 years on the pubmed central publication was used. No limits were placed on the search for South African studies. Only English studies were reviewed.

1.4.2 Epidemiology

The prevalence of *oral lichen planus* has been reported to be between 0.1 % to 2. 2 % of the general population. These rates are the results of studies conducted in Japan (Ikeda *et al;* 1991), Sweden (Axell & Rundquist; 1987), India and Malaysia (Ismail *et al;* 2007), Saudi Arabia (Salem; 1989) and Yugoslavia (Bokor-Bratik & Picuric; 2001). Dreyer in 1978 reported a prevalence of 0.1% of *oral lichen planus* in a Cape Malay population group. The earlier studies, however, failed to report the definitive histological criteria used to diagnose *oral lichen planus*. The validity of these studies has been questioned and the one by Axell and Rundquist (1987) has been used because it has fewer deficiencies than any other epidemiological study of *oral lichen planus* (McCartan & Healy; 2008)

Oral lichen planus was found to be rare in a Nigerian study which reported the condition as a rarity in black individuals. Two out of 57 patients presented with cutaneous lichen planus and *oral lichen planus* simultaneously (Daramola *et al;* 2003). An earlier American study reported on the ethnic distribution of *oral lichen planus* and found that 94% of the affected patients were White, 5% were Oriental and 1% was Black (Silverman & Lozada-Nur; 1985). In 2006, Ingafou et al reported a British study which found that the majority of the affected patients (68.7%) were Caucasian (White), 15% were of Indian origin and approximately 8% of patients were grouped together as Black, African or Caribbean decent, Chinese or Mediterranean. The ethnic origins of 7.4% of those patients were not recorded. Thirty-three cases of *oral lichen planus* within the Western Cape, South Africa reported that 94% of the patients were Caucasian (Dreyer *et al*; 1982).

A female predilection has been reported (Silverman & Lozada-Nur; 1985; Axell & Rundquist; 1987; Bokor-Bratik & Picuric; 2001; Eisen; 2002; Myers *et al;* 2002; Ingafou *et al;* 2006; Camacho-Alonso *et al;* 2007; Ismail *et al;*

2007; Mignogna *et al;* 2007). The mean age of onset has been determined to be in the fourth and fifth decades of life (Myers *et al;* 2002; Camacho-Alonso *et al;* 2007; Mignogna *et al;* 2007). A Brazilian study determined that *oral lichen planus* is the most common autoimmune disease of the oral mucosa; further findings showed that females were also more commonly affected and most were White patients. (Arisawa *et al;* 2008). These authors failed to clearly report on the ethnic distribution of *oral lichen planus* and offer no definition of any other ethnic groups represented in their study.

Although the majority of reports have been in adults, children have also been reported to be affected with *oral lichen planus*. The latter has been reported concomitantly with cutaneous disease (Sharma & Maheshwari; 1999 and Nanda *et al;* 2001). Case series of children affected with *oral lichen planus* have shown that the clinical appearances of lesions are similar to those occurring in adults. It was also suggested that *oral lichen planus* may be more common in children of Asian decent (Alam & Hamburger; 2001). There have been other case reports that highlighted the occurrence of paediatric *oral lichen planus* (Patel *et al;* 2005) but no epidemiological studies have been conducted to determine prevalence or ethnicity of *oral lichen planus* in children.

The epidemiology of *oral lichen planus* in a South African setting has been reported within a limited Cape Malay population group (Dreyer; 1978). By reviewing all diagnosed cases over the proposed study period, some light will be shed on the patient demographics of this disorder within the Western Cape.

1.4.3 Clinical features of *oral lichen planus*

Oral lichen planus is a chronic oral mucosal disorder that can involve both lining and attached gingival mucosa. The oral cavity may be the only site affected by lichen planus, (Chainani-Wu *et al;* 2001; Al-Hashimi *et al;*

2007) however, approximately 15% of patients with *oral lichen planus* may have cutaneous manifestations (Eisen *et al;* 2005). Cutaneous manifestations of lichen planus are mostly self-limiting, but unlike the cutaneous counterpart *oral lichen planus* runs a more chronic course and is often difficult to manage (Eisen *et al;* 2005; Camacho-Alonso *et al;* 2007).

Lichen planus of the genital mucosa has also been reported in the literature. Genital lesions occur in 20% of females who have *oral lichen planus* (cited in Eisen *et al;* 2005). Malignant transformation has been reported in both females and males who have genital lichen planus and highlights the need for early recognition and treatment of genital lesions (Al-Hashimi *et al;* 2007).

Lichen planus of the scalp and hair follicles causes a scarring alopecia. Nail involvement is also known to occur, but together with scalp involvement is uncommon in patients with *oral lichen planus* (Eisen; 1999). More commonly seen with *oral lichen planus* is oesophageal involvement. Symptoms of pain and dysphagia lead to this diagnosis. When left untreated, these lesions can result in chronic pain and oesophageal strictures (cited in Eisen *et al;* 2005).

Oral lichen planus has a variable clinical manifestation. In the past six clinical forms have been described, but the latest classification identifies three types of *oral lichen planus*; reticular, atrophic and erosive (Eisen; 2002; Scully & Carrozzo; 2008). The reticular form consists of white striae or lines, plaques or papules (Figures 1.1 and 1.2). The atrophic variant appears erythematous and the erosive variant may consist of ulcerations (Figure 1.3) or bullae (Figure 1.4) (Eisen; 2002; Eisen *et al;* 2005; Camacho-Alonso *et al;* 2007). Reticular lichen planus often occurs as a single manifestation of the disease, erythematous lesions however can be accompanied by reticular lesions and erosive lesions can be accompanied by both atrophic and reticular forms of the disease (Eisen *et al;* 2005). Symptoms of pain and discomfort are usually associated with the atrophic and erosive variants. The reticular variant is seldom symptomatic (Eisen

et al; 2005). Erosive lichen planus appears clinically as any other vesiculobullous disease of autoimmune origin, and thus a biopsy is mandatory to determine a definitive diagnosis.

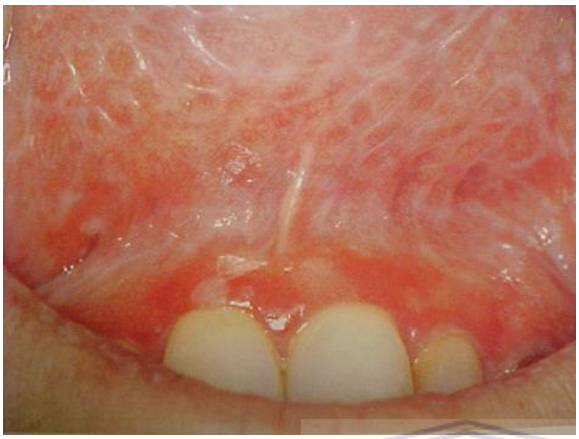

Figure 1.1
Reticular lichen planus of the labial mucosa, mixed with the atrophic variant on the anterior facial gingiva (desquamative gingivitis)

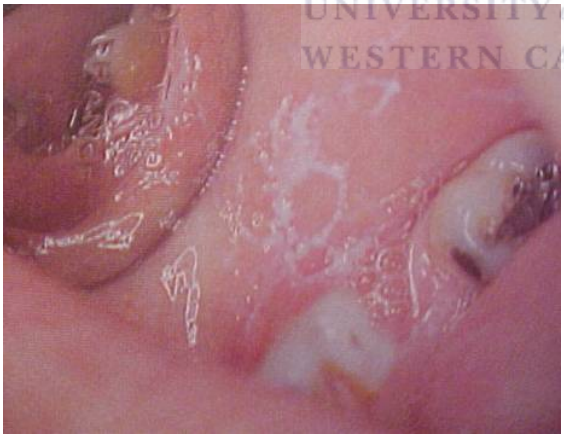

Figure 1.2
Reticular lichen planus of the buccal vestibule

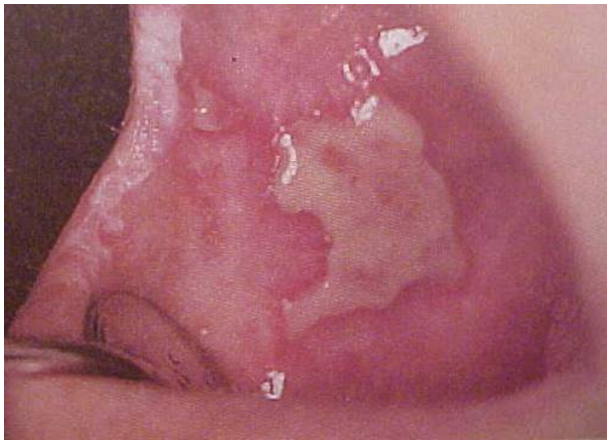

Figure 1.3
Erosive lichen planus of the buccal mucosa

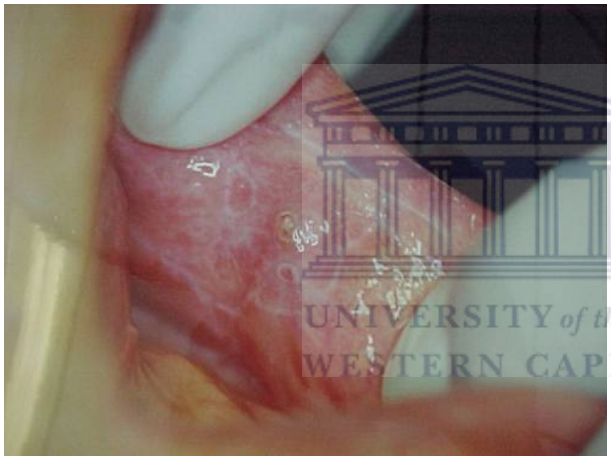

Figure 1.4
Reticular and Bullous Lichen planus

The most common intra-oral site of *oral lichen planus* is the buccal mucosa with a bilateral or unilateral distribution. (Eisen; 2002; Eisen *et al;* 2005; Scully & Carrozzo; 2008). The tongue dorsum, gingival and labial mucosae are the other sites favoured by *oral lichen planus* (Eisen; 2002; Eisen *et al;* 2005; Scully & Carrozzo; 2008). Gingival involvement may take the form of any of the clinical variants and erythematous lesions may however impart a clinical manifestation of desquamative gingivitis. As with erythematous lesions that occur elsewhere, this manifestation is not pathognomonic of *oral lichen planus* alone and other vesiculobullous diseases would have to be ruled out. White lesions of *oral lichen planus*

can mimic other intra oral diseases that manifest in the same manner. The most common being a lichenoid reaction to a known antigen. Erosive lesions of *oral lichen planus* similarly mimic other vesiculoerosive diseases such as pemphigus and mucous membrane pemphigoid. It is necessary to confirm the clinical diagnosis with the histology, as management of these entities is very different. Furthermore the debate of the potentially malignant nature of *oral lichen planus* still ensues (Sugerman & Savage; 2002; Scully and Carrozzo; 2008). Given that a leukoplakia that may have features of dysplasia can clinically resemble *oral lichen planus*, a biopsy of these lesions is compulsory.

1.4.4 The pathogenesis of *oral lichen planus*

The aetiology of *oral lichen planus* has not been identified but studies have drawn some conclusions that shed light on its pathogenesis, albeit not fully defined. Sugerman *et al;* 2002, suggest that oral lichen planus is the result of both antigen specific and non-specific mechanisms, as both antigen specific $CD4^+$ and $CD8^+$T-cell clones and non-clonal T- cells have been isolated from oral lichen planus lesions. The non-specific T-cells have been suggested as being attracted to the lesion by mechanisms associated with pre-existing inflammation (Sugerman *et al;* 2002). Evidence of pro-inflammatory events at the site of oral lichen planus lesions has supported the existence of non-specific mechanisms at work during the pathogenesis of this disorder These mechanisms include the chemotaxis and degranulation of mast cells and the release of their pro-inflammatory cytokines and the activation of matrix metalloproteinases (Sugerman *et al;* 2002).

The role of inflammatory mediators such as cytokines in the pathogenesis of oral lichen planus has also been established by other workers (Scully & Carrozzo; 2008). It is suggested that cytokines play an essential role in the activation of the T-cells and that genetic polymorphisms of T-cells appear to govern whether the disease will be limited to a particular area

such as the mouth alone or whether cutaneous involvement is also seen (Scully & Carrozzo; 2008). Lesion location, according to Sugerman *et al;* (2002), is determined by the expression of the lichen planus self peptide antigen by epithelial cells. The latter statement applies to the theory of these authors, (Sugerman *et al;* 2002), that the pathogenesis of *oral lichen planus* is initiated by the self peptide antigen specific theory. Scully and Carrozzo (2008) suggest that intercellular adhesion molecules also play a role by further attracting T- cells and aiding their migration toward the epithelium. T-cells bind to the basal cells and to cytokines such as IFN-*gamma* to cause upregulation of matrix metalloproteinases that lead to apoptosis of basal cells (Scully & Carrozzo; 2008).

1.4.5 The diagnosis of oral lichen planus

The diagnosis of *oral lichen planus* may be confused with oral lichenoid reactions (Myers *et al;* 2002; Juneja *et al;* 2006, and Ismail *et al;* 2007). This entity has been described as a diagnostic dilemma (Myers *et al;* 2002) and thus clarification on the definitive diagnosis is necessary. *Oral lichen planus* bears clinical and sometimes histological similarities to oral lichenoid reactions. Various pharmacological agents and direct contact with certain metals within dental restorations have been identified as triggers for lichenoid reactions of the oral mucosa (Scully & Carrozza; 2008). Clinically the two may be distinguished on the basis that a lichenoid reaction can be triggered by drug intake, diabetes mellitus and hypertension as well as a close approximation to a dental restoration (Scully & Carrozzo; 2008). Oral lichenoid reactions will resolve spontaneously with the cessation of the offending trigger. Lichenoid reactions are usually unilateral whereas *oral lichen planus* is often bilateral; isolated episodes of unilateral *oral lichen planus* have been known to occur (Juneja *et al;* 2006, Scully & Carrozzo; 2008).

Histologically, lichenoid reactions will show a more diffuse lymphocytic infiltrate with eosinophils, plasma cells and colloid bodies than in *oral lichen planus* (Scully *et al;* 2000).

In a study by Juneja *et al;* (2006), they further distinguished between *oral lichen planus* and oral lichenoid reaction based on certain histological characteristics. This study showed an increase in number of degranulated mast cells in areas of basal cell degeneration, an increase in vascularity and an increase in the PAS-positive basement membrane thickness was found in *oral lichen planus* as compared with oral lichenoid reaction. The epithelium was found to be reduced in thickness in the *oral lichen planus* group (Juneja *et al;* 2006). This study was however limited in the sample number and the authors advocated the use of definitive immunological markers to identify the histopathological parameters. It has, however, been suggested that the definitive histology remains subjective and that a poor clinicopathological correlation is often the order of the day (Scully & Carrozzo; 2008). These authors suggest that direct immunofluorescence be employed in instances when the clinicopathological correlation is not definitive. Direct immunofluorescence is useful in detecting auto-antibodies that may be bound within the tissue of the patient (Ismail *et al;* 2007). A linear pattern of fibrin and anti-fibrinogen deposits at the epithelial basement membrane should be seen either in conjunction with Cytoid or Russel bodies, which may be seen in isolation of the former (Ismail *et al;* 2007; Scullly & Carrozzo; 2008). Ismail *et al; (*2007) reported on earlier work that had recorded the presence of immunoglobulins and complement on the colloid bodies. IgM was more frequently found than IgA of IgG. Direct immunofluorescence is an essential diagnostic aid that is helpful in the elimination of other vesiculobullous diagnoses.

Myers *et al;* 2002 proposed a list of qualifying and disqualifying factors that aid the process of defining a diagnosis of *oral lichen planus*. Their histological qualifying factors included assimilation with clinical qualifying factors. These factors however are limited and do not make allowance for the occurrence of unilateral *oral lichen planus* and lack additional histological features that may be present. A more concise list of criteria

was suggested by Eisenberg (2000); these features include a superficial band-like infiltrate of T lymphocytes, basal cell liquefactive degeneration, and normal epithelial maturation. Additional histological features include, parakeratosis, acanthosis and jagged or saw-tooth shaped rete ridges (Eisenberg; 2000 and Sugerman *et al;* 2002). Civatte bodies and the separation of the epithelium from the lamina propria are further additional features that may be present (Eisenberg; 2000). This histological cleft formation may occur due to the weakening of the epithelial-connective tissue interface that is caused by degeneration of the basal cells. This Max-Joseph space can result in the rare occurrence of an intra-oral blister formation, pathognomic of bullous lichen planus (Sugerman *et al;* 2002). Assimilation of clinical features and behaviour with the histology is essential to arrive at a definitive diagnosis of *oral lichen planus*.

1.4.6 Systemic disease associations

Hepatitis C virus is one of the major causes of chronic liver disease worldwide (Carrozzo; 2008). Infection with hepatitis C virus can produce the extrahepatic manifestation of lichen planus (Scully & Carrozzo; 2008 and Carrozzo; 2008). A study conducted in Nigeria found hypertrophic cutaneous lichen planus to be an extrahepatic manifestation of HCV infection (Daramola *et al;* 2003). *Oral lichen planus* was found to be prevalent among patients with chronic hepatitis C infection in a Brazilian study (Grossmann *et al;* 2007). Epidemiological data suggests a significant association between *oral lichen planus* and HCV infection in the regions of southern Europe and Japan. It remains unclear, however, whether the HCV infection caused *oral lichen planus* or whether the oral lesions preceded the HCV infection. Later studies suggested that the former is more likely to be the pathogenesis of this association and is thought that an initial HCV infection initiates an immunologic pathway. The authors suggested intervention studies should be conducted to further determine the probable causal link between these two pathologies (Carrozzo; 2008).

Recent studies have established the association between HCV and *oral lichen planus* to be geographic in its presentation with the HLA-DR6 allele being implicated as the cause for this geographic heterogeneity (Ismail *et al;* 2007; Scully & Carrozzo; 2008). This geographical presentation is seen in Japan and Southern Europe. Other studies have shown that there are a higher proportion of HCV-positive patients in a lichen planus group as opposed to a control group (cited in Ismail *et al;* 2007). Other researchers believe that the interferon and ribavirin therapy used for HCV infection may be the aggravating factor that results in lichen planus (cited in Ismail *et al;* 2007).

1.4.7 Malignant transformation

It has been suggested that *Oral lichen planus* patients are at an increased risk of developing oral cancer. The reported cases of malignant transformation have been in those cases of atrophic, erosive or plaque *oral lichen planus* (Sugerman & Savage; 2002). Scully and Carrozzo; 2008, reported the rate of malignant transformation to be 0.4% to 5 % as reviewed over a period of 6 months to 20 years. Similar transformation rates were reported by Ismail et al (2007). A malignant transformation was found to be slightly higher, 0% to 12.5 %, as reported by Gonzalez-Moles *et al;* (2008). These authors report that this transformation is independent of the clinical type of *oral lichen planus*. Management of *oral lichen planus* with immunosuppressant agents may theoretically impair immunity against the potential malignant lesion (Scully & Carrozzo; 2008).

The potential malignant transformation of *oral lichen planus* remains controversial. Several studies have been conducted but inconsistencies in the diagnostic criteria for *oral lichen planus* make comparisons and certainties around this topic difficult (Ismail *et al;* 2007; Gonzalez-Moles; 2008). Universally accepted criteria for the diagnosis of *oral lichen planus* are needed to be able to validate studies conducted on its malignant transformation. True *oral lichen planus* is considered benign and many

reported cases of malignant transformation are regarded as dysplasias with lichenoid features. Conversely there have been studies that have shown malignant transformation using the present suggested diagnostic criteria for *oral lichen planus* (Mignogna *et al;* 2007). Prospective long term follow up studies with strict criteria regarding tobacco and alcohol consumption need to be conducted to fully establish the premalignant nature of *oral lichen planus*.

1.4.8 Management of *oral lichen planus*

In view of the potential malignant transformation of *oral lichen planus*, it is essential that patients be routinely followed up. The majority of cases that present as reticular *oral lichen planus* are in fact asymptomatic. No treatment other than follow up regimes is required. The erosive and atrophic forms can, however, be associated with extensive discomfort, pain and burning. Gingival involvement should have a combination management which ensures optimal oral hygiene (Eisen *et al;* 2005). Other management strategies frequently used in daily practise can include advice on avoiding irritants such as spicy foods, toothpastes that contain sodium lauryl sulphate and foods with a coarse texture.

The suppression of cell mediated immunity is required to manage *oral lichen planus* and thus corticosteroids are the most widely used agents in the management. The administration can be topical, intra-lesional or systemic depending on the severity of the disease (Ismail *et al;* 2007). It is essential to bear in mind the side effects associated with the use of systemic corticosteroids, thus as far as possible, topical regimes should be employed to minimize the possibility of these side effects such as adrenal suppression. Tracolimus, an effective steroid free topical immunosuppressant agent has been used in the management of recalcitrant ulcerative *oral lichen planus*. Some studies have reported relapses after the cessation of therapy. This therapy does have side effects which include the development of squamous cell carcinoma (Eisen

et al; 2005; Ismail *et al*; 2007). The latter should be a deterrent for its use for *oral lichen planus* given the controversy that still exists about its own malignant potential. Other than drug intervention, surgical means have also been employed in the management of *oral lichen planus*. Excisional biopsies of small lesions have been reported as curative and localised lesions have been treated with free soft tissue grafts. It has been reported that periodontal surgery can provoke *oral lichen planus* (Katz *et al;* 1988). Cryosurgery has also been used to manage *oral lichen planus,* but recurrence is common. Laser therapy appears promising, but further investigation is required (Ismail *et al;* 2007; Scully & Carrozzo; 2008).

Chapter Two

Materials and Methods

2.1 Study Design

The study design can best be defined as a retrospective descriptive analysis of all confirmed diagnosis of *oral lichen planus* from Tygerberg Oral Health Centre, Mitchells Plain Oral Health Centre and Groote Schuur Oral and Dental Department. These included oral pathology reports that had a definitive histological diagnosis of *oral lichen planus*. Reports that were excluded were those that did not define a histological diagnosis of *oral lichen planus*; namely, lichenoid reaction or lichenoid dysplasia. All reports with a suggested but uncommitted diagnosis of *oral lichen planus*; namely, "may be suggestive of *oral lichen planus*" or "may be in keeping with *oral lichen planus*" were reviewed and included only if the diagnostic criteria of *oral lichen planus* were met.

2.2 Study Sample

Archival and current oral pathology reports which showed a confirmed histological diagnosis were used. The records were from 1974 to 2008. Only reports that met the inclusion criteria were used for this study.

This resulted in a sample consisting of all available oral pathology reports from Tygerberg Oral Health Centre, Mitchells Plain Oral Health Centre and Groote Schuur Oral and Dental department.

2.3 Inclusion and exclusion criteria

The histological diagnostic criteria of a confirmed diagnosis of *oral lichen planus* was accepted as, a superficial band-like infiltrate of lymphocytes in the lamina propria, basal cell liquefactive degeneration, normal epithelial maturation with additional histological features that may or may not be present including, parakeratosis, acanthosis and jagged or saw-tooth shaped rete ridges. Civatte bodies and the separation of the epithelium from the lamina propria were further additional features that may have been present giving rise to subepithelial cleft formation (Eisenberg; 2000; Sugerman *et al;* 2002).

Reports that were excluded were those that did not define a histological diagnosis of *oral lichen planus.*

From the pathology reports the following criteria were recorded for each patient, Ethnic origin, Sex, Age and the Intra-oral location of the lesion.

2.4. Data Analysis

The data obtained from the oral pathology reports were entered in an Excel® spreadsheet and statistically analysed.

Contingency tables summarised the counts (Frequency) according to the three categorical measurements: ethnicity, sex and intra-oral location. It was not possible to study the data in one extensive three way table, but rather in descriptive marginal tables. For some of these tables the Chi-Squared test was applied to investigate the differences in the rates occurred. For the interval measurement of age, a non-parametric test, (Wilcoxon Rank Test) was applied.

2.5 Limitations

This study is limited in that it is a retrospective study of proven cases of *oral lichen planus*.

The ethnic distribution of patients within this study is not representative of the South African or the Western Cape populations as archival records used were drawn from as far back as 1974, 20 years before the democratically elected government and the end of Apartheid. A true reflection of the ethnic distribution of *oral lichen planus* can thus not be defined from this data. This study is limited in that the samples were drawn from tertiary treatment centres and is thus not a true epidemiological study.

Over the period of 34 years (1974-2008) there was variability in the terminologies used by the clinicians with regard to patient ethnicity; some failed to report on ethnicity, others reported in a variable fashion; namely, “other” or “non-white”. These reports were excluded from the statistical analysis relating to ethnicity. Furthermore other variables included for analysis, sex and age, were not always recorded.

A scientific opinion on the age and sex distribution of this condition in the general population could not be expressed from this present study population which is drawn for a tertiary treatment centre and not from a community setting, which would be a true epidemiological survey.

2.6 Ethical Considerations

Authorization to access archived oral pathology reports was given to the Dean of the Faculty of Dentistry. The oral pathology reports contained details of the patient’s name and had a registration number. The name of the patient was not recorded, the registration number of the pathology report was however included in the raw data that was entered onto the Excel® spreadsheet along with other data needed to fulfil the objectives of

this study. The confidentiality of the patients was thus maintained. The registration number was part of the raw data.

Chapter Three

Results

Two hundred and forty nine (249) confirmed diagnoses of *oral lichen planus* were retrieved from the tertiary diagnostic centres within the Western Cape.

Table 3.1:
The distribution of ethnicity within the sample (n=249)

African	Coloured	Indian	Not reported	Non-white	Other	White
2	27	9	41	1	6	163

The White individuals were in the majority at 163. Twenty-seven (27) were Coloured and only 2 African individuals were diagnosed with *oral lichen planus* within this sample. Forty-one (41) reports had no record of the ethnic origin of the patient and the terminology used to describe the ethnic origin of 7 patients provided no definitive information on their ethnicity, as they were reported as “Non- White” and “Other”. No assumptions could be made on the latter groups, namely; “non- White” and “other” as these terms was ambiguous. This data (7 pathology reports) was omitted from the analysis of the ethnic origin. Forty-one (41) records with no definitive ethnic group were omitted. The patients with a definitive report on ethnic origin were analysed and stratified by gender as shown in Table 3.2.

Table 3.2

The distribution of ethnic origin by sex (n=201)

Sex	African	Coloured	Indian	White	Total
Female	0	17	5	128	150
Male	2	10	4	35	51

There were more females than males. Females: Males = 150:51. The Chi-squared test, for the observed Sex distribution (150:51) and the expected theoretical Sex distribution (50:50) were extremely different. This supports the notion that *oral lichen planus* has a female predilection.

One hundred and Twenty Eight (128) of the females were White, 85.3% of the female population within this sample. There were 17 Coloured females, accounting for 11.3%, 5 Indian females, 3.3% of the sample. There were no African females within this sample. There were 35 White males, 71.4%, 10 Coloured males, 20.4%, and Indian males made up 8.2% of the male ethnic distribution, being 4 in number. Two (2) African males were diagnosed with *oral lichen planus* in this sample (Table 3.2).

The sex distribution differed somewhat between the ethnic groups and although 2 African males were affected by *oral lichen planus*, no African females were found within this sample. The female proportion for other ethnic groups was however higher than the male proportion in those groups.

The number of affected African individuals was so low that this data was omitted from further analysis as it was not representative.

Table 3.3

Ethnic Distribution within Sex groups

	Coloured	Indian	White	Total
Females	11.3%	3.3%	85.3%	100.0%
Males	20.4%	8.2%	71.4%	100.0%

Sex distribution differed somewhat between the ethnic groups studied (Coloured, Indian and White). The ethnic distribution of the males and females are different (Table 3.3). Chi-squared Statistic was 5.0188 with two degrees of freedom ($p < 0.1$).

The census population of South Africa (SA) and of the Western Cape (WP) is tabulated below in Tables 3.4 and 3.6, respectively. The distribution of the population groups within South Africa and the Western Cape was correlated with the sample that was diagnosed with *oral lichen planus*. The correlation of this sample (201) and the South African population distribution expectation is tabulated in Table 3.5.

Table 3.4

Population group distribution and percentage distribution as per 2001 census within SA

	African	Coloured	Indian	White	Total
Census Numbers	35,416,166	3,994,505	1,115,467	4,293,640	44,819,778
Percentages	79%	8.9%	2.5%	9.6%	100.0%

Table 3.5

The expected distribution of *oral lichen planus* according to the population distribution of South Africa

	African	Coloured	Indian	White	Total
Expected Numbers	158.8	17.9	5.0	19.3	201
Observed Numbers	2	27	9	163	201

To statistically compare the two sets of numbers and decide whether the observed numbers correspond to the distribution of the ethnic distribution

of South Africa, a Chi squared test was performed, using data from Tables 3.4 and 3.5, (Test statistic = 1235.73 with 3 degrees of freedom, highly significant difference between the two sets of numbers, expected and observed). The high significance originated from the difference between the expected and observed numbers within the African population.

Table 3.6 shows the population group distribution within the Western Cape. This was analysed due to the difference in the percentages of the ethnic groups in the Western Cape compared to the rest of South Africa.

Table 3.6

Population distribution census for the Western Cape 2001

African	Coloured	Indian	White	Total
1,207,429	2,438,976	45,030	832,901	4,524,336
26.7%	53.9%	1.0%	18.4%	100.0%

When using the population distribution of the Western Cape as an expectation of outcomes for the existing study, it would be expected that the sample of 201 individuals would have a distribution of *oral lichen planus* as depicted in Table 3.7.

Table 3.7

The expected distribution of individuals with *oral lichen planus* within the Western Cape

	African	Coloured	Indian	White	
Expected Numbers	53.6	108.4	2.0	37	201
Observed Numbers	2	27	9	163	201

Test statistic = 564.32 with 3 degrees of freedom, $p < 0.1\%$

A Chi squared test was performed to compare the expected and observed numbers, using data from Tables 3.6 and 3.7. The test statistic was less significant than that of the test of fit for Table 3.5 (SA population). The observed numbers of individuals in this study corresponded better with the Western Cape population distribution. The Ethnic distribution of *oral*

lichen planus within this sample differed from the expected distribution seen in the census for South Africa and the Western Cape; the distribution fit for the Western Cape is better than that for South Africa as a whole.

A female predilection was evident within this sample as depicted by the pie graph below (Figure 3.1).

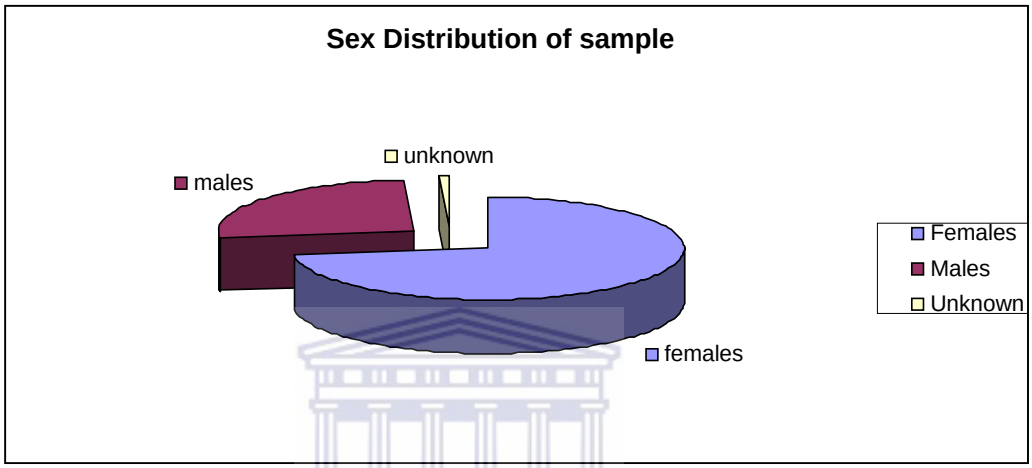

Figure 3.1:
The Sex Distribution of the sample (n= 249)

One hundred and eighty two (182) females had *oral lichen planus* and sixty-five (65) males were diagnosed. Two (2) reports did not record sex and were omitted from analysis.

The Age range of those individuals diagnosed with *oral lichen planus* was from 12 to 86 years. The female age range was 12- 86 years, and for males, 13 – 71 years. 6.4% of the sample failed to report on age of patient.

Table 3.8

Descriptive statistics of Age for Females and Males

	Females	Males
Minimum	12	13
Q1	53	36.25
Median (Q2)	59	45.5
Q3	62	54
Maximum	86	71
Averages	52.34	45.73
Standard Deviation	14.39	12.32
Dispersion above the Median to Q3	3.00	8.50
Inter-quartile range	9.00	17.75
Dispersion below the Median to Q1	6.00	9.25

Table 3.8 shows the Median of the females differed from the Average; the median was approximately six and a half years older than the Average, whereas for the males the difference was negligible. The observed age distribution of the females was skewed towards the lower ages and there was no skewness for the males. The Standard Deviation of the females and males was approximately the same, 14.39 (females), 12.32 (males). The females with *oral lichen planus* were older than the males [compare the medians, 59 (females) to 45 (males), Wilcoxon Test significant, $p<0.001$].

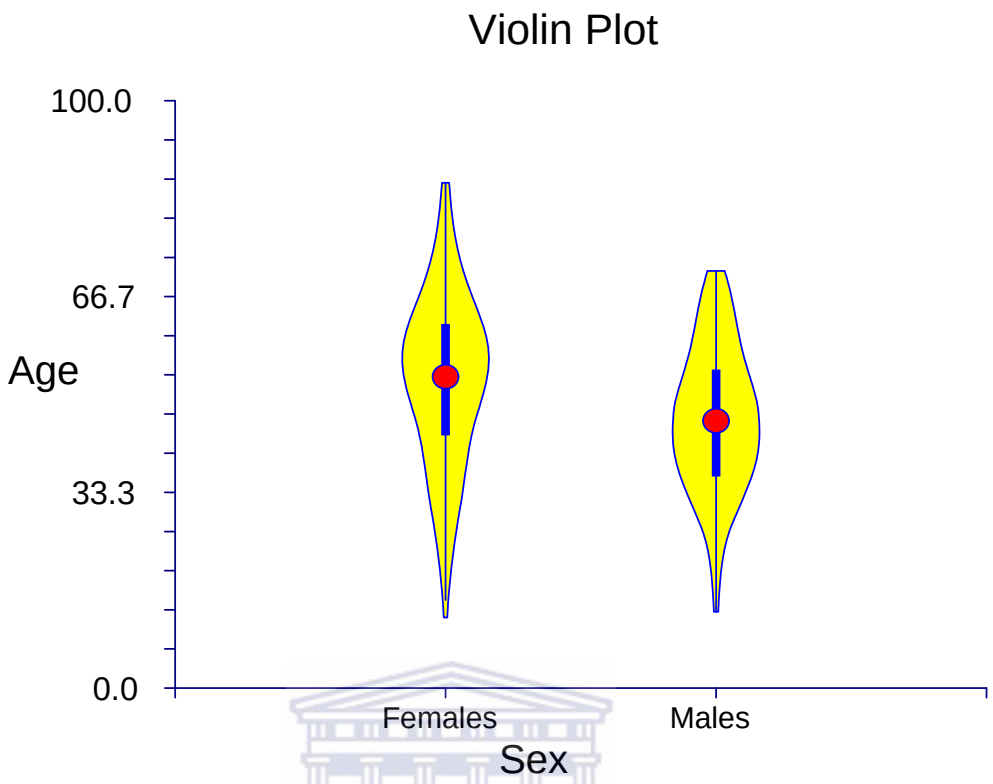

Figure 3.2:

Side-by-side violin plots of the age of the two genders (Females: Males = 150:51).

The red dot in the “middle” indicates the median of the age distribution. The thick blue bar to the bottom indicates the first quartile and the thick blue bar to the top indicates the third quartile. The distance from the bottom to the top of the thick blue line depicts the inter-quartile range.

The age distribution of both females and males are symmetrical about the median, except to a lesser extent for the females, which had a long tail toward the lower age groups.

Table 3.9

The intra-oral distribution of *oral lichen planus* in the complete sample

Intra-oral location	
Single sites	
Buccal mucosa	134
Gingiva	34
Labial mucosa	2
Palate	1
Tongue	21
Retromolar area	2
Not specified	28
Multiple sites	
Bilateral Buccal mucosa	14
Buccal mucosa and gingival	6
Buccal and labial mucosa	1
Buccal mucosa and tongue	6
Total	249

Table 3.9 shows the 249 diagnosed cases of *oral lichen planus,* 194 lesions were at a single intra-oral site. The buccal mucosa was affected in 134 of those single sites; the gingiva at 34; 2 lesions were located at the labial mucosa; 1 was situated on the palate, 21 on the tongue and 2 in the retromolar area. The location of twenty-eight (28) lesions was not recorded on the pathology reports. Of the 249 cases, 27 were located at multiple intra-oral sites. The buccal mucosa was affected bilaterally in 14 cases. Six lesions were located on both the buccal mucosa and the gingival; 6 lesions were on the buccal mucosa and the tongue. One case of lichen planus was located on both the buccal and labial mucosa. Eighty-five (85%) percent of the lesions in the females were situated on the gingiva, while the lesions at other sites in females was less than 75%.

Chapter Four

Discussion and Conclusions

4.1 Discussion

From the retrievable records from three diagnostic centres within the Western Cape, two hundred and forty nine cases of oral lichen planus were diagnosed over a 34 year (1974-2008) period. The number of *oral lichen planus* cases was low compared to the overall number of biopsy reports over the same period of time which was estimated to be from 20000 to 25000. These estimations could not be fully verified for all sites and were estimated from available records at Tygerberg Oral Health Centre. This suggested that the proportion percentage of biopsied and diagnosed cases of oral lichen planus for the province as a whole to be even lower.

The pathognomonic clinical features of reticular lichen planus may lead some clinicians to define a diagnosis on clinical manifestations only and thus not perform a biopsy. Furthermore, information regarding cases with a clinical diagnosis of *oral lichen planus* but a different definitive histological diagnosis was not available.

McCartan and Healy (2008) reviewed and critiqued studies that have been conducted on the prevalence of oral lichen planus. Several of the studies that were reviewed had not included a biopsy of oral lichen planus and the diagnosis was made on a clinical basis only. This study in the Western Cape does not truly represent all cases of *oral lichen planus* diagnosed over the 34 year period (1974-2008) as there may have been clinically diagnosed cases that were not biopsied. The McCartan and Healy (2008) review highlights that clinical diagnosis alone is not reliable and histological diagnosis is needed to

arrive at a definitive diagnosis. There is also variability within the different studies on the diagnostic criteria used for both clinical and histological diagnosis of oral lichen planus. Furthermore, this study based on histological diagnosis aimed at overcoming this variability by defining the definitive inclusion criteria.

The description of ethnicity within the sample was identified. It was clear that there was lack of uniformity in the reporting of the ethnic origins of patients. One patient was reported as “non-white”, some others as “other” and many had no report on the ethnic origin of the patients. Due to the unknown ethnic origin of those not reported, and the ambiguity of the terms “non-white and “other” these particular patients had to be excluded from further statistical analysis. This resulted in the omission of 48 out of 249 cases of oral lichen planus. The political history of South Africa during the Apartheid era, suggests that the matter of ethnicity may have been too sensitive for some clinicians to ask patients about or to report on.

The 201 cases of known ethnicity were then divided into females and males. Within the female group the majority of females were White, 128 (85.3%) as apposed to 17 (11.3%) Coloured females and 5 (3.3%) Indian females. It was interesting to note that no African females were affected within this sample. The proportion of males within the different ethnic groups was generally lower than the females, except in those who were African; 2 African males were affected and no African females. Furthermore, White males were in the majority, 35 (71.4%) and there were 10 (20.4%) Coloured males and only 4 (8.2%) Indian males.

When one looks at the population distribution within South Africa, it is clear that individuals of African origin are within an overwhelming majority. African individuals, according to the 2001 Census within South Africa as a whole make up 79% of the population, White individuals make up 9.6%, Coloureds 8.9% and Indian individuals, 2.5 % of the population. The expectation of a disease trend across the different population groups in any given sample would then be expected to follow the same percentage distribution, namely for

the given sample the expectation would have been that 159 individuals should have been African, 19 White, 18 Coloured and 5 Indian (Table 3.5). The Chi squared test (Test statistic= 1235.73) performed on this analysis resulted in a difference that was highly significant due to the difference in this expectation and the actual finding within this sample group.

When the same population statistics are analysed for the population within the Western Cape, the outcome is different. Within the Western Cape it has been established, according to census 2001, that the population proportion is different to that of the rest of South Africa. Namely, the Coloured population is in the majority at 53, 9%, followed by the African population at 26, 7%, the White population at 18, 4% and the Indian population at 1,0%. When one then uses these figures as a basis of expectation for this sample from within the Western Cape, within the sample of 201, it would be expected that 108 individuals with oral lichen planus should have been Coloured, 54, African, 37, White and 2 Indian (Table 3.7). The observed numbers of affected individuals was however very different to that which was expected. A Chi squared test was once again applied, and the outcome (564.32) was less significant in the difference that was observed than that which was expected. The distributional fit for oral lichen planus according to the population groups or ethnic origin was thus better for the Western Cape than for South Africa, yet remains a skewed distribution due to the biased sample.

Epidemiological studies conducted on *oral lichen planus* largely focus on the distribution of this disorder by sex only, few studies mention or define this disorder by ethnicity. When however, the ethnic distribution of those affected with *oral lichen planus* was reviewed in the literature, it became clear that *oral lichen planus* is a rarity in African individuals (Daramola *et al;* 2003). As early as 1985, it was recognised that the prevalence in African individuals is low, as Silverman and Lozada-Nur had 1% of their study population being Black of African decent, whereas 94% was White. In 2006, Ingafou et al established a prevalence among black (African and Carribean decent) individuals to be so low that in addition to other ethnic backgrounds such as Mediterranean and Chinese this group who made up 8% of the study population as opposed to

63,6% that were White. The ethnic or population groups within the South African context are very different to that from the studies referred to above. An earlier South African study by Dreyer *et al*, 1982, reported on 33 cases of *oral lichen planus* and found that 94% of that study population was White. However, just like similarities could not be drawn from studies within other countries, the particular study was conducted at a centre that serviced a mainly White population during that period of time as a result of the Apartheid system.

As previously highlighted in the limitations of this study, a scientific opinion on sex and age for the general population cannot be made from the data presented within this sample. The sex and age distribution within this sample are however presented for discussion below but is should be stressed that the discussion only pertains to this limited sample.

Oral lichen planus within this sample followed a female predilection. The sample expressed a female to male ratio of approximately 3:1. Within an ideal sample to determine true disease prevalence one would study a sample that has an equal number of males and females. The Chi squared test of the observed gender distribution (3:1) and the theoretical distribution (50:50) were extremely different and supported the notion that *oral lichen planus* followed a female predilection. This may be a verification of the fact that *oral lichen planus* is an oral disorder that may be patient reported or discovered by a clinician on routine dental examinations. The gender distribution of studies conducted worldwide report a female predilection; however some studies described as true population studies have reported prevalence rates to be nearly the same in females and males (McCartan & Healy, 2008). These studies were conducted in earlier years when the contention of lichenoid reactions were not yet generally recognised, furthermore there is no uniformity of diagnostic criteria used to arrive at a definitive diagnosis of *oral lichen planus.* The present study aimed to overcome this by only including those cases with a known definitive histological diagnosis.

The age range for the Western Cape sample was from 12 to 86 years. Incomplete recording of variables resulted in 6.4% of the sample with an unknown age. Descriptive statistics were applied to known ages of participants, stratified by gender. The median age of the females was six and a half years older than the average age of all the females (median= 59, average= 52.34). The median and average age of the male participants were however approximately the same (median= 45.5, average= 45.73). Analysing the values of the averages and medians shows that the average and median age of onset for the females was older than that of the males. A Wilcoxon test showed that this difference in age between the females and males was significant (p<0.001). Side by side violin plots (Figure 3.2) illustrates the age ranges for females and males within this sample. The inter-quartile range for the males was larger than that of the females. The males were younger at the time of presentation of *oral lichen planus*. The maximum age of the males was 15 years younger than that of the females.

The frequency table (Table 3.9) of the intra-oral distribution of *oral lichen planus* shows that the buccal mucosa was most frequently affected. This finding is in keeping with that of other studies (Eisen; 2002; Eisen *et al;* 2005; Scully & Carrozzo; 2008). The occurrence of *oral lichen planus* on the gingiva manifested clinically as desquamative gingivitis and this was seen more frequently in females (85%) than the other intra-oral sites.

4.2. Conclusions

There is a need for uniformity of record taking of patients who undergo intra-oral biopsies. All patient variables such as sex, ethnic origin and age need to be systematically recorded. It can be concluded that this sample is biased and no definitive conclusions regarding patient demographics of *oral lichen planus* can be extrapolated from this sample as a representation of the general population of the Western Cape or South Africa. Within the confines of these limitations, as previously highlighted, *oral lichen planus* was found to occur in individuals of all ethnic backgrounds. The latter statement remains

contentious within this particular sample. The inclusion of pre-1994 records has skewed the sample to a predominantly White distribution; however the inclusion was mandatory to provide sufficient data for statistical analysis. Even though the population demographics for the Western Cape had changed since 1994 and the influx of patients at tertiary dental institutions has also changed during this period of time, no post 1994 records included individuals of African origin. This may be due to lack of adequate record taking by attending clinicians or due to the fact that variants of *oral lichen planus* are asymptomatic and thus treatment for this disorder may not be sought. Within suburbs that are largely populated by African individuals there are community clinics equipped to treat dental pain and sepsis, thus *oral lichen planus* may be going undiagnosed in these areas, especially the asymptomatic variant. Symptomatic patients would still however need to be referred to the tertiary dental teaching institutions where biopsies would have been taken. The fact that no record of these biopsies were found for these individuals within the archives, may support the notion that *oral lichen planus* is a rarity in African individuals but the biased sample presented provides no definitive conclusion in this regard. Optimal population based studies within communities will overcome this problem.

The female to male ratio was 3:1. The average age of onset of *oral lichen planus* was older for females (52.34) than for males (45.73). The intra-oral distribution of *oral lichen planus* was most frequently found on the buccal mucosa, followed by gingival lesions. Considerably more females had gingival lesions.

Future study in this area is warranted and suggestions follow;

1. This study should be carried out in other provinces within South Africa that are predominantly African in its population breakdown. This will give a true reflection if *oral lichen planus* is a feature in this population group.
2. Ideally community, rather than treatment centre based studies should be conducted in this regard for a true epidemiological reflection of *oral*

lichen planus. Clinical diagnoses in this setting should however be verified by a histological diagnosis.

3. Protocols should be constituted so that patients who present with *oral lichen planus* can be included in prospective studies and the course of their disease can be monitored, thus shedding light on other topical issues that abound this disease process, such as its malignant potential and the association it may have with Hepatitis C infection.

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