An Oral Health Survey among HIV-infected children younger than twelve years of age presenting at the Paediatric Infectious Diseases Clinic at Tygerberg Hospital.

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A mini-thesis submitted in partial fulfilment of the requirements for the degree of MSc in Paediatric Dentistry.

DR OLORATO P. MATHIBA

Student ID: 3515495

Supervisor: Dr. Nadia Mohamed

Co-supervisor: Dr. Riaan Mulder

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Olorato Patience Mathiba

KEYWORDS

HIV/AIDS

HAART

Oral health

Orofacial manifestations

Orofacial lesions

Dental caries

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ABSTRACT

Background: HIV/AIDS remains a global health problem. Orofacial manifestations of HIV/AIDS have been found to be among the first signs of immune suppression and have been used in the clinical staging of the disease. Infants and children are prone to opportunistic infections because of the immature immune system. Orofacial manifestations of HIV can therefore be used to predict prognosis and progression of infection. The introduction of highly active anti-retroviral therapy (HAART) has since seen a decline in the development of opportunistic infections and HIV-related orofacial manifestations.

Aim: The aim of this study was to determine the oral health status of HIV-infected children at the Paediatric Infectious Diseases Clinic at Tygerberg Hospital.

Method: A cross-sectional survey among HIV-infected children aged between 2 and 12 years presenting at this clinic. The parents/guardians were interviewed to obtain information regarding health seeking behaviour, oral hygiene practices and dietary behaviour. A standardized clinical examination was performed on a random sample of children by the principal researcher who is a qualified dentist. The World Health Organization criteria (with modifications) was followed. Medical records were retrieved to obtain information on medications, co-morbidities and immune-deficiency status. The prevalence of orofacial lesions and dental caries as well as the mean decayed (D-/d-), missing (M-/m-) and filled (F-/f-) teeth were calculated with 95% confidence intervals (95% CI). Poisson regression was used to analyze the association between the presence of orofacial lesions and children's characteristics.

Results: Out of the 66 children who were recruited for this study, 28 (42.4%) were female and 38 (57.6%) were male. One or more orofacial lesions were found in 31.8% of the sample. The presence of orofacial lesions was found to be independently associated with the $CD4^{+}$ counts and viral load (p values of 0.715 and 0.638 respectively). The study population was found to have a high prevalence of dental caries (78.8%) and an unmet treatment need of 90.4%. Approximately 60% of the children had never had a dental visit since birth, whilst the 20.2% who have been to the dentist in the past 12 months mainly presented for emergency care.

Conclusion: Orofacial manifestations of HIV still occur in children despite the availability of HAART, but to a lesser extent. The high prevalence of severe dental caries in this population high-

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lights the need for oral health awareness and the inclusion of oral health care in the comprehensive care of children with HIV.

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DECLARATION

I, the undersigned, Olorato Patience Mathiba, hereby declare that the work contained in this dissertation titled; "An Oral Health Survey among HIV-infected children younger than twelve years of age presenting at the Paediatric Infectious Diseases Clinic at Tygerberg Hospital" is my original work and has not been previously submitted in its entirety or in any part at any university for any degree or examination.

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DEDICATION

This dissertation is in honour of my late father ***Professor G.A. Sekgoma***, may your soul rest in peace.

To my rock, my mother; ***Ms O.K. Mathiba***, without your love and support nothing would have been possible.

And to my amazing siblings; ***Shasha*** and ***Lefhika***, your immeasurable moral support through this journey is greatly appreciated.

Thank You

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LIST OF ABBREVIATIONS

AIDS: Acquired Immune Deficiency Syndrome

ART: Anti-retroviral Therapy

CI: Confidence Interval

CMV: Cytomegalovirus

DMFT/dmft: Decayed (D-/d-); Missing (M-/m-) or Filled (F-/f-) Teeth

EBV: Epstein Barr Virus

HAART: Highly Active Anti-retroviral Therapy

HHV: Human Herpes Virus

HIV: Human Immuno-deficiency Virus

HPV: Human Papilloma Virus

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HSV: Herpes Simplex Virus

LGE: Linear Gingival Erythema

LRTI: Lower Respiratory Tract Infections

n: Number of cases

NHL: Non-Hodgkins Lymphoma

NS: Necrotising Stomatitis

NUG: Necrotising Ulcerative Gingivitis

NUP: Necrotising Ulcerative Periodontitis

OHL: Oral Hairy Leukoplakia

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PIDC: Paediatric Infectious Diseases Clinic

SD: Standard Deviation

UNAIDS: United Nations joint program on HIV/AIDS

URTI: Upper Respiratory Tract Infections

WHO: World Health Organization

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DEFINITION OF TERMS

Caries Experience is defined as the presence of either untreated or treated caries, expressed as DMFT/dmft indices.

CD4$^+$: CD4 (cluster of differentiation) is a glycoprotein found on the surface of T-helper cells, monocytes, macrophages and dendritic cells. CD4$^+$ T-helper cells are white blood cells that form a crucial part of the immune system.

Prevalence is defined as the percentage of the population affected by a given condition at a specific point in time.

Co-morbidity is the presence of one or more additional diseases occurring concurrently with the primary condition.

Orofacial manifestation: a lesion appearing on the oral, peri-oral, facial and head and neck region associated with HIV.

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Trans.CD4$^+$: Transformed CD4$^+$ calculated as the square root of the CD4$^+$ cell count.

Trans.Viral Load: Transformed Viral Load calculated as Log (Viral Load+1); note that log is the natural log.

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CHAPTER 1: INTRODUCTION

Ever since the discovery of the Human Immuno-Deficiency Virus (HIV) in 1981, the virus has continued to wreak havoc globally with new infections continuing to surface and HIV-related deaths still being registered (World Health Organization, 2014). The United Nations' joint programme on HIV/AIDS (UNAIDS) Gap Report (2014) estimated that by the end of 2013 there were 35 million people living with HIV/AIDS. The impact of HIV has continued to be hard-felt in Sub-Saharan Africa; with the region accounting for 71% of the global HIV infections (UNAIDS Gap Report, 2014). South Africa on the other hand has an estimated 6.3 million people living with HIV; making it the highest prevalence of people living with HIV/AIDS in the world (UNAIDS Gap Report, 2014).

Children constitute a vulnerable population as they continue to suffer from the impact of the HIV/AIDS pandemic. A study carried out in the Western Cape, South Africa reported on the prevalence of HIV and estimated a prevalence of 0.7% in children between the ages of 2 and 15 years of age (South African National HIV Survey, 2012). The most recent report on HIV/AIDS in children between the ages of 0 and 14 depicted an overwhelming 3.2 million children living with HIV, and out of this population, 2.9 million (91%) are living in Sub-Saharan Africa. In South Africa, an estimated 360,000 children were living with HIV/AIDS by end of 2013 (UNAIDS Gap report, 2014).

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There is a well-known cliché that the mouth is a mirror reflecting an individual's general health or disease. Oral manifestations of HIV/AIDS have been found to be among the earliest signs of the disease and may be markers of disease progression in both adults and children (Coogan *et al*., 2005; Miziara & Weber, 2008). HIV-infected children may experience an increase in caries experience and orofacial lesions, compared to their healthy peers (Howell *et al*., 1992; dos Santos Pinhero *et al*., 2009; Orenuga *et al.,* 2011). The presence of these lesions in children impact on the quality of life as they cause discomfort, impairment in function as well as disabilities in extreme cases (Yengopal & Naidoo, 2008). Oral health should be taken into consideration when dealing with the overall management of HIV-infected paediatric patients. Early recognition of these oral lesions allows for early intervention which helps with better clinical staging of the HIV infection. This leads to an improved prognosis, reduced morbidity and subsequently, an improved quality of life for the child.

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CHAPTER 2: LITERATURE REVIEW

Children acquire the HIV infection perinatally through three main ways. These include intra-uterine mother to child transmission, i.e. during pregnancy, passage through the birth canal during labour and during breastfeeding (Jetpurwala & Jain, 2011). HIV infection is characterized by suppression of the immune system. The virus targets the $CD4^+$ T-helper cells of the immune system the main function of which is to help the body fight infections. The virus replicates within the $CD4^+$ T-helper cell and eventually destroys the $CD4^+$ lymphocyte (Calles *et al.*, 2006). This is evident through a decrease in the amount of $CD4^+$ T-helper lymphocytes and an increase in the viral load (Wilson *et al*., 2002).

The normal $CD4^+$ cell count for adolescents and adults ranges between 500 and 1200cells/mm^3 (Bofill, 1992). Infants and young children normally have high $CD4^+$ counts when compared to adolescents and adults. $CD4^+$ counts slowly decline to adult values by the age of 6 years (Shearer *et al*., 1997). This signifies the need to take age into consideration when dealing with immunological status in children. The percentage $CD4^+$ cell count is more valuable when doing the immunological staging in children as depicted in Appendix 1 (WHO Case Definitions of HIV, 2007).

The viral load is a blood test carried out to determine the concentration of HIV copies in the blood plasma (Wilson *et al*., 2002). Clinicians use this result to assess the severity of the infection. The viral load is expressed as copies/mL or as a $\log_{10}$ value (Wilson *et al*., 2002). For a patient on antiretroviral medication, ideally, the viral load should remain undetectable; or recorded as LDL (lower detection limit) when it is below 50 copies/mL (Carter, 2012). A rising viral load is often indicative of drug failure (Bofill, 1992).

2.1 Oral lesions as predictors of HIV infection

A decrease in $CD4^+$ cells and an increase in the viral load make the body susceptible to opportunistic infections (Wislon *et al*., 2002; Yengopal *et al*., 2011). Some of these infections result from commensal micro-organisms which take advantage of the immune suppression and manifest as infections ranging from fungal, viral and bacterial infections to neoplastic lesions (Coogan *et al*., 2005; Yengopal *et al.*, 2011). These opportunistic infections often manifest in the oral cavity. $CD4^+$ counts of less than 200 cells/mm^3 and viral loads greater than 3000 copies/ml are among some the factors found to predispose the expression of orofacial lesions (Reznik & O'Daniels, 2007).

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It has been established in the literature that the $CD4^+$ count by itself is not a reliable marker for HIV progression in paediatric cases (Ramos-Gomez, 1996), hence the inclusion of oral lesions in the WHO clinical staging of HIV (Appendix 2). The inclusion of orofacial lesions in the WHO clinical staging of HIV/AIDS plays a significant role in developing countries with poor resource settings where laboratory services are not easily accessible and those with long laboratory turnaround time for blood tests (Yengopal *et al*., 2016). The presence of such lesions can and have been used as clinical signposts of the presence and progression of immunodeficiency (Baghirath *et al.*, 2013; Yengopal *et al*., 2016).

In children, this effect is more pronounced as their immune system is not fully mature (Jetpurwala & Jain, 2011). This means that the interval between acquisition of the infection, incubation, progression to AIDS and subsequent death is compressed and very short (Prabhu *et al.*; 2013). Infants and children with lower $CD4^+$ counts are more prone to opportunistic infections (Arrive *et al*., 2016). Orofacial manifestations have been reported to be the earliest signs indicative of a paediatric HIV infection (Ramos-Gomez *et al*, 1999) and can therefore help determine the prognosis and progression of the HIV infection (Coogan *et al*., 2005).

The use of oral lesions as predictors of the progression of the HIV infection in adults has been thoroughly investigated and documented, but a paucity of data is available for the paediatric population (dos Santos Pinheiro *et al.*, 2009; Rwenyonyi *et al.*, 2011; Oladokun *et al.*, 2013; Meless *et al.*, 2014).

2.2 Highly Active Anti-retroviral Therapy (HAART)

The introduction of highly active anti-retroviral therapy in 1996 saw an improvement in the immune status of its recipients. This was signified by an increase in the $CD4^+$ count and suppression of viral replication in patients on the medication (Hamza *et al*., 2006). This regimen improves immune function therefore reducing the risk of opportunistic infections (Baghirath *et al*., 2013).

South Africa conforms to the WHO consolidated guidelines on the use of anti-retroviral drugs updated in 2015 (The South African Anti-retroviral Treatment Guidelines, 2015). The guideline states that all children below the age of five years are eligible for anti-retroviral treatment (ART) irrespective of the $CD4^+$ cell count or the WHO clinical stage. The WHO clinical staging is based on clinical findings and does not require the $CD4^+$ cell count (WHO Clinical staging of HIV, 2007). This staging system is widely used to determine the eligibility for HAART (Munthali *et al*., 2014).

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According to the current guidelines, children between the ages of 5 and 15 years with a WHO clinical stage 3 or 4 or a $CD4^+$ cell count less than 350 cells/mm^3 should receive HAART (WHO Global update on HIV treatment, 2013). HAART should be provided to all HIV-infected pregnant and breastfeeding women irrespective of the $CD4^+$ cell count or the WHO clinical stage (South African Anti-retroviral Treatment Guidelines, 2015; WHO guidelines, 2015). This is to minimize and/or prevent the chances of mother to child transmission.

Despite all these standardized ART guidelines there are still quite a number of infants born with HIV. The number of children receiving ART is reported to be at an appallingly low rate of 24% (UNAIDS Gap Report, 2014). This means that approximately 76% of children living with HIV are not receiving treatment. With these low numbers of children on HAART one can deduce that the prevalence of orofacial manifestations of HIV in children is likely to be high.

2.3 Oral aspects of HIV therapy (HAART)

Since the introduction of ART and HAART a number of studies have reported a marked decline in HIV-related orofacial manifestations (Coogan *et al.*, 2005; dos Santos Pinhero *et al.*, 2009). Several studies concluded that the presence of oral lesions in children coincided with immunosuppression and could therefore be used as a proxy for treatment failure among patients on HAART (Miziara & Weber, 2008; Rwenyonyi *et al*., 2011, Ponnam *et al*., 2012). In line with this finding, a study by Gaitan-Cepeda *et al* (2010) concluded that the presence of oral lesions was significantly correlated to treatment failure in patients on anti-retroviral medication.

A study by Oladukon *et al* (2013) in Nigeria revealed a higher occurrence of oral manifestations of HIV in children not on anti-retroviral treatment when compared to those on the medication. Other studies have however reported no significant change in the prevalence of orofacial manifestations of HIV in certain lesions such as aphthous ulcers and parotid gland swelling (MacPhail & Greenspan, 1997; Greenspan *et al*., 2001).

Over the years, several studies noted that as patients on HAART displayed an improved immune status, there was an increased occurrence of outbreaks of infectious opportunistic diseases (Shelburne *et al*., 2002; Gaitan-Cepeda *et al*., 2010). The terms immune reconstitution inflammatory syndrome (IRIS) and immune reconstitution disease (IRD), among other terms, were used to describe this phenomenon (Gaitan-Cepeda *et al*., 2010). In an attempt to establish whether oral lesions could be used as predictors for the development of IRIS, Ramirez-Amador *et al* (2011) found that several studies reported the occurrence of a high prevalence of human papillomavirus (HPV)-

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related lesions in the oral cavity among patient receiving HAART (Patton *et al*., 2000; Greenspan *et al*., 2001). Other studies reported an increase in the incidence of salivary gland disease with the incidence of HAART (Ortega *et al*., 2008; dos Santos Pinhero *et al*., 2009). This led to a conclusion that HPV-related oral lesions and salivary gland disease may be considered as a form of immune reconstitution syndrome; a belief also shared by Flint *et al* (2006).

However, due to the paucity of data on the oral manifestations of IRIS and the conflicting reports on oral lesions with HAART, the correlation of IRIS and oral lesions has not been fully established (Ramirez-Amador *et al*., 2011; Yengopal *et al*., 2016).

2.4 HIV-associated orofacial lesions

The World Health Organization (WHO) published a set of guidelines for carrying out epidemiological studies on oral manifestations of HIV. Highlighted within those guidelines was the need to target certain conditions expected to be most prevalent (Petersen *et al*., 2005). There is a need to understand the classifications and diagnostic criteria of these lesions when doing a prevalence study. This will help to determine which lesions to target. There have been a number of classification systems for orofacial lesions associated with HIV. Out of these classification systems, two stand out. The first is based on the aetiology of the lesion and classifies lesions into bacterial, viral, fungal, neoplastic or other conditions (Vaseliu *et al.*, 2006). The second classification system was proposed by the European Collaborative Clearing on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of HIV in 1993. This more widely used classification system organizes orofacial lesions into three categories based on the frequency of their association with HIV/AIDS (Ramos-Gomez *et al.*, 1999).

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The Collaborative Workgroup on the Oral Manifestations of Paediatric HIV Infections developed a framework for diagnosis for HIV-related oral diseases (Appendix 3). These guidelines were adapted from the classification system proposed in 1993 (Prabhu *et al.*, 2012; Ramos-Gomez *et al.*, 1999). According to this classification, Group 1 comprises of orofacial lesions commonly associated with a paediatric HIV infection. Group 2 lesions are those lesions that are less commonly associated with a paediatric HIV infection and Group 3 lesions are those lesions that are strongly associated with an HIV infection but are rarely seen in children (Ramos-Gomez *et al.*, 1999; Prabhu *et al.*, 2012).

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2.5 Diagnostic criteria of orofacial lesions in HIV-infected children

For diagnostic purposes, the Collaborative Workgroup on the Oral Manifestations of Paediatric HIV Infections describes a presumptive and a definitive criteria. A presumptive diagnostic criteria takes into consideration the clinical presentation of the particular lesion whereas a definitive diagnosis involves deriving a differential diagnosis from the presumptive criteria and performing laboratory tests to confirm the diagnosis (Ramos-Gomez *et al.*, 1999).

2.5.1 Oral candidiasis

This fungal infection is caused by Candida albicans presenting orally in different forms. Pseudomembranous candidiasis (thrush) is the most common form in children, with prevalence rates ranging between 6 and 72% (dos Santos Pinhero *et al*., 2009; Oladokun *et al.*, 2013; Meless *et al*., 2014; Nabbanja *et al*., 2013). Thrush presents clinically as white plaques on the buccal mucosa, tongue, palate, tongue, or oropharynx. One distinct feature that can help with the diagnosis is that the plaques can be easily wiped off, leaving a reddish/ ulcerated surface. The presence of oral thrush has been strongly associated with rapid progression of HIV (Nokta, 2008; Coogan *et al.*, 2005). Erythematous candidiasis presents as red patches on the tongue and palate whereas angular cheilitis presents as linear fissures on both corners of the mouth with a tendency of delayed healing due to the repeated mouth opening (Ramos-Gomez *et al.*, 1999; Flaitz & Hicks, 2003).

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2.5.2 Salivary gland disease

Schiodt and colleagues (1992) first described HIV-related salivary gland as swelling of one or both of the parotid glands. Parotid enlargement initially presents as a soft tissue swelling beside or beneath the ear, which gradually increases in size and may eventually cause facial asymmetry (Vaseliu *et al.*, 2006). It may occur either unilaterally or bilaterally. There may also be associated pain and xerostomia (Wilson *et al*., 2002). This condition generally appears to be a common phenomenon among HIV-infected children (Schiodt *et al*., 1992) and is reported to occur late in the HIV infection, marking a slower progression to AIDS (Jetpurwala & Jain, 2011). Schiodt *et al* (1992) suggested that the HIV infection itself does not directly attack the salivary gland. The parotid enlargement arises from CD4/CD8 infiltration into the salivary gland. In the era of HAART, the prevalence of parotid enlargement has been successfully reduced (Mandel & Vakkas, 2005). The action of HAART results in the halting of viral replication, a reduction in the viral load and subsequent stabilization of the CD4/CD8 cell counts (Ebrahim *et al*., 2014).

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2.5.3 Gingival and periodontal diseases

Gingival and periodontal diseases associated with HIV include linear gingival erythema (LGE), necrotising ulcerative gingivitis (NUG), necrotising ulcerative periodontitis (NUP) and necrotising stomatitis (NS) (*Classification and diagnostic criteria for oral lesions in HIV infection*, 1993; Robinson, 2002). Linear gingival erythma has been reported to be the most common HIV-related disorder of the gingiva in children (Ramos-Gomez, 2002). It presents as a band of redness along the margins of the unattached gingiva especially from canine to canine. It is usually painless although some patients report bleeding on brushing (Prabhu *et al*., 2012).

Necrotizing diseases of the periodontium associated with HIV are not commonly seen in children (Ryder *et al*., 2012). These conditions appear to be different stages of the same disease, the only distinction being their severity (Robinson *et al*., 2002). Several studies reported cases of NUG that progressed to necrotizing stomatitis (Robinson *et al*., 1998; Patton & McKaig, 1998). NUG and NUP are characterized by rapid destruction of the periodontal tissues and is associated with severe immunosuppression (Nokta, 2008). NUG presents as necrotic sloughing and ulceration of the interdental papilla accompanied by pain and halitosis whereas NUP on the other hand is far more destructive than NUG presenting with extensive loss of the gingiva, periodontal ligament and alveolar bone (Vaseliu *et al.*, 2006). Necrotizing stomatitis (NS) is a rare aggressive form of periodontal disease characterized by necrosis of the oral mucosa resulting in exposure of the underlying bone (Ramos-Gomez, 2002). Severe malnutrition, bad hygiene and poverty have been reported to have association with an increased risk for NS (Barrati-Mayer *et al*., 2013; Ashok *et al*., 2016).

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2.5.4 Ulcerative lesions

Any breach in the epithelial lining of the oral mucosa is referred to as ulceration (Regezi *et al*., 2007). There is a whole array of aetiological factors associated with ulceration. Some ulcers may occur as a result of an infection and may be viral, bacterial, fungal or atypical in origin, or may arise as a result of medication (Vaseliu *et al.*, 2006) and nutritional deficiencies (MacPhail & Greenspan, 1997). Ulcerative lesions may mimic each other, for example, ulcerations resulting from cytomegalovirus can mimic a number of persistent ulcerations such as aphthous ulcers and recurrent Herpes Simplex Virus (HSV) infection. The diagnosis of these ulcerations should therefore be definitive, i.e. confirmed by a laboratory test result (Ramos-Gomez *et al.*, 1999).

Recurrent Aphthous Ulcers constitute of a group of intra-oral ulcerative lesions commonly associated with a paediatric HIV infection. They can be classified as minor, major and herpetiform depending on their size, number and duration (Vaseliu *et al.*, 2006). In HIV-infected individuals these ul-

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cerations tend to be larger, more painful, slow-healing and tend to recur more frequently (Flaitz & Hicks, 2003). The cause of these non-specific ulcers is not well understood but some investigators attributed them to an adverse reaction to anti-retroviral drugs such as Didanosine (Jetpurwala & Jain, 2011). Recurrent aphthous ulcers are reported to occur in approximately 2% to 6% in the HIV-infected adult population (Ramos-Gomez *et al.*, 1999).

Herpes Simplex Virus (HSV) infection is a common condition affecting all children and is not specific to HIV. It presents in two forms, namely, primary herpetic gingivostomatitis and secondary herpes (Prabhu *et al.*, 2012). The primary form is most common among children. It presents initially as vesicles which rupture, leaving multiple ulcerations of the oral mucosa and lips. This condition is usually associated with systemic symptoms of fever and malaise (Vaseliu *et al.*, 2006).

2.5.5 Other Viral Infections

The Epstein Barr Virus (EBV) presents orally as Oral hairy leukoplakia (OHL). Though rarely seen in children it is a common oral manifestation associated with HIV. It presents bilaterally on the lateral border of the tongue as white, corrugated "hair-like" lesions that cannot be wiped off (Ramos-Gomez *et al.*, 1999). Since OHL is associated with immune suppression, its appearance in patients receiving anti-retroviral treatment may indicate non-adherence, treatment failure or disease progression (Nokta, 2008). In children, the clinical significance of OHL is not yet well documented. Chigurupati *et al* (1996) stated that the low prevalence of OHL in children could be because exposure to the Epstein Barr Virus does not occur in younger children. Dias *et al* (2006) hypothesized that the low prevalence can be explained by the high occurrence of candidiasis infection overlaying OHL resulting in OHL being clinically mistaken for candidiasis infection.

Human papilloma virus (HPV), also known as oral warts, present as cauliflower-like, spiked or raised lesions. They frequently appear in children as multifocal flat lesions resembling lesions of focal epithelial hyperplasia (Nokta, 2008). There have been reports of an increase in the prevalence of oral warts in HIV-infected individuals (Ryder *et al.*, 2012; Jetpurwala & Jain, 2011). Ryder *et al* (2012) linked the development of oral warts and other HPV-related lesions to the decrease in the $CD4^+$ count and a decrease in the viral load in HIV-infected individuals. The mechanism in which the reduction of the viral load leads to an increased risk of oral warts remains unclear. One study suggested that it may be due to the immune reconstruction taking place with anti-retroviral therapy (Reznick, 2006).

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Molluscum contagiosum is a superficial, benign condition caused by a pox virus, presenting clinically as either single or numerous pearl-white or skin-coloured papules (WHO Guideline, 2014). Among people living with HIV, its prevalence has been estimated at 5 to 18% (Gur *et al*., 2008). Immunocompromised children between the ages of 2 and 11 years are the most commonly affected (Brown *et al*., 2006). This condition commonly appears on the face and trunk. A more disseminated form of the disease may be indicative of advanced immunodeficiency (Vander & Tyring, 2002). Molluscum contagiosum is spread via direct skin-to-skin contact and has been found to be common among institutionalized patients (Wilson *et al*., 2002).

2.5.6 Malignancies associated with HIV

Although HIV-associated malignancies are not as common among the paediatric population as in adults, they are reported to affect HIV-infected children more than uninfected children (Davidson & Eley, 2010). Their prevalence is estimated to be 40 times more than in the general population (Mehta, 2006). Non-Hodgkin Lymphoma (NHL) and Kaposi sarcoma (KS) are among the most commonly reported HIV-linked malignancies. Kaposi sarcoma results from an exuberant expression on the Human herpetic-virus (HHV-8) as a result of the immune suppression. The clinical presentation varies from reddish-purple skin lesions to erythematous lesions in the oral mucosa (Mehta, 2006. The incidence of KS is reported to be substantially low especially in children on HAART (Davidson & Eley, 2010). The clinical presentation of NHL is indistinguishable from HIV, more so due to the fact that at the time of its diagnosis, children tend to have extra-nodal manifestation (Mehta, 2006).

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2.6 HIV and caries risk in children

The prevalence of dental caries has been a problem in children with HIV especially in the developing world. This has been attributed to the socio-economic factors, such as poor access to medical resources and preventive measures (Ramos-Gomez & Folayan, 2013). The DMFT/dmft index has been used in several studies to record the caries experience, expressed as DMFT for permanent teeth and dmft for primary teeth. This index is used to record the total number of decayed (D-/d-) missing (M-/m-) or filled (F-/f-) teeth in an individual (Klein *et al.*, 1938). The result is reported as a percentage of the total number of teeth present intra-orally.

Immunocompromised children in resource-limited populations have been found to have a higher caries experience than their unaffected peers (Naidoo & Chikte, 2004; Ramos-Gomez, 2002). Madigan *et al* (1996) reported an increased caries rate in HIV-infected children mainly because of

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the inappropriate dietary habits brought on by the failure to thrive. Some studies suggested that the caries experience in children is related to the acidic and sugary syrup medications consumed by these HIV patients, opportunistic infections and reduction in the salivary flow rate (dos Santos Pinhero *et al.*, 2009; Jetpurwala & Jain, 2011). An increased incidence has also been attributed to irresponsibility on the caregiver's part concerning oral health and dietary habits of the child (Nokta, 2008).

2.7 Motivation for the study

Several studies have been carried out on oral manifestations of paediatric HIV infection in developing countries such as Brazil (dos Santos Pinhero *et al.*, 2009), India (Ponnam *et al.*, 2012), Nigeria (Adebola *et al*., 2012; Oladokun *et al*., 2013), Uganda (Rwenyoni *et al*., 2011; Nabbanja *et al*., 2012), Mali, Cote d'Ivore and Senegal (Meless *et al.*, 2014). There is a paucity of data on orofacial manifestations of paediatric HIV infection in South Africa. South Africa has seen a significant increase in access to ART since 2004, with the introduction of new national guidelines.

The purpose of this study was to conduct an oral health survey among HIV-infected children younger than twelve years of age presenting at the Paediatric Infectious Disease Clinic at Tygerberg Hospital and to determine the factors contributing to the oral health status.

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CHAPTER 3: RESEARCH METHODOLOGY

Children living with HIV/AIDS in the city of Cape Town receive medical care from various health care facilities. Tygerberg Hospital is one of these institutions with a Paediatric Infectious Diseases Clinic (PIDC) dedicated to providing care for children with HIV/AIDS. The hospital has approximately 300 children enrolled in their programme. These children are cared for by general medical practitioners, paediatricians and the nursing staff who perform general medical assessments and reviews which may include various blood tests and enrolment of suitable candidates into the HAART programme. However, the oral health status of children living with HIV/AIDS currently enrolled with the Tygerberg Paediatric Infectious Diseases Clinic is unknown.

3.1 Aims and Objectives

The main aim of this study was to determine the oral health status and determinants of oral health of HIV-infected children at the PIDC at Tygerberg Hospital. The objectives of the study were to determine the following in the study population;

- the caries experience
- the dental treatment need
- the prevalence of orofacial lesions
- factors contributing to the oral health status

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3.2 Research design

This research was a carried out as a cross-sectional descriptive study.

3.3 Study Population

In an average year, Tygerberg PIDC sees and records viral load results of approximately 200 children younger than 16 years of age. This study, however, included children aged between 2 and 12 years currently enrolled with the hospital. The reason for this being that the upper age limit for paediatric dental patients at the Tygerberg Dental Faculty is 12 years of age.

3.4 Ethical considerations

Approval to conduct the study was sought from the University of the Western Cape Research Ethics Committee (Project Registration Number: **15/6/83**, Appendix 4). Permission to carry out the re-

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search at the Paediatric Infectious Diseases Clinic was obtained from the relevant authorities at Tygerberg Hospital (Appendix 5).

Participants were made aware of the study and given all the relevant information both verbally and in writing. Participation for the study was entirely voluntary, with participants were given the freedom to withdraw from the study at any point in time. For each child recruited for this study, informed consent was obtained from the parent/ legal guardian or caregiver before the questionnaire was administered. A written consent form (Appendix 6) was issued to each parent/ guardian in English and thoroughly explained verbally. In an effort to protect the identity and the confidentiality of the participants of this study, the patients' names were not recorded on the data capture sheet. Instead, the patients' medical record numbers were used for identification purposes. The data capture sheets for each patient enrolled in this study were kept safely in a locked cabinet in the Principal Researcher's office. This was done to protect the privacy of information collected from participants' medical records.

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3.5 Sampling criteria

A convenient sampling method was employed to select candidates who fit the selection criteria. Children living with HIV/AIDS are seen at Tygerberg PIDC from Monday to Wednesday. On the days of the examination, all patients who attended the outpatient clinic who were eligible for inclusion in the study were recruited.

3.5.1 Inclusion criteria

The criteria for inclusion into the study included;

- Children between the ages of 2 and 12 years of age with a confirmed HIV positive status
- Children with signed consent from a legal guardian
- Recorded viral load or $CD4^+$ count results obtained between August 2015 and June 2016

3.5.2 Exclusion criteria

Children from whom consent could not be obtained from the legal guardian were not included in this study. Children who did not comply with clinical examination as well as those who were unable to communicate, were excluded from the sample. Brief oral health advice was however given to all the children.

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3.6 Sample size

A statistician was consulted to assist with the estimation of the sample size. After doing a power calculation, 50 patients were found to be representative of the study population. A total number of 66 patients were recruited for the study. Between August 2015 and July 2016, the hospital recorded the viral loads of 190 children aged between 0 and 16 years. From this total, only 140 patients were between the ages of 2 and 12 years but only 66 met the inclusion criteria.

3.7 Data collection technique

The data collection process consisted of both quantitative and qualitative aspects. The former was used to capture the $CD4^+$ count and viral load of the patient as well as the DMFT/dmft. Socio-demographic aspects of oral health and diagnosis of the orofacial lesions were recorded through qualitative methods. Data collection was done through the use of a questionnaire, a clinical examination and a review of the patients' medical records.

3.7.1 Questionnaire

A structured questionnaire adapted from the WHO Oral Health Surveys-Basic Methods (2013) was administered verbally through an interview conducted with the child and their legal guardian or caregiver (see Appendix 7). The interview was conducted in English. The data captured from the interview included an inquiry on the child's oral hygiene practices, dietary habits and any past experiences of dental and orofacial ailments.

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3.7.2 Clinical examination

A standardized clinical examination was carried out on all participants by the principal researcher who is a qualified dental practitioner. For each child, a basic examination pack consisting of an explorer, a mirror, gauze and a head-light was used for the examination. A data capture sheet was used to record the information obtained from the clinical assessment (Appendix 8). The data capture sheet was generated by the principal researcher through an amalgamation of the basic charting format used in the Paediatric Dentistry Department of UWC and a form adapted from the WHO Oral Health Surveys-Basic Methods (2013).

The examination looked at the facial, extra-oral and the intra-oral tissues and included an inspection and palpation of the mouth and facial structures. The soft tissue oral lesions were diagnosed using a presumptive diagnostic criteria described by the Collaborative Workgroup on the Oral Manifestation of Paediatric HIV infections. A visual reference chart for health care workers depicting com-

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mon oral lesions in children with HIV/AIDS (Wilson *et al*., 2002) was also used as a reference for pictorial comparison of lesions to help with the presumptive diagnosis of lesions (Appendix 9).

To assess the dentition of the child, the WHO Oral Health Survey-Basic Methods criteria was followed. Each tooth was examined using a mirror and an explorer. All the carious lesions, restorations and missing teeth were recorded.

3.7.3 Medical Records

Each patient's demographic information and medical history was recorded from the hospital folder. This captured the patient's age, gender and date of birth. The immunological status, i.e. the $CD4^+$ count, viral load and clinical stage of the disease was also recorded from the medical folder. The HAART regimen the patient was taking as well as other co-morbidities and past medical conditions were also captured.

3.8 Pilot Study

A pilot study was carried out on 5 patients in March 2016, with the help of a co-supervisor (RM). The purpose of this process was to test the feasibility of the questionnaire and the adequacy of the data capture sheet. This session also provided an estimate of the time required to carry out the data collection on one patient. Unnecessary questions were omitted from the questionnaire and it was restructured (Appendix 7).

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3.9 Validity and Reliability

The methodology followed in this study was on par with the WHO Oral Health Survey: Basic Methods (2013). This allowed for a standardized procedure which is reproducible and comparable internationally.

3.9.1 Inter-examiner calibration

The five children (10% of the estimated sample size), all fitting the selection criteria, were examined following the outlined procedure. The children were then re-examined by another examiner (RM), who was familiar with the data capture sheet, to ensure consistency in the diagnosis.

3.9.2 Intra-examiner calibration

In order to maintain consistency throughout the study the extra-oral and intra-oral examinations as well as the data recording were carried out by the primary researcher.

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4.0 Data analysis

The data was entered into a Microsoft Excel 2010 spreadsheet. Statistical analysis was performed using R-project program (R Core Team, 2014). Descriptive statistical analyses were done for quantitative variables in the form of means, standard deviations (SD) and 95% confidence intervals (CI). The General Linear Models approach of the Poisson family was used to determine the association between orofacial lesions and children's characteristics. Frequency tables were used to summarize and identify the most common orofacial lesions and children's characteristics.

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CHAPTER 4: RESULTS

4.1 Characteristics of the sample

4.1.1 Characteristics of the sample according to age, gender, anti-retroviral medication, immune status

Table 1: The frequency distribution of children according to age, gender, anti-retroviral status, $CD4^+$ cell count and viral load.

Characteristics	Number of participants (%)
Gender	
Male	38 (57.6%)
Female	28 (42.6%)
Age Group (years)	
2-6	34 (51.5%)
7-12	32 (48.5%)
Anti-retroviral status	
On HAART	63 (95.5%)
Not on HAART	3 (4.5%)
$CD4^+$ count (Cells/mm^3)	
Unknown	14 (21.2%)
<200	1 (1.5%)
200-500	6 (9.1%)
500	45 (68.2%)
Viral load (Copies/mL)	
<50	31 (47%)
50-1000	18 (27.3%)
1000-10 000	8 (12.1%)
>10 000	9 (13.6%)

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4.2 Prevalence of orofacial lesions

4.2.1 Frequency of orofacial lesions

Table 2: The frequency distribution of orofacial lesions

Lesion type	**Frequency** ***n***	**% Sample** ***n=66***	**% Lesions** ***n=30***
Candidiasis	12*	18.2	44.4^
Pseudomembranous	3	4.5	10
Erythematous	1	1.5	3.3
Angular cheilitis	11	16.7	36.7
Parotid enlargement	1	1.5	3.3
Herpes labialis	3	4.5	10
Linear gingival erythema	2	3	6.7
ANUG	1	1.5	3.3
Atypical oral ulcers	4	6.1	13.3
Molluscum contagiosum	3	4.5	10
Non Hodgkin lymphoma	1	1.5	3.3

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*Three children presented with two concomitant types of candidiasis
n=27 lesions for this line ONLY, to account for the 3 children (30-3)

4.2.2 Distribution of lesions

Table 3: Distribution of lesions according to each child

Number of lesions	**0**	**1**	**2**	**3**
Observed frequency	45	13	7	1
% total sample	68.2	19.7	10.6	1.5

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4.2.3 Lymphadenopathy

Table 4: Distribution of lymphadenopathy among the sample population

Presence of lymphadenopathy	Frequency (%)
N	42 (63.6)
Y	24 (36.4)
Total	66

4.3 Factors associated with orofacial lesions

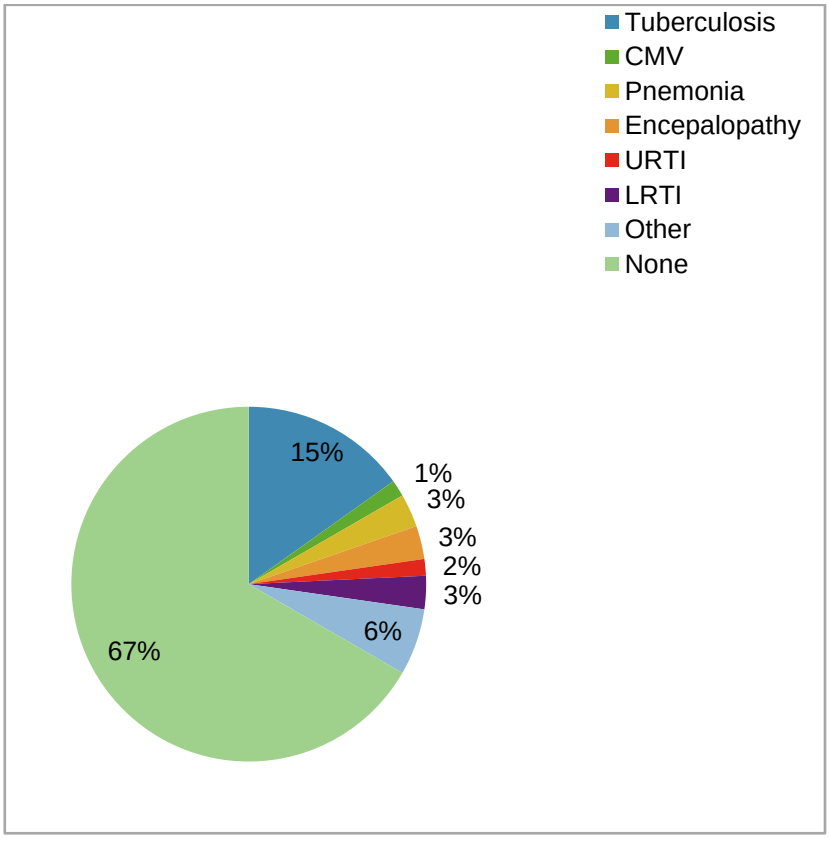

Figure 1: Comorbidities among participants

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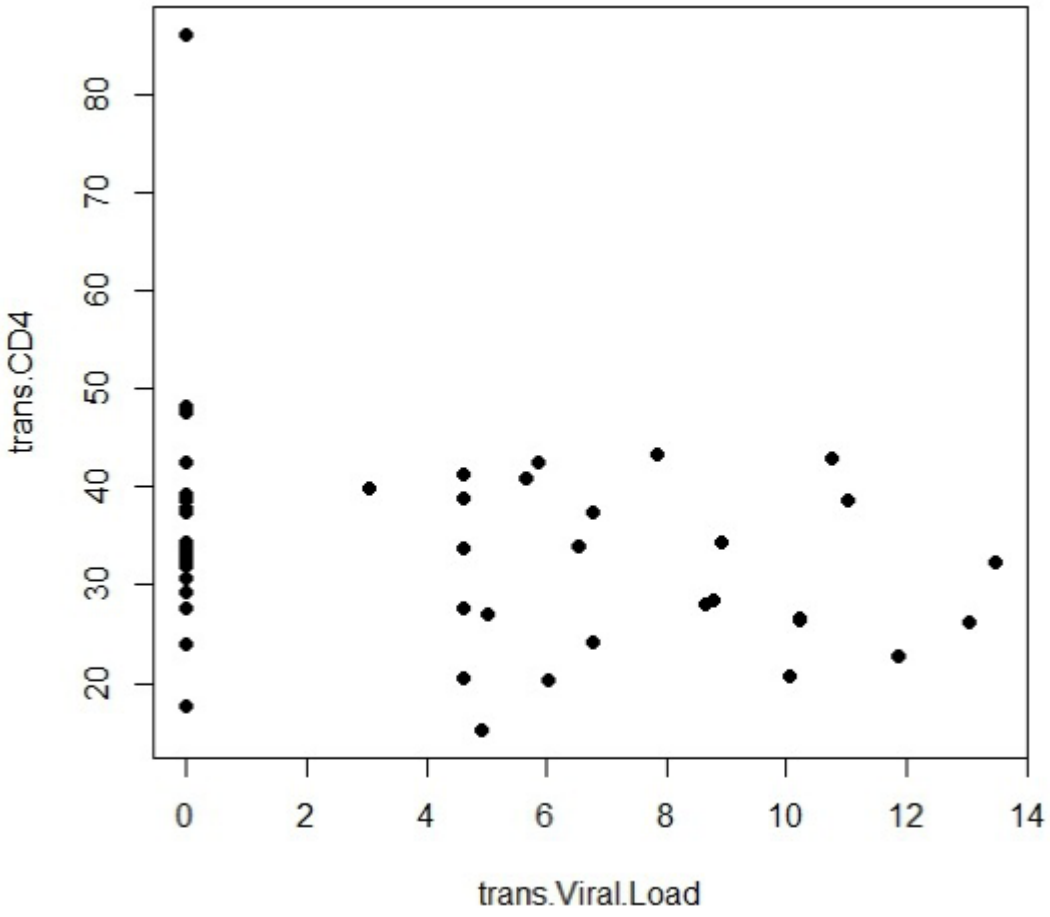

Figure 2: Association between $CD4^+$ count and Viral Load

Figure 2 is a plot of trans.$CD4^+$ vs trans.Viral.Load. According to this graph there is little or no correlation between the two variables; the (Pearson) correlation coefficient between them is -0.264, p-value=0.073.

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4.3.1 Orofacial lesions and CD4^{+} cells/mm^{3} of blood

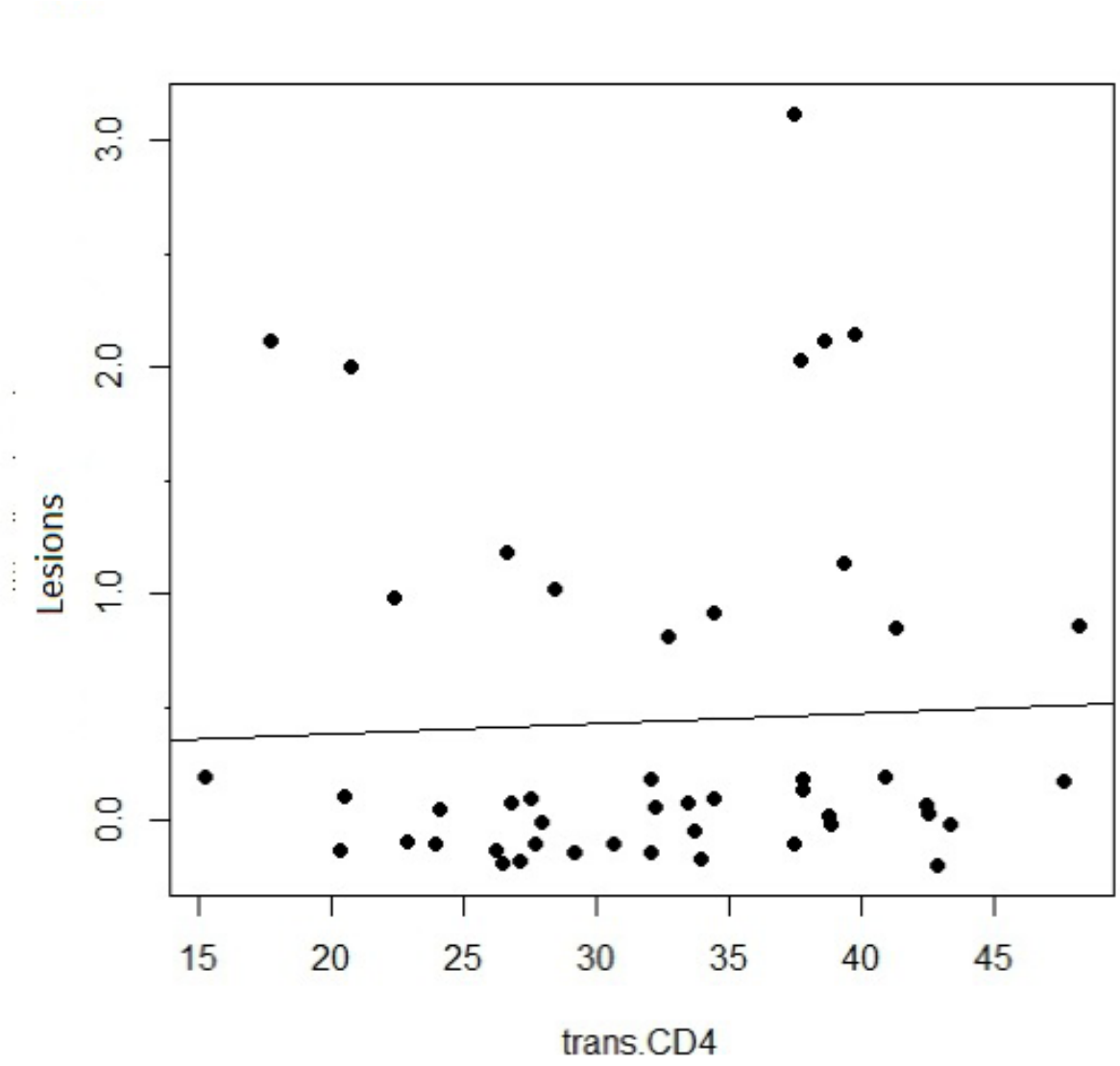

Figure 3 Association between orofacial lesions and CD4^{+} count

Figure 3 is a plot of Lesions vs trans.CD4^{+} The result of fitting a linear regression with dependent variable Lesions, and predictor trans.CD4^{+}, is that the effect of CD4^{+} is not significant; P=0.715. The General Linear Models approach, family=Poisson, was used in this analysis. It clearly illustrates the lack of correlation between the two variables; note that the lesion points are slightly offset from the integer values so as to make all observations visible.

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Table 5: Distribution of orofacial manifestations with respect to $CD4^+$ count

Lesion type	**>500** (%)	**500-200** (%)		**<200** (%)	**Unknown (%)**
Candidiasis					
Pseudomembranous	2 (6.7)	-		-	1 (3.3)
Erythematous	-	1 (3.3)		-	0
Angular cheilitis	8 (26.7)	2 (6.7)		1 (3.3)	-
Parotid enlargement	-	-		-	1 (3.3)
Herpes labialis	3 (10)	-		-	0
Linear gingival erythema	1 (3.3)	-		-	1 (3.3)
ANUG	1 (3.3)	-		-	0
Atypical oral ulcers	1 (3.3)	-		-	3 (10)
Molluscum contagiosum	2 (6.7	-		-	1 (3.3)
Non Hodgkin's lymphoma	-	-		-	1 (3.3)
Total	**18 (60)**	**3 (10)**		**1 (3.3)**	**8 (26.7)**

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4.3.2 Orofacial manifestations and Viral load copies/mL of blood

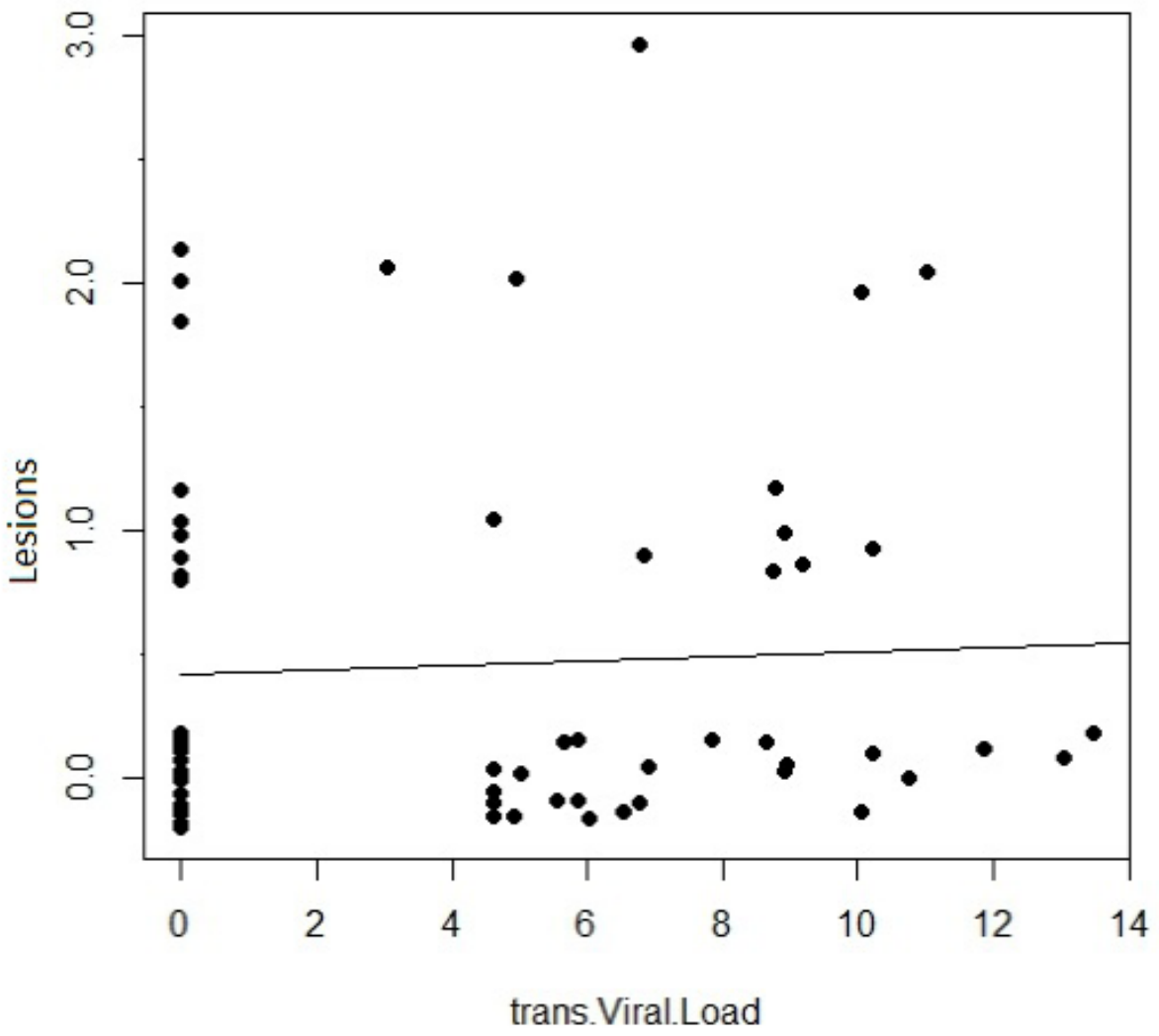

Figure 4: Association between orofacial lesions and viral Load

Figure 4 is a plot of Lesions vs trans.Viral.Load. The line on this graph represents the fitted model, using the same technique as for Lesions vs trans.$CD4^{+}$. Its slope is not significantly different from zero, indicating non-significant association between the two variables; P=0.638.

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Table 6: The distributions of orofacial manifestations with respect to the viral loads

Lesion type	<50 (%)	<1000 (%)	1000-10,000 (%)	>10,000 (%)
Candidiasis				
Pseudomembranous	-	2 (6.7)	-	1 (3.3)
Erythematous	-	-	-	1 (3.3)
Angular cheilitis	3 (10)	5 (16.7)	2 (6.7)	1 (3.3)
Parotid enlargement	-	-	1 (3.3)	-
Herpes labialis	2 (6.7)	1 (3.3)	-	-
Linear gingival erythema	2 (6.7)	-	-	-
ANUG	-	1 (3.3)	-	-
Atypical oral ulcers	3 (10)	1 (3.3)	-	-
Molluscum contagiosum	2 (6.7)	1 (3.3)	-	-
Non Hodgkin's lymphoma	-	-	-	1 (3.3)
Total	**12 (40)**	**11 (36.7)**	**3 (10)**	**4 (13.3)**

4.3.3 Association between orofacial lesions, CD4$^+$ count and viral load

Table 7: Association between orofacial lesions, CD4$^+$ count and viral load

Variable	Presence of Oral lesion	Mean (SD)	p-value
CD4$^+$ count	Yes	1176.9 (±561.5)	0.701
	No	1296.8 (±1390.9)	
Viral Load	Yes	8330.0 (±14,727.9)	0.176
	No	55,369.1 (±148,753.5)	

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4.4 Dental caries experience

4.4.1 Caries experience in primary teeth

Table 8: Caries experience in the primary dentition according to gender and age group

Characteristic		dmft		
		dmft = 0	dmft > 0	Mean dmft ± STD
Gender	Female	7 (10.9%)	19 (29.7%)	5.46 ± 4.95
	Male	7 (10.9%)	31 (48.4%)	6.37 ± 4.55
Age group	2-6	10 (15.6%)	24 (37.5%)	5.88 ± 5.34
	7-12	4 (6.3%)	26 (40.6%)	6.13 ± 3.94

Two children were in the permanent dentition (n=64)

The overall caries experience in primary teeth (dmft>0) is 78.1% (95% CI 66.0-87.5)

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4.4.2 Caries experience in permanent teeth

Table 9: Caries experience in the permanent dentition according to gender

Characteristic		DMFT		
		DMFT = 0	DMFT > 0	Mean ± STD
Gender	Female	11 (30.6%)	7(19.4%)	0.89 ± 1.37
	Male	10(27.8%)	8 (22.2%)	0.83 ± 1.20

30 children were still in the primary dentition (n=36).

The caries experience (DMFT>0) is 41.7% (95% CI= 25.5-59.2)

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4.4.3 Distribution of Decayed (D-/d-), Missing (M-/m-) and Filled (F-/f-) Teeth

Table 10: Distribution of decayed, missing and filled teeth according to age group

	D-/d-	M-/m-	F-/f-	DMFT/dmft
2-6 year	5.12 ± 5.44	0.74 ± 2.08	0	5.97 ± 5.43
7-12 year	5.09 ± 4.28	1.38 ± 3.18	0.125 ± 0.71	6.63 ± 4.53
Overall DMFT-/dmft-				6.30 ± 4.99

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4.5 Factors associated with the caries experience

4.5.1: Oral health determinants as reported by children's caregivers

Table 11: Oral health determinants as reported by children's caregivers

Variable	Categories	Frequency n (%)
Guardian	Parent Relative Other	44 (66.7) 8 (12.1) 14 (21.2)
Discomfort in the mouth	Often Occasionally Rarely Never Don't Know	3 (4.5) 15 (22.7) 1 (1.5) 40 (60.6) 7 (10.6)
Previous dental visits	Once More than once None in the past 12 months Never Don't know	11 (16.7) 3 (3.5) 7 (10.6) 40 (60.6) 5 (7.6)
Reason for visit	Discomfort Check-up Follow-up Don't know N/A	9 (13.6) 2 (3.0) 2 (3.0) 2 (3.0) 51 (77.3)
Frequency of tooth brushing	Never Once a day Two or more times a day Occasionally	6 (9.1) 28 (42.4) 26 (39.4) 6 (9.1)
Toothpaste used	Adult toothpaste Baby toothpaste None	40 (60.6) 19 (28.8) 7 (10.6)
Problems experienced	Aesthetics Chewing Sleep disturbance School attendance Don't know None	6 (9) 8 (12.1) 1 (1.5) 1 (1.5) 4 (6.1) 46 (69.7)

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4.5.2 Dietary habits of participants

Table 12: Dietary determinants as reported by children's caregivers

Variable	Categories	Frequency n (%)
Fresh fruit	Never Everyday Once a week Several times a week Several times a month	1 (1.5) 1 (1.5) 1 (1.5) 41 (62.1) 22 (33.3)
Sugary snacks	Never Everyday Several times a day Several times a week Several times a month	1 (1.5) 22 (33.3) 36 (54.5) 1 (1.5) 6 (9.1)
Sugary drinks	Never Everyday Several times a day Several times a week	1 (1.5) 28 (42.4) 20 (30.3) 17 (25.8)
Candy/Sweets	Never Several times a day Several times a week Several times a month	3 (4.5) 2 (3.0) 15 (22.7) 46 (69.7)
Coffee/tea with sugar	Never Everyday Several times a day Several times a week Several times a month	2 (3.0) 32 (48.5) 1 (1.5) 9 (13.6) 22 (33.3)

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CHAPTER 5: DISCUSSION

5.1 Characteristics of participants

A total of 66 (47.1%) children were recruited for this study. Table 1 shows the gender distribution of the sample. The M:F ratio was 1.36:1. The mean age of participants was 6.167 (±2.726); 5.292 (±2.827) among female participants and 6.342 (±2.674) in males. The majority of the participants were on HAART (95.5%), refer to Table 1.

5. 2 Prevalence of orofacial manifestations of HIV

At the time of the study, 21 children (31.8%) presented with at least one orofacial lesion (95% CI: 21.9-44.4). A total of 30 lesions were diagnosed among the 21 children. Table 2 displays the distribution of orofacial lesions among the children. The majority of the children had a single type of lesion. Eight (38.1%) children had more than one lesion in their mouths (Table 3). The prevalence of orofacial manifestations of HIV in children varies significantly among resource-limited countries. Studies reported prevalence rates ranging from as low as 8.3% in West Africa (Meless *et al*., 2014) to as high as 77.4% in Uganda (Nabbanja *et al*., 2013).

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The prevalence of orofacial manifestations of HIV in this study corroborates a prevalence of 31.4% reported in Brazil (Miziara *et al*., 2005). However, this finding is significantly lower than those found in Tanzania, India, Nigeria and Uganda (Hamza *et al*., 2006; Kaul *et al*., 2009; Oladokun *et al*., 2013; Rwenyonyi *et al*., 2011). The lower prevalence in this study may be explained by the fact that in the aforementioned studies, a large number of participants were not on HAART. Another factor contributing to the relatively low prevalence of oral manifestations of HIV in this study is the exclusion of cervical lymphadenopathy (Table 4). In studies where cervical lymphadenopathy was included, the reported prevalence of orofacial manifestation ranged between 64% and 78% (Kaul *et al*., 2009; Rwenyonyi *et al*., 2011; Nabbanja *et al*., 2013). Close to 40% of the sample in the current study presented with lymphadenopathy. Several children in this study were found to have other co-morbidities (Figure 1) which could present with lymphadenopathy thereby leaving room for bias. One such case was of a child with submental lymphadenopathy who was found to have concomitant ulcerative infections and multiple carious teeth (Appendix 10), which made it difficult to pinpoint the exact cause of the lymphadenopathy. The following table summarizes several studies highlighting the prevalence of orofacial lesions in children with HIV in various countries.

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Reference	Country	Age group	(n)	Prevalence
Olaniyi *et al. (*2005)	Nigeria	18-168 months	36	41.7% prevalence of orofacial lesions.
Hamza *et al.* (2006)	Tanzania	2-17 years	51	43,1% had at least one orofacial lesion
Miziara *et al.* (2006)	Brazil	0-12years	459	31.4% prevalence of oral lesions (excluding cervical lymphadenopathy)
Kaul *et al.* (2009)	India	2-12 years	48	64.58% prevalence of orofacial lesions including cervical lymphadenopathy accounting for 14.58%)
Duggal *et al*. (2010)	South Africa	0-4 years	56	51.8% had oral mucosal lesions
Rwenyonyi *et al.* (2011)	Uganda	1-12 years	237	73% had at least one orofacial manifestation of HIV (including cervical lymphadenopathy accounting for 60.8%)
Adebola *et al*. (2012)	Nigeria	2-156 months	105	61.9% prevalence of orofacial lesions
Sale-Peres *et al*. (2012)	Mozambique	1.7-16 years	90	13.3% oral mucosal lesions
Oladokun *et al*. (2013)	Nigeria	3-204 months	127	55.9% had at least one orofacial manifestation of HIV
Nabbanja *et al*. (2013)	Uganda	1.5-17 years	368	77.4% prevalence of orofacial mucosal lesions (including cervical lymphadenopathy, accounting for 28.5% of the cases.
Meless *et al*. (2014)	West Africa	5-15 years	420	Oral mucosal mucosal lesions present in 8.3% of the patients (cervical lymphadenopathy excluded)
Present study	South Africa	2-12 years	66	31.8% had at least one orofacial lesion (excluding lymphadenopathy)

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5.2.1 Oral Candidiasis

Frequencies of orofacial lesions in the present study are summarized in Table 2. Candidal infections were the most common lesions encountered, accounting for 44.4%. Several studies reported a wide variability in the prevalence of oral candidiasis among children, ranging from 22.5% to 83.3% (Naidoo & Chikte, 2004; Samarayanake *et al*., 1992). Pseudomembranous candidiasis was reported to be the most prevalent variant among children, with values ranging between 6% and 72% (Meless *et al*., 2014; Oladokun *et al*., 2013; Nabbanja *et al*., 2013). Contrary to the aforementioned studies, the current study found angular cheilitis to be the most common form of candidiasis. This variation may be attributed to a number of factors, among them being the diagnostic methods used and clinical and demographic features of the study group (Campo *et al*., 2002; Samarayanake *et al*., 1992). With respect to diagnostic methods applied, some studies included a definitive laboratory test which was not part of this study.

Three children presented with two concomitant types of candidiasis. Oral candidiasis has been found to be a good indicator of immune suppression, thus seen commonly in patients who have progressed to AIDS (Coogan *et al*., 2005; Gaitán-Cepeda *et al*., 2014; Nittayanata, 2016). In this study, 75% of children with candidal infection had viral loads above 50 copies/mL (which is indicative of immune suppression). Gaitán-Cepeda and colleagues (2014) observed a high prevalence of oral candidiasis among severely immunodeficient children with viral loads above 100,000 copies/mL. The current study found one child with a concomitant infection of median rhomboid glossitis (erythematous candidiasis) and angular cheilitis who was severely immunocompromised, with a viral load above 100,000 copies/mL (Appendix 10)

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5.2.2 Parotid Enlargement

The prevalence of salivary gland enlargement varies significantly among paediatric populations, with prevalences ranging from 0% to 58% (Schiodt *et al*., 1992). With respect to parotid enlargement, the current study found a lower prevalence as compared to studies conducted in Tanzania, India, Uganda, Nigeria and West Africa (Hamza *et al*., 2006; Kaul *et al*., 2009; Rwenyonyi *et al*., 2011; Oladokun *et al*., 2013; Meless *et al*., 2014). There were suggestions that HIV-associated salivary gland disease is associated with a favourable prognosis (Schiodt *et al*., 1992). However, in the present study, the only child who had parotid enlargement was severely immunocompromised with a high viral load. This finding correlates with conclusions from studies that HIV-associated parotid enlargement occurs late in the infection, marking a progression to AIDS and immune failure (Jetpurwala & Jain, 2012; Prabhu *et al*., 2013).

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5.2.3 Gingival and periodontal disease

The prevalence of linear gingival erythema (LGE) in children with HIV varies between populations and can range from 0 to 48% (Ramos-Gomez *et al*., 1999; Hamza *et al*., 2006; Kaul *et al*., 2009; Rwenyonyi *et al*., 2011). In this study, two children (3%) were found to have LGE, both of whom had an undetectable viral load. However, several children had poor oral hygiene and increased dental plaque, making LGE difficult to distinguish from conventional gingivitis. Studies comparing the prevalence of LGE in HIV-infected and HIV-negative participants found that not only was LGE equally common in the two groups but was associated with plaque in both groups (Grbic *et al*., 1995; Robinson *et al*., 1998). This led to a suggestion that HIV gingivitis (LGE) may be indistinguishable from conventional gingivitis, hence the wide variability in the prevalence (Robinson, 2002).

Acute necrotizing ulcerative gingivitis (ANUG) and acute necrotizing ulcerative periodontitis (ANUP) are far less common in children, with a prevalence varying between 0.2% and 5% (Ramos-Gomez et al., 1999; Ranganathan *et al*., 2006; Flaitz *et al*., 2001). This study found a prevalence of 1.5%, corroborating the 1.7% reported by Meless and colleagues (2014). Studies have linked the occurrence of gingivitis and periodontal disease in HIV-infected individuals to other relevant factors such as poor oral hygiene (Robinson, 2002; Leão *et al*., 2009). This adds to the conclusion that HIV infection alone does not predispose patients to periodontal disease (Samarayanake *et al*., 1992).

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5.2.4 Ulcerative Lesions

In the current study, 6.1% of the sample population was found to have oral ulceration. Without definitive diagnostic aids in this study, ulcerative lesions could not be distinguished from each other. Naidoo and Chikte (2004) reported a prevalence of 6% for atypical ulcerative lesions among outpatient children in South Africa, corroborating findings of the current study. As definitive diagnoses could not be reached due to the fact that ulcerative lesions seldom mimic each other, all ulcerative conditions were lumped together in the present study with the exception of recurrent aphthous ulcers and herpes labialis, a form of Herpes Simplex Virus.

Several studies reported a higher prevalence of recurrent aphthous ulcerations, ranging between 0.4% and 14.1% (Oladukon *et al*., 2011; Rwenyonyi *et al*., 2011; Nabbanja *et al*., 2013; Meless *et al*., 2014). This study did not find any cases of recurrent aphthous ulcerations. The correct diagnosis of recurrent aphthous ulcers is dependent upon an accurate and detailed clinical history to complement the clinical findings (Tarakji *et al*., 2015). Atypical oral ulcers could have potentially been

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recurrent aphthous ulcers; but due to the difficulty in eliciting a detailed history from the paediatric population and their guardians, proper diagnosis could not be reached. Studies report the prevalence of Herpes Simplex Virus (HSV) infection to be between 1.7% and 24 % (Ramos-Gomez *et al.*, 1999; Flaitz & Hicks, 2003; Rwenoynyi *et al*., 2011; Bodhade *et al*., 2011). In the current study 4.5% presented with herpes labialis.

5.2.5 Viral Lesions

With respect to orofacial lesions resulting from viral infections, in this study molluscum contagiosum was the most common lesion with a prevalence of 4.5%. This is higher when compared to the 0.9% and 3% reported by Ranganath *et al*., (2010) and Flaitz *et al*., (2001) respectively. The higher prevalence may be explained by the fact that most children live in crowded households and institutions. Several factors have been found to encourage the spread of molluscum contagiosum. Outbreaks of this condition have been noted where there is poor hygiene, low socioeconomic status and overcrowded households (Naidoo & Chikte, 2004; Brown *et al.*, 2006; Reynolds *et al*., 2009).

5.2.6 Malignancies

HIV associated malignancies are generally uncommon in the paediatric population (Davidson & Eley, 2010). Most studies found Kaposi sarcoma (KS) to be the most common neoplastic lesion (Hamza *et al*., 2006; Oladukon *et al*., 2013; Nabbanja *et al*., 2013). In the current study, one child (1.5%) was found to have a Non-Hodgkin's Lymphoma (NHL). This child had a very high viral load despite being on HAART, signifying immune failure. NHL is usually seen in late stages of AIDS where $CD4^+$ counts are below 100 cells/mm^3 (Bajpai & Pazare, 2010). In this era of anti-retroviral treatment most patients tend to maintain high $CD4^+$ counts and low viral loads. This may explain the low prevalence rate of NHL.

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5.3 Factors associated with orofacial lesions

In an effort to assess factors associated with the occurrence orofacial lesions, the level of immunosuppression was assessed. The $CD4^+$ count and viral load, although measuring different aspects of immunity, should have an inverse relationship (HIV-ibase, 2016). Ideally, when the viral load is low, the $CD4^+$ count should be high and vice versa. The current study however found that there was little or no correlation between $CD4^+$ counts and viral load. Figure 2 is a plot of trans.$CD4^+$ vs trans.Viral.Load. According to this graph, there is little or no correlation between the two variables. The Pearson correlation coefficient between them is -0.264 and a P-value=0.073. A study by Shah (2006) also found no significant correlation between the two variables in their study.

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It has been hypothesized that the presence of orofacial lesions in patients with HIV coincides with a deterioration of the immune status, i.e. low $CD4^+$ count and a high viral low (Baghirath *et al*., 2013). Ideally, a lower $CD4^+$ count is expected predispose one to a high susceptibility for orofacial lesions (Adebola *et al*., 2012; Sale-Peres *et al*., 2012). Figure 3 is a plot of Lesions vs trans.$CD4^+$. The result of fitting a linear regression with a dependent variable (lesions) and predictor (trans.$CD4^+$) is that the effect of $CD4^+$ is not significant on the presence of orofacial lesions; p-value=0.715. The General Linear Models approach of the Poisson family, was used in this analysis. This study corroborates findings from Nabbanja *et al* (2012) where no significant correlation was found between $CD4^+$ count and oral lesions among a group of Ugandan children. Gaitan-Cepeda *et al* (2010) also concluded that the presence of oral lesions was a poor predictor of lowered $CD4^+$ counts.

A study by Rwenyonyi and colleagues (2011) explored factors influencing the distribution of oral lesions in children aged between 1 and 12 years of age with HIV/AIDS. They found that even though there are confounding factors associated with the presence of oral lesions, children with $CD4^+$ counts below 500 cells/mm^3 had more lesions than those with $CD4^+$ counts above 500 cells/mm^3. Contrary to the aforementioned study, the current study surprisingly found that 60% of the lesions were present in children with $CD4^+$ counts above 500 cells/mm^3 (Table 5).

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With respect to the correlation between viral load and the presence of orofacial lesions, this study did not find any significant association. Figure 4 is a plot of lesions vs trans.Viral Load. The line on this graph represents the fitted model. Its slope is not significantly different from zero, indicating a non-significant association between the two variables; p=0.638. In the present study, children with a viral load less than 50 copies/mL had more orofacial lesions (Table 6). These patients are clinically described as doing well and adhering well to the HAART medication. Oladokun and colleagues (2013) investigated the type of oral lesions seen in HIV-positive patients in Nigeria, as well as their correlation to the patient's clinical stage, viral load and $CD4^+$ count. Their study found no significant correlation between the viral load and orofacial lesions, corroborating findings from this study. Their study among several other studies concluded that the $CD4^+$ count was a better indicator of the disease progression than the viral load (Bodhade *et al*., 2011; Rwenyonyi *et al*., 2011; Sale-Peres *et al*., 2012; Adebola *et al*., 2012).

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Table 7 shows a comparison between the mean $CD4^+$ counts and mean viral loads of children with and without orofacial lesions. The difference between these the two groups were not statistically significant, i.e. p=0.701 and p=0.176 respectively. This highlights the lack of a significant correlation between immunosuppression and presence of orofacial lesions. Contrary to the current study, a study done by Duggal *et al* (2010) among South African children with HIV found an association between the viral load and $CD4^+$ counts and the presence of oral lesions. The results of the present study corroborate findings from Meless and colleagues (2014) that the occurrence of orofacial lesions is independently associated with immunosuppression. These findings suggest that the $CD4^+$ count and viral load are not indicators of disease progression.

5.4 Caries prevalence and experience

A high proportion of children in this study presented with a severe pattern of dental caries. An overall prevalence of 78.8% (95% CI=67.0-87.9) was recorded among the study population. In the primary dentition, a prevalence of 78.1% (95% CI= 66.0-87.5) was found; significantly higher than the 41.7% (95% CI= 25.2-59.2) found in the permanent teeth. The results of this study corroborate reports of a high caries experience amongst HIV-infected children, especially in the primary dentition (Howell *et al*., 1992; Nabbanja *et al*., 2013; Yengopal *et al*., 2016). Studies have reported caries prevalence ranging from 40% to 86% in the primary dentition (Beena, 2011; Rwenyonyi *et al*., 2011; Nabbanja *et al*., 2013; Meless *et al*., 2014).

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Looking at the severity/caries experience in the deciduous dentition (Table 8), the mean dmft was 6.0 ± 4.70 with no significant difference between males (6.37 ± 4.55) and females (5.46 ± 4.95). There was no significant difference in the mean dmft of the two age groups, i.e. 2 to 6 years and 7 to 12 years. In the scientific literature, the reported mean dmft ranges between 1.5 and 11.8 (Madigan *et al*., 1996; dos Santos Pinhero *et al*., 2009; Cerqueira *et al*., 2010; Meless *et al*., 2014). Contrary to the findings of the current study, Sahana *et al* (2013) found the dmft in children with perinatally acquired HIV was significantly lower and comparable to that of normal children. A meta-analysis by Oliveira and colleagues (2015) concluded that even though studies reported a high dmft, there was no significant association between the caries experience and HIV-infection.

In the permanent dentition (Table 9), the mean DMFT for the sample population was 0.86 ± 1.29. There was no significant variation between girls (0.89 ± 1.37) and boys (0.83 ± 1.20). Several stud-

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ies have reported mean DMFT ranging from 0.5 to 4.0 (Madigan *et al*., 1996; dos Santos Pinhero *et al*., 2009; Cerqueira *et al*., 2010; Sahana *et al*., 2013; Meless *et al*., 2014). The results of the current study highlighted an overall low caries experience (mean DMFT) in the permanent dentition. Oliveira and colleagues (2015) found that the data on the caries experience in the permanent dentition although insufficient, revealed a low mean DMFT.

Table 10 depicts the distribution of mean decayed (D-/d), missing (M-/m-) and filled (F-/f-) teeth among the different age groups. The mean number of decayed, missing and filled teeth (DMFT/dmft) amongst the participants was 6.30 ± 4.99 (Table 10). The older age group, 7 to 12 years had a higher mean decayed (D-/d-) variable. This substantiates conclusions that older children have more decayed teeth compared to the younger children because their teeth are exposed to environmental risk factors longer (Ferraro & Vieira, 2010; Wang *et al*., 2012). In the present study, decayed teeth accounted for 82.2% of the total number of DMFT/dmft. According to literature the F-/f- component is rarely reported in children. If reported, the values are usually low (Rwenyonyi *et al*., 2011; Nabbanja *et al*., 2013). Only one child had received restorative treatment, represented by a low mean filled index (F-/f-) of 0.125. The most popular form of treatment for dental caries received by children in this study was extraction. The undesirable consequences of premature loss of deciduous teeth have been thoroughly discussed in the literature. Early loss of primary teeth may predispose one to crowding and malposition of permanent teeth (Ahamed *et al*., 2012).

Of the 52 children (78.8%) with dental caries experience, 47 had untreated carious teeth. This value, described as "Unmet Treatment Need (UTN)", is calculated by dividing the percentage of untreated caries by the caries prevalence (Van Wyk & Van Wyk, 2004). In the current study, an UTN of 90.4% was found among participants. This correlates to the 92% UTN among 4-to-5-year-old children reported by Van Wyk & Van Wyk (2004). Joosab and colleagues conducted two studies in 2012 investigating the caries experience among children living with HIV in South Africa. They found prevalences of 62.9% and 70.9% and mean dmft indices of 4.2 and 5.1 respectively. The UTN among children in this study ranged from 87.8% to 100%. The report on the National Children's Oral Health Survey (South African Department of Health, 2003) concluded that approximately 45%-60% of children in South Africa required treatment for dental caries. In the Western Cape Province, this UTN was reported to be as high as 80% (Singh, 2011; Ramphoma, 2016). The results of the current study are therefore no different from other findings with regards the caries experience among children in South Africa.

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5.5 Factors associated with caries experience

Medically compromised children who are on long-term medication are generally classified as having a high caries risk (Foster & Fitzgerald, 2005). Children living with HIV have been found to be susceptible to dental caries (Leão *et al*., 2009). Studies have established a direct relationship between caries risk and HIV, particularly with respect to the potentially cariogenic and xerostomic anti-retroviral medication (Nittayananta *et al*., 2010; Oliveira *et al*., 2015; Nittayananta, 2016). Other factors implicated in the heightened prevalence of dental caries among children with HIV include diminished flow of saliva and a reduction in the salivary antibodies (dos Santos Pinhero *et al*., 2009; Oliveira *et al*., 2015). Due to the absence of an HIV-negative control group in this study, a direct relationship between the HIV infection and caries prevalence/severity could not established.

Control of oral disease is often dependent upon several environmental factors such as dietary factors, family factors, behavioural factors and access to oral health services (Hashim *et al*., 2006). Table 11 summarizes some of these factors. The family and social environment include the child's caretaker, the number of siblings in a household as well as household crowding (Petersen *et al*., 2005; Wang *et al*., 2012). In this study, 21.2% of children were under the care of an institution or foster care, categorized as 'other'. The institutionalized children were orphaned and had concomitant ailments. Children under the care of a relative were cared for by a grandparent, an aunt or an uncle. Most of the children hailed from poor households. The association between poor oral health in children and low socioeconomic status of the family has been widely documented in the literature (Petersen *et al*., 2005; Castilho *et al*., 2013).

Access to oral health care is a crucial factor in the prevention and management of dental caries (Singh, 2011). In the present study, out of the entire sample, only 21.2% had had a dental visit in the previous year; 60.6% had never been to the dentist nor had a dental check-up. Negligence towards oral health has been shown to be among the leading factors related to the development and progression of dental caries (Castilho *et al*., 2013). In addition, oral hygiene practices as well as exposure to fluoride have been shown to play a key role as protective factors in minimizing the caries risk (Yengopal *et al*., 2016). In the present study, 42.4% of the sample admitted to brushing their teeth only once a day, while 18.2% either brushed occasionally or had never brushed. These inadequate toothbrushing practices could be linked to the high caries experience.

The impact of diet and nutrition, especially the role played by refined sugary substances on the development and progression of dental caries has been widely discussed in literature (Rwenyonyi *et al*., 2011). The dietary habits of children were explored, particularly the consumption of sugary

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food substances. In this study, 54.5% of the children were reported to consume sugary snacks several times a day (Table 12). In summation, the results of this study corroborate conclusions that HIV-infected children have an increased caries experience due to poor access to oral health services and inadequate access to protective measures such as professionally applied fluoride.

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CHAPTER 6: CONCLUSION

This study was aimed at highlighting the oral health status among children living with HIV, with regard to orofacial lesions associated with HIV and dental caries. In a nutshell, while orofacial manifestations of HIV were observed in a portion of the study population, candidal infection and particularly angular cheilitis were the most common lesions despite the use of HAART. The presence of orofacial lesions had no significant correlation with the immunosuppression status of the patient. A significant number of children presented with dental caries, the majority of which was untreated. The lack of restorative treatment was quite evident. Among the factors relevant to the increased prevalence of dental caries in children with HIV, lack of awareness on oral health issues and inadequate access to oral health services were quite prominent.

6.1 Limitations of the study

One great limitation of this study in terms of the hospital's patients in relation to the provincial applicability, was the small sample size. A larger sample size would have been more reflective of the oral health status of children in the Western Cape. However, at some point during the data collection period, the same children were seen, thus depicting sample saturation.

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6.2 Recommendations

This study highlights the need for oral health awareness and access to oral health services for children with HIV. Most of the caregivers in this study were unaware of services offered at Tygerberg Dental Faculty, UWC. The need for restorative treatment can never be over emphasized. Tygerberg Dental Faculty has a fully functional paediatric department offering comprehensive restorative treatment. The notion that primary teeth are just temporary teeth and therefore does not require dental care still resonates among most parents and caregivers/ guardians.

This data also reflects the need for a collaborative effort between the Paediatric Infectious Diseases Clinic and paediatric dental clinics to provide oral health services to children with HIV.

Early recognition of orofacial lesions and carious lesions will go a long way to providing appropriate management. This can only be necessitated by improved screening and referral processes between the two departments.

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APPENDICES

Appendix 1

Immunological Staging of HIV in Infants and Children (WHO Case Definitions of HIV, 2007)

	< 11 months (% $CD4^+$)	12-35 months (%$CD4^+$)	36-59 months (% $CD4^+$)	> 5 years ($CD4^+$ cells/ mm)
Non-symptomatic	>35	<30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-29	20-24	15-19	200-349
Severe	< 25	<20	<15	<200 or < 15%

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Appendix 2

WHO Clinical staging of HIV/AIDS (WHO Case Definitions of HIV, 2007)

CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS
Clinical stage 1	-Asymptomatic -Persistent generalized lymphadenopathy
Clinical Stage 2	-Moderate unexplained weight loss (<10% of presumed or measured body weight -recurrent respiratory infections (sinusitis, tonsilitis, otitis media, and pharyngitis) -Angular cheilitis -Recurrent oral ulceration -Papular pruritic eruptions -Seborrheic dermatitis -Fungal nail infections

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CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS
Clinical Stage 3	-Unexplained severe weight loss -Unexplained chronic diarrhoea for >1 month -Unexplained persistent fever for > 1 month -Persistent oral candidiasis (thrush) -Oral hairy leukoplakia -Acute Necrotizing Ulcerative Gingivitis or Periodontitis -Lymph node tuberculosis -Severe recurrent bacterial pneumonia -Unexplained anaemia (haemoglobin <8g/dL) -Neutropenia (neutrophils <500 cells/microlitre) -Chronic thrombocytopenia (platelets <50 000 cells/ microlitre)

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CLINICAL STAGE	CLINICAL CONDITIONS OR SYMPTOMS
Clinical Stage 4	-Unexplained severe wasting, stunting, malnutrition not responding to standard therapy -Pneumocystis pneumonia -Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection or menginitis but excluding pneumonia) -Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month duration) -Oesophageal candidiasis (or candidiasis of the trachea, bronchi or lungs) -Extrapulmonary tuberculosis -Kaposi's sarcoma -Cytomegalovirus infection: retinitis or CMV affecting another organ with onset at any age older than 1 month -Extrapulmonary cryptococcosis (including meningitis) -HIV encephalopathy -Disseminated endemic mycosis (coccidiomycosis or histoplasmosis) -Disseminated non-tuberculous mycobacterial infection -Chronic cryptosporidiosis (with diarrhoea) -Chronic isosporiasis -Cerebral or B-cell non-Hodgkin's lymphoma -Progressive multifocal leukoencephalopathy -Symptomatic HIV-associated neuropathy or HIV-associated cardiomyopathy

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Appendix 3

Consensus classification of orofacial lesions associated with paediatric HIV infection (Ramos-Gomez *et al*, 1999)

GROUP 1	**Lesions commonly associated with paediatric HIV infection**
	1. Candidiasis Pseudomembranous Erythematous Angular Cheilitis b) Herpes Simples Virus Infection c) Linear Gingival Erythema d) Parotid enlargement e) Recurrent Aphthous Ulcers Minor Major Herpetiform
GROUP 2	**Lesions less commonly associated with paediatric HIV infection**
	• Bacterial infections of oral tissues • Periodontal Disease Necrotising Ulcerative Gingivitis Necrotising Ulcerative Periodontitis Necrotising Stomatitis • Seborrheic dermatitis • Viral infections Cytomegalovirus Human Papilloma Virus Molluscum Contangiosum Varicella-Zoster Virus -Herpes Zoster -Varicella • Xerostomia
GROUP 3	**Lesions strongly associated with HIV infection but rare in children**
	• Neoplasms Kaposi's sarcoma Non-Hodgkin's lymphoma • Oral Hairy Leukoplakia • Tuberculosis-Related ulcers

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Appendix 4

Ethics Approval

Office of the Deputy Dean
Research
Faculty of Dentistry & WHO Collaborating Centre for Oral Health

UNIVERSITY OF THE WESTERN CAPE
Private Bag X1, Tygerberg 7505
Cape Town
SOUTH AFRICA

Date: 4th September 2015

For Attention: Dr O Mathiba
Department of Paediatric Dentistry
Faculty of Dentistry
Tygerberg Campus

Dear Dr Mathiba

STUDY PROJECT: An oral health survey among HIV-infected children younger than twelve years of age presenting at the paediatric infectious diseases clinic at Tygerberg Hospital

PROJECT REGISTRATION NUMBER: 15/6/83

ETHICS: Approved

At a meeting of the Senate Research Committee held on Tuesday 1st September 2015 the above-mentioned project was approved. This project is therefore now registered and you can proceed with the study. Please quote the above-mentioned project title and registration number in all further correspondence. Please carefully read the Standards and Guidance for Researchers below before carrying out your study.

Patients participating in a research project at the Tygerberg and Mitchells Plain Oral Health Centres will not be treated free of charge as the Provincial Administration of the Western Cape does not support research financially.

Due to the heavy workload auxiliary staff of the Oral Health Centres cannot offer assistance with research projects.

Yours sincerely

Professor Sudeshni Naidoo

Tel -27-21-937 3148 (w); Fax -27-21-931 2287 e-mail: suenaidoo@uwc.ac.za

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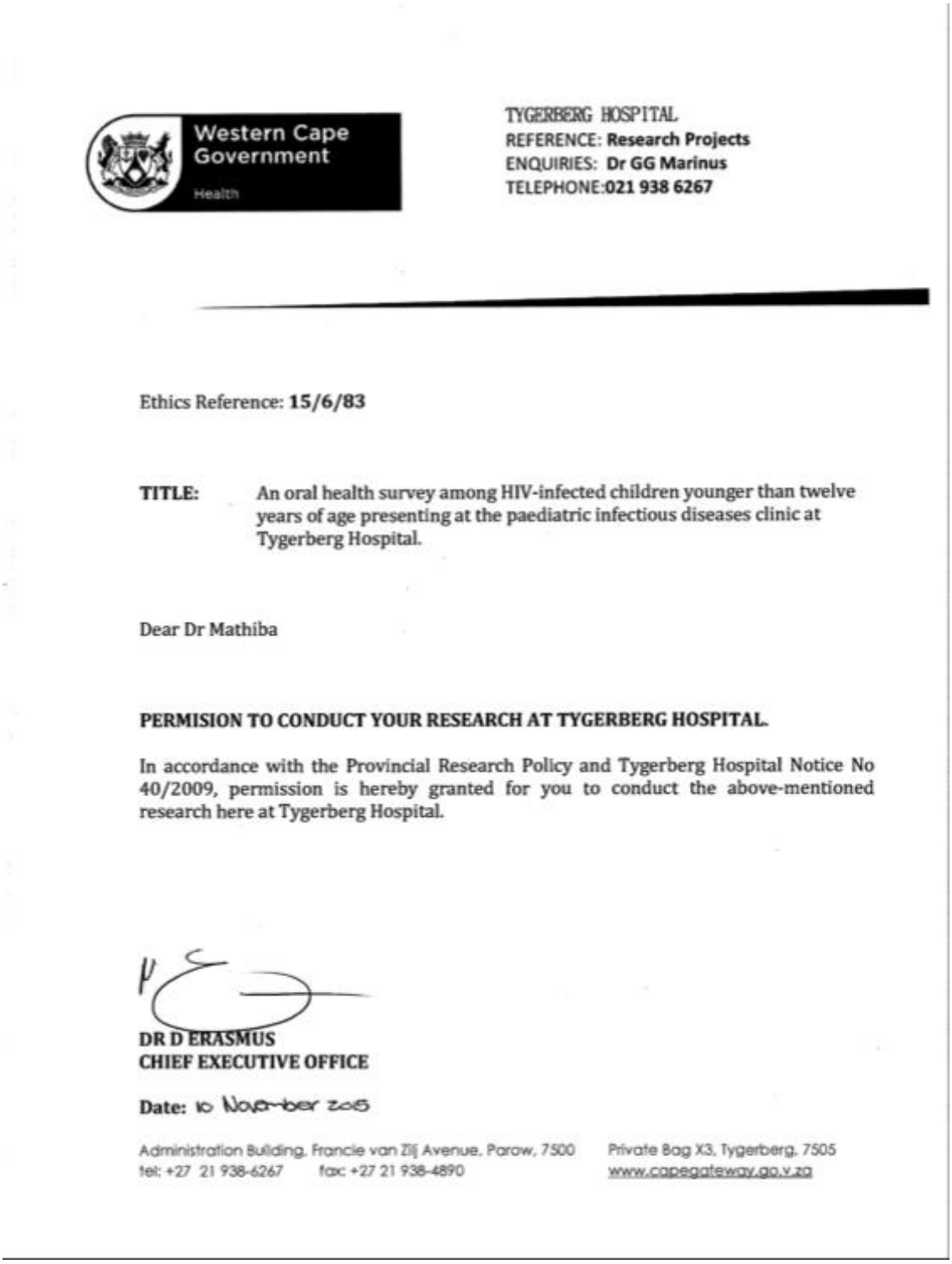
Appendix 5

Tygerberg Hospital Approval Letter



Western Cape Government
Health

TYGERBERG HOSPITAL
REFERENCE: **Research Projects**
ENQUIRIES: **Dr GG Marinus**
TELEPHONE:**021 938 6267**

Ethics Reference: **15/6/83**

TITLE: An oral health survey among HIV-infected children younger than twelve years of age presenting at the paediatric infectious diseases clinic at Tygerberg Hospital.

Dear Dr Mathiba

PERMISION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL.

In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital.

DR D ERASMUS
CHIEF EXECUTIVE OFFICE

Date: 10 November 2015

Administration Building, Francie van Zijl Avenue, Parow, 7500 Private Bag X3, Tygerberg, 7505
tel: +27 21 938-6267 fax: +27 21 938-4890 www.capegateway.gov.za

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Appendix 6

Consent form

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Faculty of DENTISTRY share your Smile

CONSENT FORM FOR PARTICIPTION IN A RESEARCH STUDY
FACULTY OF DENTISTRY

UNIVERSITY OF THE WESTERN CAPE

PROJECT TITLE: An Oral Health Survey of HIV-infected children younger than 12 years of age presenting at the paediatric infectious disease clinic at Tygerberg Hospital.

You are invited to participate in a research study conducted by myself, Dr Olorato Mathiba, a qualified dentist currently enrolled as a Masters student in the Department of Paediatric Dentistry at the University of the Western Cape. The purpose of this study is to determine the oral health status of HIV infected children.

Participation involves an interview followed by a clinical examination of your child's mouth. The study should only take about 15 to 20 minutes of your time. There are no risks associated with this research.

Potential benefits: The appropriate dental treatment will be provided for your child if any oral health problems are identified.

To maintain patient confidentiality, no names will be recorded thus protecting your identity and that of your child. Your participation in this study is entirely voluntary. You may choose not to participate and may withdraw your child from the study at any time. You will not be disadvantaged in any way should you decide not to participate or withdraw your child from the study.

The examination will be free of charge and no child will be turned away, even if the child does not participate in the study. Your child can still be referred to the Tygerberg Oral Health Centre if he/ she is in need of dental treatment. No form of compensation will be given for participation.

This study has been ethically reviewed and approved by the UWC Senate Biomedical Research Ethics Committee (Approval no: **15/6/83**)

In the event of any problems or concerns, you may contact the researcher at nr: 0711168305 email: 3515495@myuwc.ac.za) or the supervisors of this study: Dr. N. Mohamed (021 937 3073, email: namohamed@uwc.ac.za) or Dr R. Mulder(021 937 3107, email: rmulder@uwc.ac.za)

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a place to grow, from hope
to action through knowledge

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Appendix 7

QUESTIONNAIRE

Patient's Medical Record Number: ☐

1. Demographics

(a).Patient's Age: _____

(b). Gender F ☐ M ☐

2. Parent/Guardian

(a) How are you related to the child?

Mother ☐ Grandparent ☐

Father ☐ Other_____

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3. How often during the past 12 months did you have toothache or feel discomfort due to your teeth? (Put a tick/cross in one box)

(a) Often…… ☐

(b) Occasionally…… ☐

(c) Rarely…… ☐

(d) Never…… ☐

(e) Don't know …… ☐

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4. How often did you go to the dentist during the past 12 month?
(Put a tick/cross in one only)

(a) Once…… ☐

(b) More than once…… ☐

(c) I had no visit to the dentist during the past 12 months…… ☐

(d) I have never received dental care/visited the dentist…… ☐

(e) I don't know…… ☐

If you did not see a dentist during the past 12 months, go on to question 6

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5. What was the reason for your last visit to the dentist?
(Put tick/cross in one box only)

(a) Pain or trouble with teeth, gums or mouth……. ☐

(b) Treatment/follow-up treatment…… ☐

(c) Routine check-up of teeth/treatment……. ☐

(d) I don't know/don't remember…….. ☐

(e) Other, specify_____

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6. How often do you clean your teeth?
(Put tick/cross in one box only)

(a) Never…….. ☐

(b) Several times a month (2-3 times)……. ☐

(c) Once a week…….. ☐

(d) Several times a week (2-6 times)…… ☐

(e) Once a day…….. ☐

(f) 2 or more times a day…… ☐

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7. Do you use any of the following to clean your teeth or gums?
(Put ticks/crosses on all those that apply)

(a) Toothbrush…… ☐

(b) Toothpick…… ☐

(c) Thread (dental floss)…… ☐

(d) Other; Please specify_____

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8. What type of toothpaste do you use to clean your teeth?

(a) None…….. ☐

(b) Baby toothpaste with fluoride……. ☐

(c) Adult toothpaste with fluoride…… ☐

(d) Other; please specify_____

(e) Don't know…….…… ☐

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9. Because of the state of your teeth and mouth, which of the following problems have you experienced during the past year?
(Put ticks/crosses on all those that apply)

(a) I am not satisfied with the appearance of my teeth…….. ☐

(b) I often avoid smiling and laughing because of my teeth…… ☐

(c) Other kids make fun of my teeth…… ☐

(d) Toothache or discomfort caused by my teeth forced me to miss classes at school or miss school for whole days …….. ☐

(e) I have difficulty biting hard foods…….. ☐

(f) I have difficulty chewing…… ☐

(g) Other, specify_____

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10. How often do you eat or drink any of the following foods, even in small quantities?
(Put a tick/cross on all those that apply)

	Several times a day	Everyday	Several times a week	Once a week	Several times a month	Never
(a) Fresh fruit……	☐	☐	☐	☐	☐	☐
(b) Biscuits, cakes, cream, Cakes, sweet pies, buns Milk tart etc……	☐	☐	☐	☐	☐	☐
(c) Lemonade,Coca Cola, Juice or other soft drink……	☐	☐	☐	☐	☐	☐
(d) Jam/ honey……	☐	☐	☐	☐	☐	☐
(e) Sugar free/xylitol Chewing gum……	☐	☐	☐	☐	☐	☐
(f) Sweets/candy……	☐	☐	☐	☐	☐	☐
(g) Milk with sugar or nesquik or syrup……	☐	☐	☐	☐	☐	☐
(h) Tea with sugar……	☐	☐	☐	☐	☐	☐
(i) Coffee with sugar……	☐	☐	☐	☐	☐	☐

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That completes our questionnaire

Thank you very much for your cooperation!

Date:……

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Appendix 8

DATA CAPTURE SHEET FOR A CLINICAL EXAMINATION

Patient Medical Record Number: ☐

1. General Information:

(a) $CD4^+$ count: ……

(b) Viral load:……

(c) Clinical Stage:……..

2. Medical History

(a) Past illnesses……

(b) Medication……

3. Extra Oral Assessment:

		Normal	Abnormal	Description
(a)	Lips	☐	☐	……..……..……
(b)	Salivary Glands	☐	☐	……..……
(c)	Lymph Nodes	☐	☐	……

4. Intra Oral

		Normal	Abnormal	Description
(a)	Tongue	☐	☐	……
(b)	Gingiva	☐	☐	……
(c)	Buccal mucosa	☐	☐	……
(d)	Palate	☐	☐	……
(e)	Pharynx	☐	☐	……

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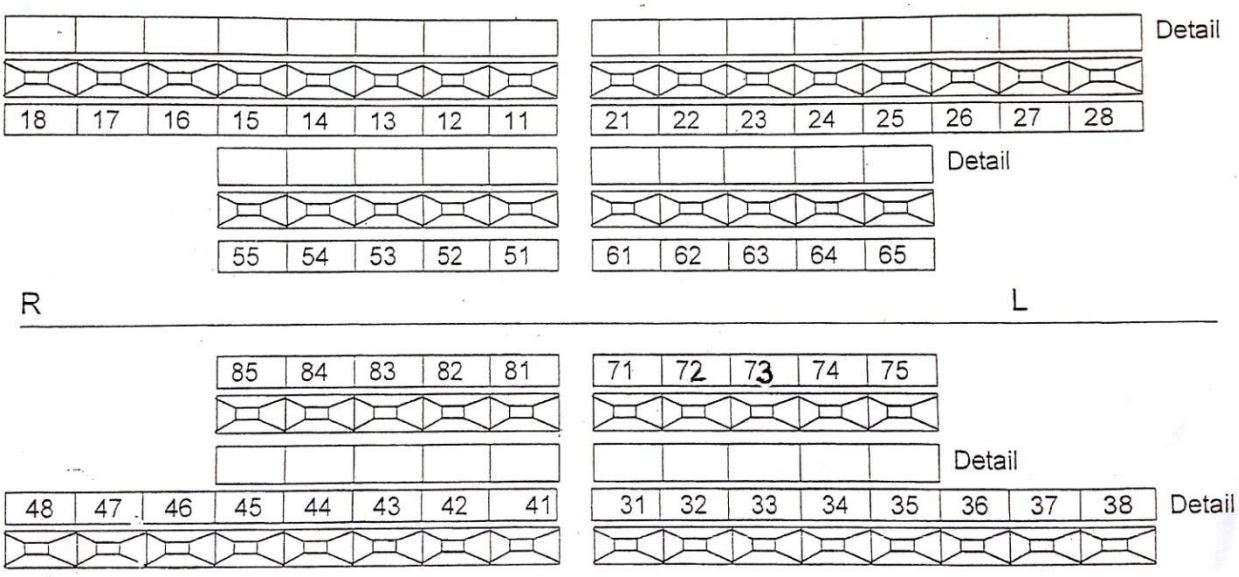
5. Teeth



DMFT/dmft/:……..

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6. Orofacial lesions

	Present	Absent
(a). Oral Candidiasis		
(i) Pseudomembranous	☐	☐
(ii) Erythematous	☐	☐
(iii) Angular Cheilitis	☐	☐
(b). Herpes Simplex Virus		
(i) Primary Herpetic Gingivostomatitis	☐	☐
(ii) Herpes Labialis	☐	☐
(c). Linear Gingival Erythema	☐	☐
(d). Recurrent Aphthous Ulcers		
(i) Minor	☐	☐
(ii) Major	☐	☐
(iii) Herpetiform	☐	☐

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(e). Periodontal Disease

(i) Necrotising Ulcerative Gingivitis ☐ ☐

(ii) Necrotising Ulcerative Periodontitis ☐ ☐

(f). Other Ulcerations ☐ ☐

(g). Viral Infections

(i) Warty-like/human papillomavirus ☐ ☐

(ii) Molluscum Contangiosum ☐ ☐

(h). Neoplasms

(i) Kaposi's sarcoma ☐ ☐

(ii) Non-Hodgkin's lymphoma ☐ ☐

(iii) Oral Hairy Leukoplakia ☐ ☐

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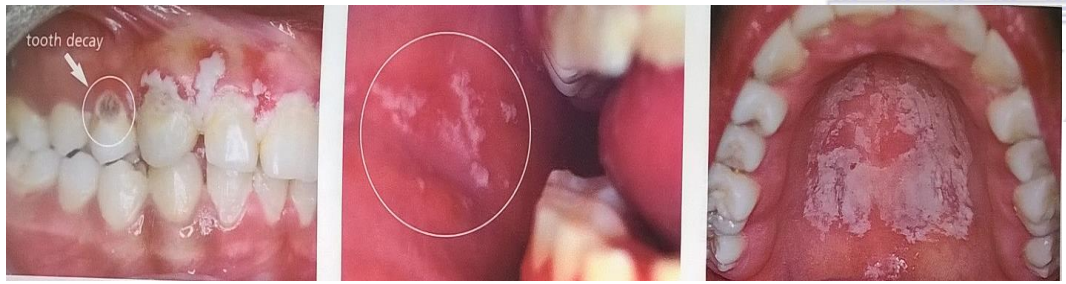
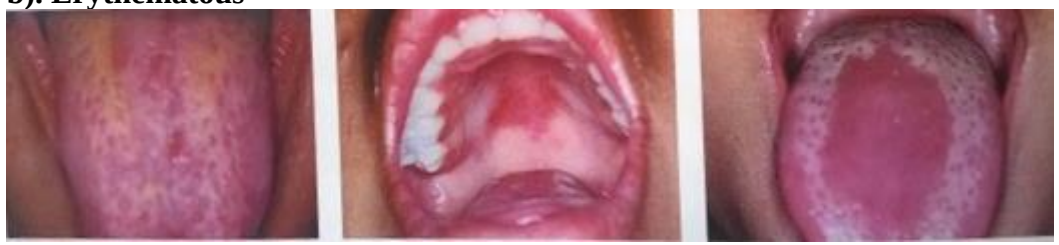
Appendix 9

CRITERIA FOR DIAGNOSIS OF PAEDIATRIC OROFACIAL LESIONS ASSOCIATED WITH PAEDIATRIC HIV/AIDS INFECTION

(Ramos-Gomez *et al*, 1999; Naidoo *et al*, 2001)

LESION	CRITERIA
Group 1: Lesions commonly associated with paediatric HIV infection	
1.CANDIDIASIS **a). Pseudomembranous Candidiasis** 	• Multifocal, nonadherent • Creamy white papules or plaque • Can be wiped off • Leaving an erythematous base with or without bleeding
b). Erythematous 	• Multiple red patches • Commonly located on palate • Variant: Median rhomboid glossitis; a red, smooth depapillated patch on the mid-dorsal tongue. • Tenderness or burning sensation may be experienced

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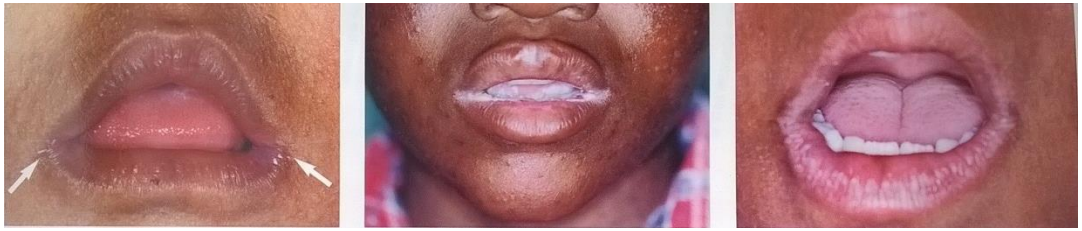
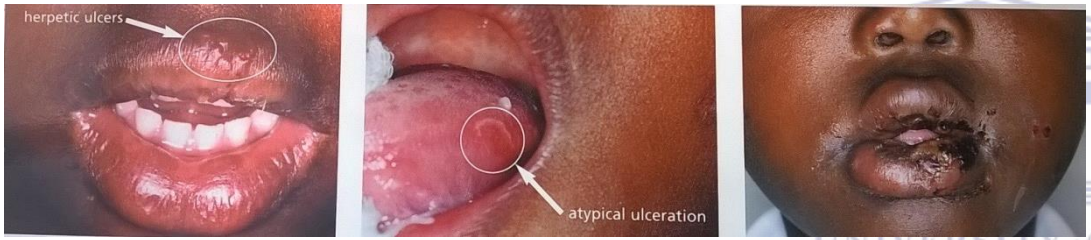
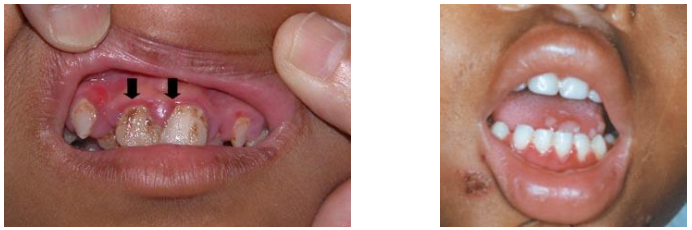
c). Angular cheilitis 	• Bilateral linear red or ulcerated fissures radiating from the corners of the mouth • Tendor • Hyperkeratosi may be present at the periphery of the lesion
2. HERPES SIMPLEX VIRUS 	Herpes Simplex Virus • Initially present as vesicles which rupture to become painful irregular vesicles • Intraoral and perioral lesions on the gingival, hard palate and vermilion border. • Patients exhibit fever and malaise, swollen and tendor lymph nodes
3. LINEAR GINGIVAL ERYTHEMA 	• A fiery red, linear band 2 to 3 mm wide • On the marginal gingival • Accompanied by petechiae-like or diffuse red lesions on the attached gingival and oral mucosa. • Maybe accompanied by bleeding gums on brushing

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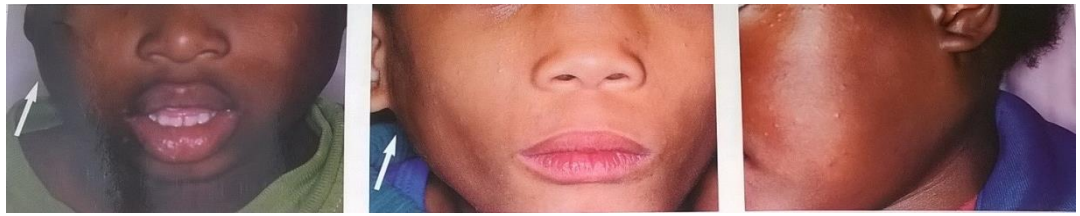
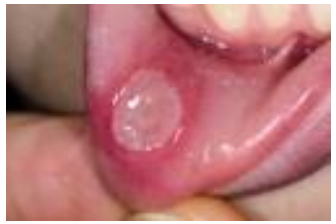
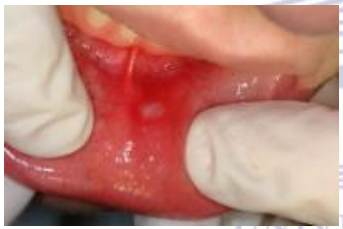
4. PAROTID ENLARGEMENT 	• Unilateral or bilateral diffuse soft-tissue swelling • Result in facial disfigurement • May be accompanied by pain • May cause dry mouth
5. RECURRENT APTHOUS ULCERS  	**Minor recurrent aphthous ulcers** • Small ulcer <5mm in diameter • Covered with a pseudomembrane and surrounded by an erythematous halo. **Major recurrent aphthous ulcers** • Larger approximately 1 to 2 cm in diameter • Painful and may interfere with mastication and swallowing **Herpetiform recurrent aphthous ulcers** • Clusters or cropsof tiny recurrent aphthous ulcers • 1-2mm in diameters • Tend to occur in areas where they hinder eating and speaking

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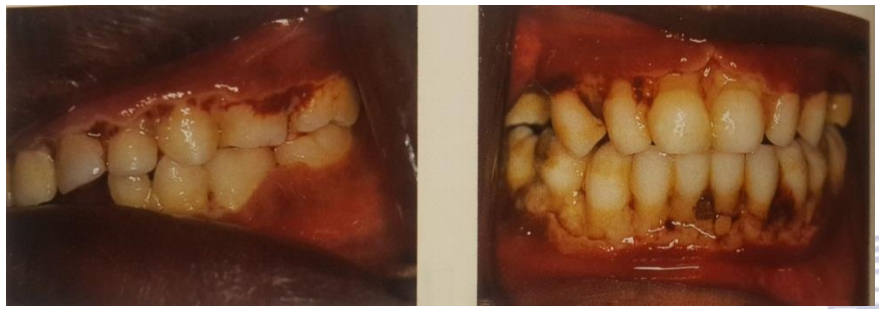
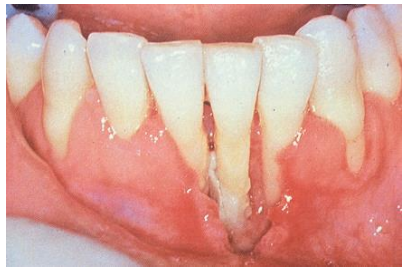
Group 2: Orofacial lesions less commonly associated with HIV infection in children	
NECROTISING ULCERATIVE GINGIVITIS (NUG) 	• Destruction of inter-dental papillae • Accompanied by necrosis, ulceration and sloughing • Symptoms: bleeding on brushing, pain and halitosis.
NECROTISING ULCERATIVE PERIODONTITIS (NUP) 	• Severe soft tissue necrosis along with destruction of periodontal attachment and bone • Patients experience spontaneous gingival bleeding • Bleeding on brushing • Severe gingival recession resulting from rapid bone loss and soft tissue necrosis
HUMAN PAPILLOMA VIRUS (HPV) 	• Raised, irregular, flesh-colored warts

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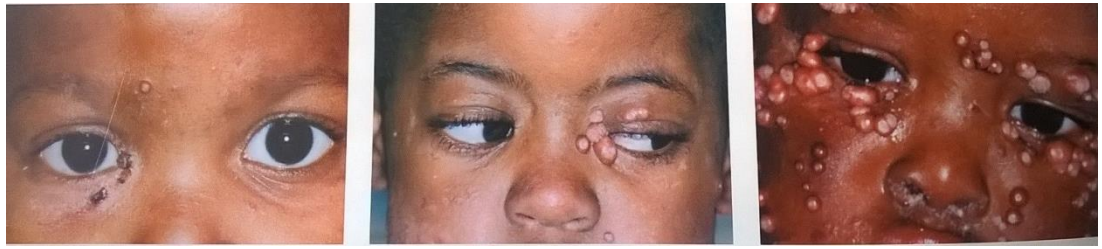
MOLLUSCUM CONTANGIOSUM 	• Small discrete dome shaped • Pearly white to skin color • In HIV positive children they may be numerous and unusually large
Group 3: Orofacial lesions strongly associated with HIV infection but rare in children	
ORAL HAIRY LEUKOPLAKIA	• White, nonremovable lesions • with a corrugated surface • appear bilaterally • on lateral borders of the tongue
KAPOSI SARCOMA & NON-HODGKIN'S LYMPHOMA	• Both far less common in children and adults • Hyperpigmented nodular lesions

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Appendix 10

CLINICAL PHOTOGRAPHS OF CHILDREN SEEN AT TYGERBERG PIDC

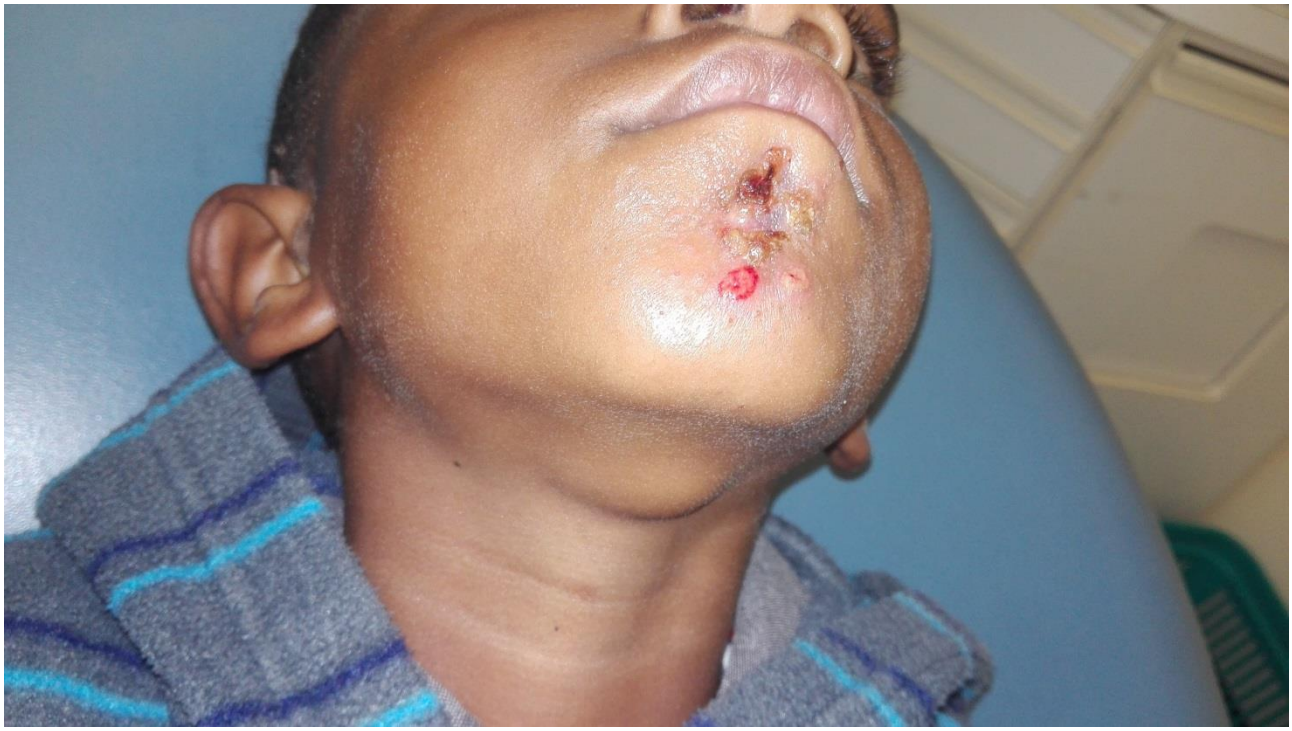
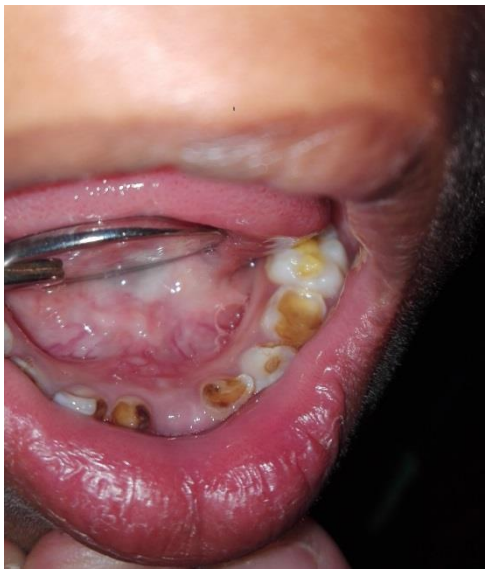
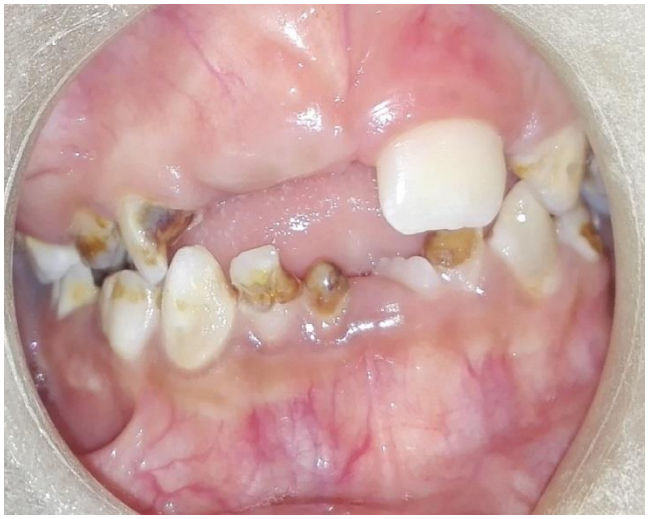


Figure 6: A child with submental lymphadenopathy, ulcerative lesion





Dental caries in the same child with submental lymphadenopathy

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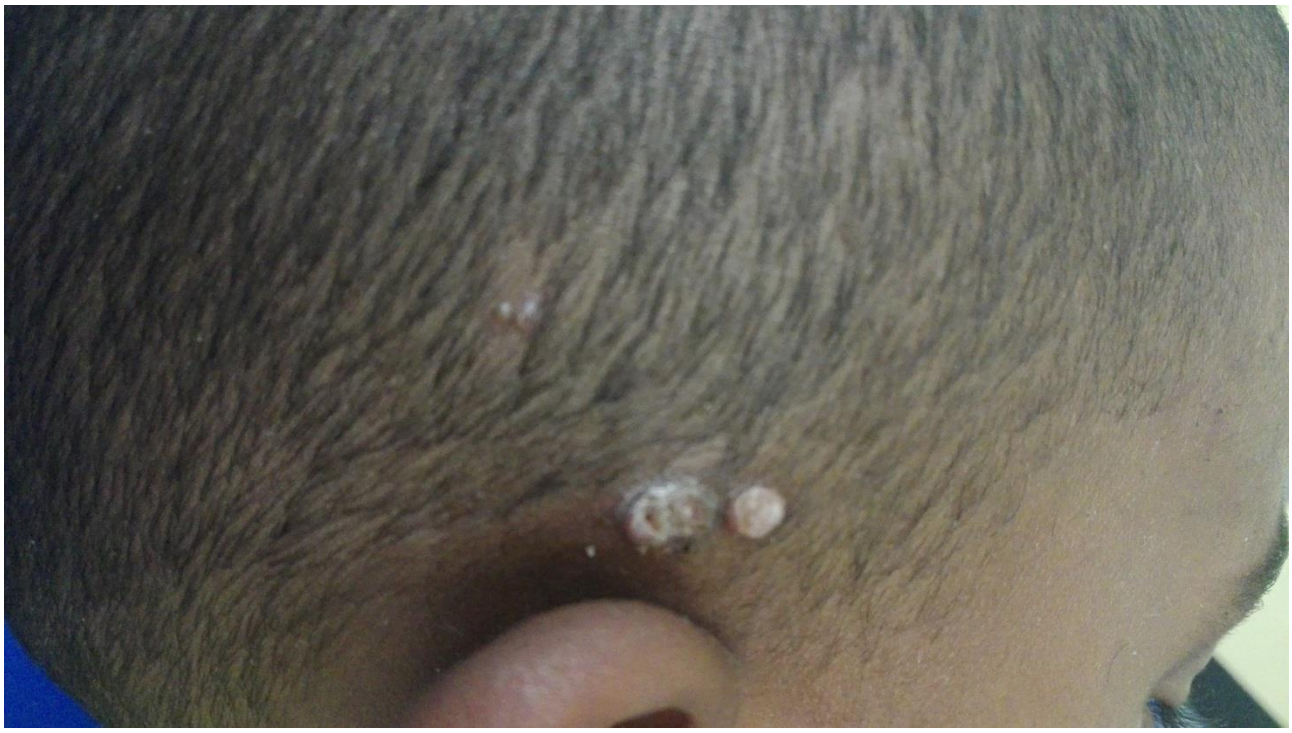

Molluscum contagiosum on a child with HIV

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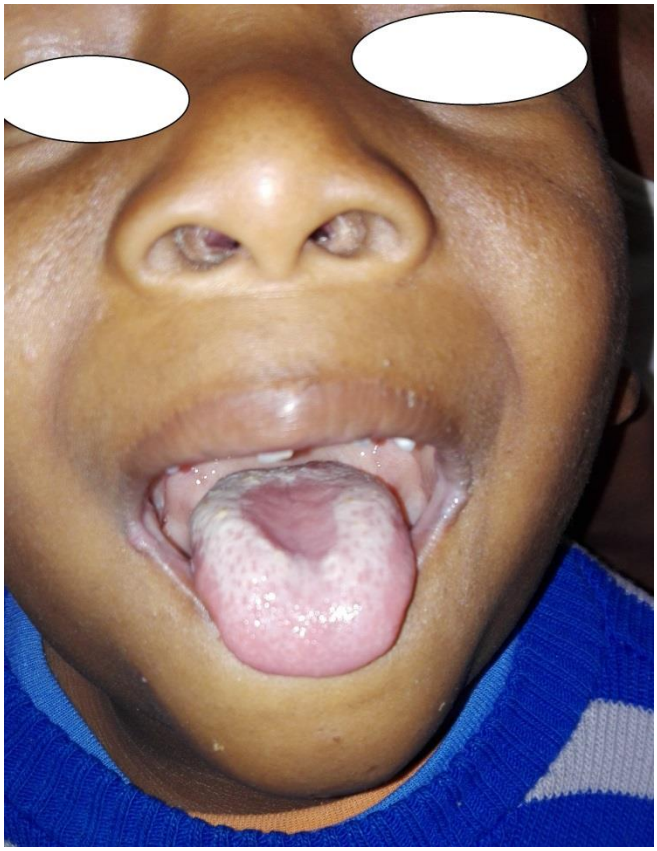
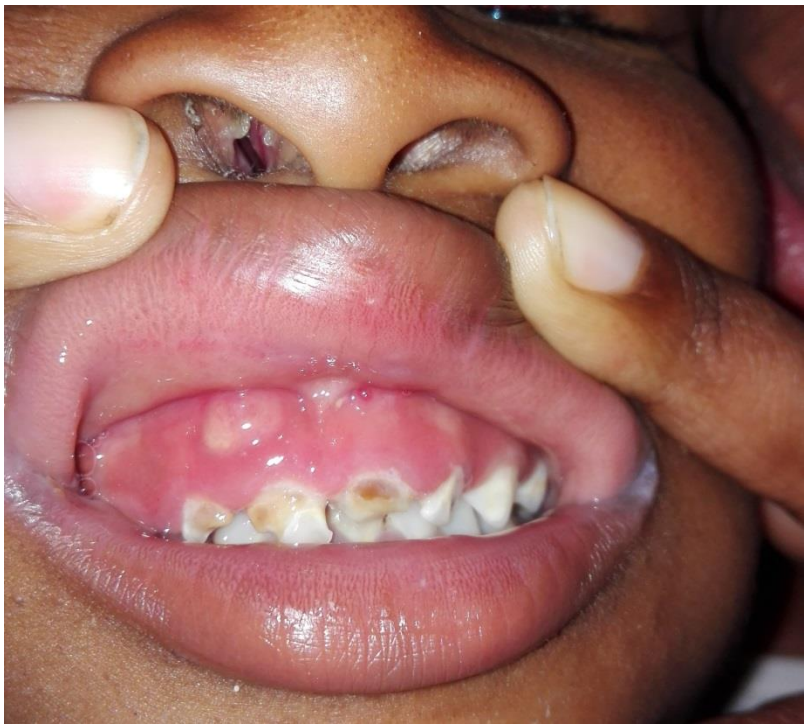


A child with median rhomboid glossitis (erythematous candidiasis)



Multiple carious lesions, dental abscesses adjacent to the 51 and 52 and scarring as a result of angular cheilitis.

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