

UNIVERSITY OF NAMIBIA
FACULTY OF HEALTH SCIENCES

**PREVALENCE OF ORAL LESIONS IN ADULT PATIENTS INFECTED BY
THE HUMAN IMMUNODEFICIENCY VIRUS AND ITS ASSOCIATION
WITH CD4 COUNTS IN OSHAKATI HOSPITAL, NAMIBIA**

**A THESIS SUBMITTED IN PARTIAL FULFILLEMENT OF THE
REQUIREMENTS FOR THE DEGREE
MASTERS IN PUBLIC HEALTH**

BY

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MARCH 2013

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ABSTRACT

In dentistry HIV/AIDS patients with oral lesions are encountered regularly, hence early diagnosis and appropriate treatment is important so as to prolong patient's life. The researcher had noticed over time, what appeared to be a significant number of patients with oral lesions who were eligible for highly active antiretroviral therapy treatment, but who were not initiated. Applicable guidelines were available on how to manage patients with oral lesions as well as recommendations to initiate these patients on highly active antiretroviral therapy, even without the recommended CD4 counts. There were also no studies in Namibia on the prevalence of HIV/AIDS associated oral and peri-oral lesions and their association with CD4 counts.

It is against this background that this study was conducted to explore and describe the magnitude and prevalence of the different types of oral manifestations of HIV/AIDS and their association with CD4 counts among adult patients attending the *Communicable Disease Clinic* at the Oshakati Hospital.

A quantitative cross sectional design was used in this study, and 360 patients, representing a 96% participation rate, were included in the study. Examinations of these patients for oral lesions were done using a checklist based on European Community Clearinghouse criteria. In addition CD4 count results were obtained from patient's health passports or laboratory results.

It emerged that out of the 360 patients examined, 54.7% had oral lesions, of which 62.9% were females and 37% were males. Cheilitis accounted for the highest number of lesions, namely 20.9%, followed by pseudomembranous candidiasis occurring in 5% of patients. Herpes simplex lesions were the least seen with only one patient. Furthermore, a statistical significant association between the development of oral lesions and CD4 counts was found.

In conclusion, the prevalence of HIV associated oral lesions (54.7%) was lower than reported studies of other African countries. The strong positive association between the occurrence of oral and peri-oral lesions and low CD4 cell counts found in this study could be regarded as an important result in the light of the need for inexpensive surrogate markers of HIV disease progression in resource-poor countries, where the measurement of CD4 cell counts is expensive and in some areas not available.

Recommendations were submitted to the Ministry of Health and Social Services, with the emphasis on health education and involvement of dental personnel in HIV/AIDS programmes.

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
ARVs	Antiretrovirals
HAART	Highly active antiretroviral therapy
CDC	Centre for Disease Control
CD4	Cluster Designate 4
HIV	Human immune virus
MoHSS	Ministry of Health and Social Services
IHO	Intermediate Hospital Oshakati
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNAM	University of Namibia
USAID	United States Agents for International Development
PMTCT	Prevention of mother to child transmission

ACKNOWLEDGEMENTS

Glory to God, Mohamed (S.A.W.) who gave me health and strength to reach this far.

I wish to express my sincere gratitude to the following people:

- My supervisors, professors LF Small, and S Yigeremu for guiding me meticulously throughout my work.
- Mr N Tshifugula my co-supervisor, for his patient guidance, advice and encouragement throughout the course of this work.
- I humbly thank the administrators at the University of Namibia for allowing me to study at this institution.
- My special thanks goes to the patients who agreed to participate in the study and to all the nurses and doctors working in the *Centre for Disease Control* pre HAART clinic during 2012, and who took the time to assist in either the translations, or explanations during the period of data collection. To you I wish to express a hearty “thank you”, without you this study would not have been a success or even possible.
- I would also like to thank Leonie Munro for editing my thesis. I am responsible for the final version.
- I thank all my colleagues, relatives and friends who assisted and wished me well during this endeavor.

May almighty God bless you all.

DEDICATION

This thesis is dedicated to my husband, Mr. A. A. Mfinanga, for his love, support and encouragement to me to pursue the course and to my beloved daughters and son, Rahima, Leila, Ally, Amina and Abdul. Let this accomplishment be a source of inspiration.

DECLARATION

I hereby declare that this thesis is a true reflection of my own research work and efforts, and that this work has not been submitted anywhere for a degree in any other institution of higher education. No part of this thesis may be reproduced, stored in a retrieval system, or transmitted in any form, or by any means (e.g. electronic, mechanical, photocopying, recording, or otherwise) without the prior permission of the author, or the University of Namibia on her behalf. Where other sources of information have been used, they have been acknowledged. I grant the University of Namibia the right to reproduce this thesis in any manner or format which the University of Namibia may deem fit.

Signature.....

Date.....

CHAPTER ONE

INTRODUCTION AND BACKGROUND OF THE PROBLEM

1.1 INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is a set of symptoms and infections resulting from the damage to the human immune system caused by the human immunodeficiency virus (HIV) (Online medical dictionary, 2010). HIV is considered to be one of the most deadly diseases affecting humans. White blood cells are an important part of the immune system, and when HIV invades the body it targets specific white blood cells called CD4 cells. These cells are involved in antibody (agglutinin) production which is responsible for the one of the body's most important defense mechanisms against infective materials (antigens). If too many CD4 cells are destroyed, the body can no longer defend itself against infections, leaving an individual susceptible to opportunistic infections and tumors (Essig & Els, 2008). The term AIDS is then used when the human physiology is adversely affected by these infections and tumors.

Since the introduction of laboratory identification of HIV, it has become possible to quantify its exponential growth and the results indicated that it had literally affected millions of people in the world. During 2008 alone, 2 million people died worldwide due to HIV/AIDS and another 33.4 million were living with HIV/AIDS, while 2.7 million people were newly infected with the virus in the same year. Of all the people

affected with AIDS, more than 90 percent are living in the developing world (UNAIDS, 2009).

As a developing region, Africa, and specifically sub-Saharan Africa, has been most profoundly affected. The 2007 statistics for HIV/AIDS puts this impact in perspective since an estimated 1.5 million adults and children died as a result of AIDS in sub-Saharan Africa. The severity of this impact in sub-Saharan Africa was underscored when the data show that two-thirds of all people living with HIV were found in this area, yet this region contains not more than 10% of the world's population (UNAIDS, 2005).

However, the HIV prevalence rates and the number of people dying from AIDS vary considerably between African countries. In Somalia and Senegal the HIV prevalence is under 1% of the adult population, whereas in Namibia, South Africa, Zambia and Zimbabwe, around 15-20% of adults are infected with HIV. In three southern African countries the national adult HIV prevalence rate now exceeds 20%. These countries are Botswana, with a prevalence rate of close to 24%, Lesotho with 23%, and Swaziland with a 26% prevalence rate (UNAIDS, 2008). West Africa had been less severely affected by HIV and AIDS, but countries in this region had witnessed rising HIV prevalence rates. For example, in Cameroon the HIV prevalence is now estimated at 5.1% and in Gabon it stands at 5.9%. A country that seems to have escaped this rise in HIV/AIDS, is Nigeria (the most populated sub-Saharan country), where the prevalence is only 3.1%, as compared to the rest of Africa and in view of Nigeria's large population, this equates to around 2.6 million people living with HIV

(UNAIDS, 2008). East Africa is also not spared as the adult HIV prevalence exceeds 5% in Uganda, Kenya and Tanzania (UNAIDS, 2008).

1.2 NAMIBIA AND HIV/AIDS

Namibia is located in the south-western part of Africa and has a population of approximately 2,000,000 (National Planning Commission, 2004). After Windhoek, Oshakati is the second largest populated town in Namibia. Oshakati is, however, growing at a staggering rate with a recorded annual population increase of 5.5% since Namibia's independence (CIA World Fact Book, 2008).

According to the Kaiser Family Foundation (2005), Namibia has one of the highest HIV/AIDS prevalence rates in the world, which at that time was just more than 21%. With this high prevalence rate, the epidemic poses significant challenges to this middle-income country as it also struggles with high levels of unemployment and income disparity which may lead to even further spread of diseases such as HIV/AIDS (UNAIDS, 2004).

1.3 HIV/AIDS AND DENTISTRY

The oral cavity is one of the sites where HIV infections and AIDS manifest through the development of a number of oral lesions. Oral health problems were identified as a significant issue early in the AIDS epidemic and they continue to be so today. Problems in the mouth not only may be the first symptom of a HIV infection, but

also can signify clinical progression. Thus access to oral health care is critical both from an early detection perspective as well as the early treatment of those lesions for persons at risk of HIV infection, and, for individuals already living with HIV. Although HIV-related oral conditions occur in a large proportion of patients, they are frequently misdiagnosed or inadequately treated.

Dental expertise is necessary for an appropriate diagnosis and management of oral manifestations of HIV/AIDS, but many patients do not receive adequate dental care. Some of the common or notable HIV-related oral conditions include xerostomia, candidiasis, oral hairy leukoplakia, periodontal diseases such as linear gingival erythema and necrotizing ulcerative periodontitis. Added to these are Kaposi's sarcoma, human papilloma virus-associated warts and ulcerative conditions including herpes simplex virus lesions, recurrent aphthous ulcers and neutropenic ulcers (Reznik, 2005). Other oral lesions are also well documented and some are discussed in the literature review in the next chapter.

As stated in the previous paragraph, oral lesions not only indicate HIV infections, but are also among the early clinical features of the infection that can predict progression of the disease to AIDS. These lesions can therefore be used as entry, or end-points in therapy and vaccine trials, and can also be the determinants for anti-HIV therapy, and in addition they can also be used in the staging and classification systems. These lesions parallel the decline in the number of CD4⁺ cells and an increase in viral load, hence they are independent indicators of disease progression (Hodgson, Greenspan & Greenspan, 2006; WHO, 2005).

1.4 PROBLEM STATEMENT

Numerous studies on oral manifestations of HIV/AIDS had been done in different countries in Africa, and the world in general. However, there is no evidence of published studies undertaken in Namibia which underscores the need for research to be done in this area. In addition, a lot of discrepancies on the prevalence of oral manifestations of HIV/AIDS between different countries were observed, and there is a need to know what the situation is in Namibia. Also, the information on the association of CD4 counts and the presence of oral lesions had never been confirmed in a Namibian context. Furthermore it was noted that a substantial number of HIV patients with oral lesions who were clinically eligible to start highly active antiretroviral therapy (HAART) were seen in a dental clinic but were not yet on HAART. It is against this background that this study was conducted. Knowing the magnitude of oral lesions associated with HIV/AIDS should assist the Ministry of Health and Social Services in future planning and budgeting for management of these lesions. Apart from highly active antiretroviral therapy, there are other supportive medications needed for such oral lesions. Once the prevalence of these conditions is known, the ministry should be in a position to investigate why patients who are clinically eligible to highly active antiretroviral therapy, are not.

1.5 PURPOSE OF THE STUDY

The purpose of this study is to explore and describe the magnitude and prevalence of the different types of oral manifestations of HIV/AIDS and their association with

CD4 counts among adult patients attending the communicable disease clinic (CDC) at the Oshakati Hospital.

1.5.1 OBJECTIVES

- To determine the prevalence and types of oral lesions among patients diagnosed with HIV/AIDS.
- To determine the association between CD4 counts and oral lesions among patients diagnosed with HIV/AIDS.

1.6 SIGNIFICANCE OF THE STUDY

It is essential to know the prevalence and magnitude of the different types of oral lesions in order to identify and prioritize treatment budgets based on the prevalence pattern of these lesions seen. Such data can help to set priorities for resource allocation in HIV/AIDS programmes and to ensure availability of appropriate medication. Furthermore, oral health care is an essential part of HIV primary care, therefore early diagnosis and management of oral manifestations (opportunistic infections) is crucial to prevent complications and prolong the lives of patients. Additionally, if patients with oral lesions get appropriate treatment, and are free of pain and discomfort caused by these oral lesions, then their nutritional intake will improve and it will become possible to fulfill the overall aim of highly active antiretroviral treatment, which is to prolong a patient's life.

1.7 DEFINITION OF CONCEPTS

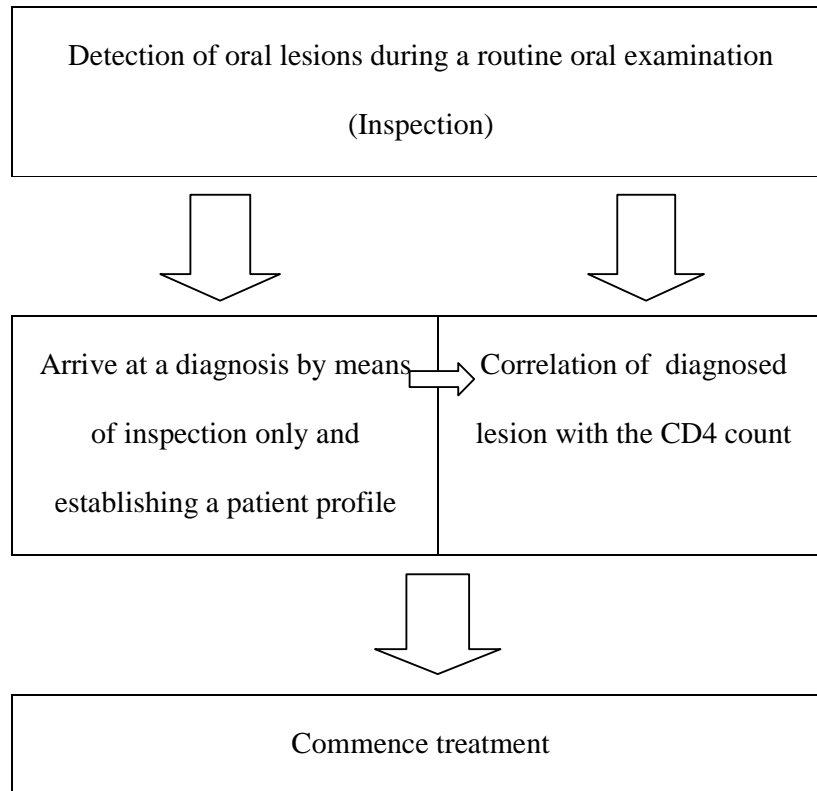
- The human immunodeficiency virus (HIV) is the cause of acquired immune deficiency syndrome (AIDS). By infecting CD4 T-lymphocytes, a type of white blood cell, HIV weakens the immune system and leaves the infected individual open to deadly infections (Encarta Encyclopedia, 2005).
- Acquired immune deficiency syndrome (AIDS) is a clinical syndrome, a group of various illnesses that together characterize a disease, resulting from damage to the immune system caused by infection with HIV (Encarta Encyclopedia, 2005).
- Oral manifestations are the presence of the signs, symptoms and lesions of a systemic disease in and around the oral cavity. In this study the term “*oral*” will also include *peri-oral* lesions

1.8 THEORETICAL FRAMEWORK

A theory is a set of statements or principles devised to explain a group of facts or phenomena. Most theories that are accepted by scientists have been repeatedly tested by experiments and can be used to make predictions about natural phenomena (The American Heritage Science Dictionary, 2010). This study is not positioned within a traditional theoretical framework, instead an eclectic pragmatic approach is used to link with the purpose and objectives of the study. This link is called a theoretical framework. Such a framework is a summary of a researcher’s theory regarding a particular problem, developed through a review of previously tested knowledge of

the variables involved. It identifies a plan for investigation and how to interpret the results. A theoretical framework involves a well-supported rationale, it is organized in a manner that helps the reader understand and assesses a researcher's perspective. The purpose is to demonstrate that the proposed relationships are not based on personal instincts or guesses, but rather formed from facts obtained from authors of previous research (Creswell, 2009).

The classical epidemiological approach would have been to look for association/cause-effect relationships. In this study the relationship between HIV/AIDS and oral lesions is known, but this association has not necessarily been officially documented in Namibia especially with regard to the relationship between CD4 count values and oral lesions. The classical epidemiological approach had thus not been used in this study, as the approach had been slightly altered, to allow for an earlier highly active antiretroviral therapy intervention (see Table 1.1).

Table 1.1 The adapted epidemiological framework of the study

1.9 SUMMARY

In chapter one an introduction to the study was presented, followed by the problem statement, purpose and objectives. The significance of the study, as well as a short explanation of the framework to be used, was briefly discussed. Chapter two covers the literature review within the context of the purpose of the study.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

The discussion of the literature is based on how HIV lowers the body's immunity and thus leading to opportunistic infections, such as oral candidiasis. A description of the different types of oral lesions that are associated with HIV, and the prevalence of oral manifestations of HIV/AIDS and its association with CD4 counts, are presented. In addition the literature review also focuses on other related factors, such as oral hygiene, nutritional intake and taking of antiretroviral therapy, which are affected by the presence of these oral lesions. This is done to stress the importance of early initiation of highly active antiretroviral therapy to achieve its overall aim: *to prolong a patient's life*.

The discussion will be positioned within the outline of the framework, although not necessary in the exact order. The first discussion point will therefore be about the relationship between CD4 counts and HIV/AIDS.

2.2 HIV, AIDS AND THE CD4 COUNT

The immune system has a vast number of cells for general defense and specific responses. Only a few specific defensive cells are activated when a specific antigen appears, and they are stimulated to multiply and to mount a response to the foreign

antigen. Immune cells are originally produced in bone marrow stem cells. Their descendants become either lymphocytes or phagocytes. The two main classes of lymphocytes are B cells that remain in the bone marrow to complete their maturation, and T cells that migrate to the thymus gland where they mature. In the thymus gland the T cells acquire an ability to distinguish self, from the non-self. The T cells form part of cell mediated immunity. There are three types, cytotoxic T cells, helper T cells and supporter T cells. Helper T cells regulate the immune response by stimulating B cells to differentiate into plasma cells and to begin antibody production. Helper T cells are also called CD4 cells (Urden, Stacey & Lough, 2006). The latter is a type of white blood cell that fights infection and is produced in the spleen, lymph nodes, and thymus gland, which are all part of the lymph or infection-fighting system. CD4 cells move throughout the body helping to identify and destroy germs such as bacteria and viruses (Bridges, 2009). The CD4 count measures the number of such cells in a sample collected by means of a venopuncture. Along with other tests, the CD4 count helps to indicate how strong the immune system is, the stage of the HIV disease, guides treatment and predicts how the disease may progress. Keeping the CD4 count high, can reduce complications of the HIV disease and extend a patient's life (Johnson, 2012).

2.2.1 HOW HIV AFFECTS CD4 CELLS

HIV targets CD4 cells by binding to them and entering them to become a part of them. As CD4 cells multiply to fight infection, they also make more copies of HIV,

and as the virus continues to replicate it lead to a gradual decline of CD4 cells. HIV can destroy entire ‘families’ of CD4 cells so that the diseased ‘families’ designed to fight can easily be taken over. In such a situation this is when opportunistic infections are likely to develop (Johnson, 2012).

2.2.2 WHEN TO HAVE A CD4 COUNT TEST

The CD4 count test is recommended when someone is diagnosed with HIV. This is called a baseline measurement which allows making comparisons against future measurements about two to eight weeks after starting or changing treatment. Thereafter the test should be done every three to six months, as this is a reasonable time interval (Johnson, 2012).

2.2.3 WHAT DOES THE CD4 COUNT TEST RESULTS MEAN?

A CD4 count is reported as the number of cells per micro-liter of blood (cells/ μ l). A normal CD4 count is from 500 to 1,500 cells/ μ l of blood. It is more relevant to pay attention to the pattern of results, than to any one test result. In general, if the HIV disease is progressing, the CD4 count decreases. This means the immune system is getting weaker and the patient is more likely to get sick. In some people, CD4 counts can drop dramatically, even going down to zero (Johnson, 2012). The test does not always correspond with how well the patient is feeling. For example, some people can have high CD4 counts and do poorly. Others can have low CD4 counts and have few complications. If the CD4 counts decrease over several months, the

doctor may recommend beginning, or changing the antiretroviral therapy and starting preventive treatment for opportunistic infections. Public health guidelines recommend prescribing preventive antiretroviral therapy if CD4 counts are fewer than 200, whether or not a patient has symptoms. This is a late stage of HIV infection called AIDS. Some doctors start therapy earlier when the CD4 count reaches 350. If therapy is effective, the CD4 count increase or become stable (Johnson, 2012).

2.2.4 FACTORS THAT CAN AFFECT THE CD4 COUNT

There are a number of factors that can influence fluctuations in CD4 counts. These factors are the time the blood is taken, as CD4 counts tend to be lower in the morning and higher in the evening, and in addition acute illnesses such as pneumonia, influenza, or herpes simplex virus infections can cause CD4 counts to decrease for a while. If one is vaccinated or when the body starts to fight an infection, then the CD4 counts can go up or down. Cancer chemotherapy can cause CD4 counts to decrease and fatigue and stress can also affect test results (Johnson, 2012).

Should the CD4 counts decline substantially, the possibility exists for the manifestations of oral lesions, which could be detected by dentists. The next discussion point is therefore on the different types of oral lesions that manifest in HIV/AIDS.

2.3 DIFFERENT TYPES OF ORAL LESIONS THAT MANIFEST IN HIV/AIDS

Oral manifestation is the presence of the signs, symptoms and lesions of a systemic disease in and around the oral cavity (Online Dictionary, 2009). These lesions give a clue that there is an underlying systemic disease which need not necessarily be HIV. In HIV these lesions signify a deficient immunity as well as disease progression to AIDS. A number of studies have demonstrated that about 40-50% of HIV positive persons with oral fungal, bacterial or viral infections that these often occurred early in the course of the disease, or extremely late as the patient progress to AIDS (WHO, 2005). At present, three groups of oral manifestations of AIDS are defined based on their strength in its association with HIV (European Community Clearing-House, WHO, 1993). These groups are discussed below.

2.3.1 GROUP 1

This group is composed of eight cardinal lesions, namely oral candidiasis, hairy leukoplakia, Kaposi sarcoma, non-Hodgkin lymphoma and periodontal disease. The latter includes linear gingival erythema, necrotizing ulcerative gingivitis and necrotizing ulcerative periodontitis. These are strongly associated with HIV infection.

2.3.1.1 ORAL CANDIDIASIS (OC)

Oral candidiasis is caused by one of the *Candida* species, usually *Candida albicans*, which is a normal inhabitant of the oral cavity in many healthy individuals. In individuals infected with HIV, the development of oral candidiasis may be an indication of immune deterioration and has prognostic significance for the development of AIDS. Oral candidiasis may precede other signs of immune deficiency and is one of the clinical indicators for initiating antiretroviral therapy. Diagnosis of oral candidiasis is made by the identification of clinically distinctive lesions. It is the most prevalent oral lesion associated with HIV/AIDS. The following three forms of oral candidiasis are frequently associated with HIV infection:

- Pseudomembranous candidiasis;
- Erythematous candidiasis; and
- Angular cheilitis.

Another form, namely the chronic hyperplastic type, had been described, but this finding is rare. The clinical appearance of each form is different, as are the criteria for diagnosis (WHO, 2005). Pseudomembranous candidiasis is discussed first.

a) PSEUDOMEMBRANOUS CANDIDIASIS

The pseudomembranous type of candidiasis (thrush) is generally diagnosed on the basis of its characteristic clinical appearance, namely a white curd-like material that may be easily wiped off, and when removed reveals an erythematous mucosa (see Figure 2.1).



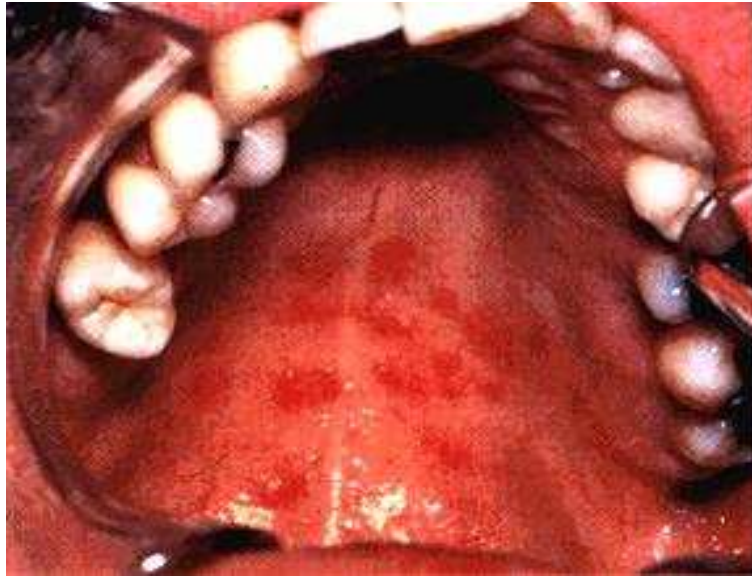
(HIV/AIDS Image Library (Oral), 2010)

Figure 2.1: Pseudomembranous candidiasis in the palate, tongue and cheek mucosa

b) ERYTHEMATOUS CANDIDIASIS

The erythematous type presents as flat, clinically red, sometimes painful macules that may first appear on the soft palate and oropharynx (see Figure 2.2). This type of candidiasis can appear as areas of mucosal erythema, or on the dorsal tongue as

irregular, depapillated, erythematous, sometimes painful areas. It may occur independently or simultaneously with pseudomembranous candidiasis (WHO, 2005).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.2: Erythematous candidiasis appearing as red plaques on the palate

c) ANGULAR CHEILITIS

Angular cheilitis is diagnosed on the basis of its clinical appearance. It appears as erythema or fissures of the labial commeasures, and frequently accompanies intra-oral candidiasis. In patients with deeply pigmented skin, depigmentation may occur at the site of angular cheilitis (Figure 2.3). Angular cheilitis is quite common among dental patients, regardless of their HIV status. It had been associated with certain anemia and nutritional deficiencies as well as decreased vertical dimension of occlusion (WHO, 2005).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.3: Angular cheilitis on the angle of the mouth

The next discussion is on the second example from the first group of oral manifestations of HIV/AIDS, namely hairy leukoplakia.

2.3.1.2 HAIRY LEUKOPLAKIA

Hairy leukoplakia most commonly presents as a white, ragged, corrugated, or irregular lesion involving the lateral and dorsolateral tongue (see Figure 2.4). Lesions may be unilateral or bilateral. Hairy leukoplakias involving other mucosal surfaces also had been reported. It is caused by infection of the lesional epithelial cells with the Epstein-Barr virus (EBV) and is associated with immune deterioration. Diagnosis of oral hairy leukoplakia in patients known to be HIV infected should be confirmed by identification of the distinct clinical lesions. If the lesions are

clinically consistent with hairy leukoplakia and the patient is known to be HIV infected, no further diagnostic procedure is necessary (Jair, Leao, Camila, Ribeiro, Alessandra, Carvalho, Cristina & Stephen, 2009).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.4: Hairy leukoplakia on the lateral border of the tongue

The next discussion is on the third example from the first group of oral manifestations of HIV/AIDS, namely Kaposi's sarcoma.

2.3.1.3 KAPOSI'S SARCOMA (KS)

Kaposi's sarcoma had been the most common malignant tumor associated with HIV infection. Since the introduction of antiretrovirals the occurrence of Kaposi's sarcoma seems to be rare. Herpes viruses (HHV-8) have been implicated in the etiology of Kaposi's sarcoma. Kaposi's sarcoma's oral lesions may interfere with function, be cosmetically objectionable, and proliferate uncontrollably (see Figure 2.5). The palate is by far the most commonly affected oral site, followed by the maxillary gingival. The lesions are often multifocal and usually present as flat purple plaques or raised nodules. The diagnosis of Kaposi's sarcoma should be confirmed by the identification of distinct clinical appearances (Jair et al., 2009).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.5: Kaposi's sarcoma occurring in the gingival

2.3.1.4 PERIODONTAL DISEASE

This is a chronic inflammatory process involving specific bacteria and affecting the tissue and bone supporting the teeth which includes linear gingival erythema, necrotizing ulcerative gingivitis and necrotizing ulcerative periodontitis. While periodontal disease can occur in anyone regardless of their HIV status, one particularly severe form known as necrotizing ulcerative periodontitis and a related condition, linear gingival erythema, appear to be unique to those with compromised immune systems (Jair et al., 2009).

a) LINEAR GINGIVAL ERYTHEMA

Linear gingival erythema, also called HIV gingivitis, is a brightly inflamed erythematous band of marginal and papillary gingiva. It is disproportional to the visible amount of plaque and bleeding. Pain is not a prominent feature and it does not resolve despite periodontal debridement.

b) NECROTIZING ULCERATIVE GINGIVITIS

Necrotizing ulcerative gingivitis is an aggressive type of gingivitis, it can be acute or chronic and is characterized by redness, swelling, and necrosis extending from the interdental papillae along the gingival margins leading to rapid loss of gingival tissue, and thus exposing the teeth. Pain, haemorrhage, necrotic odour, and often a pseudomembrane is its characteristic feature. The condition may extend to the oral

mucosa, tongue, palate or pharynx. The etiology is somewhat unclear, but may involve a complex of *Fusobacterium nucleatum* along with spirochetes like *Borrelia* or *Treponema* (Labome.Org, 2011).

c) **NECROTIZING ULCERATIVE PERIODONTITIS**

Necrotizing ulcerative periodontitis, previously called HIV-periodontitis, is the advanced form of necrotizing ulcerative gingivitis. Necrotizing ulcerative periodontitis in HIV is a severely painful gingival tissue, with severe loss of periodontal attachment & alveolar bone destruction with eventual necrosis. Rapid progression and spontaneous bleeding during minor probing are its characteristics (see Figure 2.6).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.6: Necrotizing ulcerative periodontitis

2.3.1.5 LYMPHOMA

Lymphoma is a common malignancy occurring in patients with HIV. Most AIDS patients with lymphoma develop lesions in sites other than the lymph nodes. Most AIDS-related lymphomas are of *B*-lymphocyte origin. Plasmablastic lymphoma of the oral cavity is an aggressive neoplasm derived from B cells, considered to be the second most common among HIV-associated malignancies, and the Epstein-Barr virus had been found in the lesions. The development of lymphoma in a patient with HIV is an AIDS-defining event. The clinical appearance of oral lymphoma varies from irregular, necrotic, ulcerated masses to non-ulcerated masses covered by normal or erythematous mucosa. The lesions may be painful (see Figure 2.7, L and R). Diagnosis of an oral mucosal lymphoma should be made by a biopsy and histological examination (Ferrazzo, Mesquita, Aburad, Nunes & De Sousa, 2007).



(Nikesh, Mohammad, Mrcpi & James, 2008)

Figure 2.7 (L and R): HIV associated non Hodgkin's lymphoma on the gingival area. Left nodular and right the ulcerative type.

The next discussion will be on the group 2 types of oral lesions.

2.3.2 GROUP 2

This group includes atypical ulcers, salivary glands diseases, viral infection such as cytomegalovirus (CMV), herpes simplex virus (HSV), papillomavirus (HPV), and herpes zoster virus (HZV).

2.3.2.1 ATYPICAL ORAL ULCERS

Mouth ulcers can be extremely painful and affect a person's ability to eat, and can be due to viral infections like herpes simplex ulcers or cytomegalovirus ulcers. These ulcers present as red lesions characterized by a halo of inflammation, often with a yellow-grey covering. The most commonly reported oral ulcers seen in patients with HIV are herpes simplex ulcers and aphthous ulcers. The ulcers can appear on the floor of the mouth, gum tissue adjacent to the teeth, on the tongue and inside the cheeks. Mouth ulcers can be associated with a compromised immune system, HIV drug side-effects and localized trauma to the area. They can also be symptoms of other viruses such as a cytomegalovirus infection, or herpes zoster and other diseases like histoplasmosis and lymphoma. With an accurate diagnosis and appropriate treatment, most oral ulcers resolve in a short time. Diagnosis of oral ulcers should be based on the characteristic clinical appearance, the results of cytological smears, viral culture (isolation), and biopsy and microscopic examination or the response to therapy. If an ulcer does not respond to treatment within two weeks, a biopsy and histological examination should be performed. If the decision is made not to obtain a

biopsy of an ulcer that is non-responsive to treatment, the provider should document the reason for the decision (Greenspan, 2006).



(Jair et al., 2009)

Figure 2.8: A necrotic oral mucosal ulceration, possibly associated with a cytomegalovirus infection

2.3.2.2 HERPES SIMPLEX ULCERS

The herpes simplex virus (see Figures 2.9 and 2.10), types 1 and 2, cause both primary (primary herpetic gingivostomatitis) and recurrent oral and genital diseases. The primary infection most commonly occurs in children, but may also occur in adults. Recurrent ulcers occur due to the reactivation of a latent infection. The herpes simplex virus usually appears as a vesicular eruption of the mucous membranes of the oral or peri-oral area, vulva, peri-anal skin, rectum, and occasionally the inguinal or buttock areas. The eruption develops into tender or

painful ulcerated lesions that are frequently covered with a clear yellow crust. In some patients, however, the typical painful vesicular or ulcerative lesions may be absent. Persons with HIV disease and low CD4 counts have more frequent recurrences of the herpes simplex virus and more extensive ulcerations than HIV-uninfected people. These ulcers differ from herpes simplex ulceration in immune competent individuals in that they are larger, can occur anywhere in the oral cavity, present for longer periods and are non-responsive to routine therapy. Furthermore, in immune competent individuals, these ulcers follow a predictable course and usually resolve spontaneously in seven to 10 days. Atypical herpetic ulcers presentations may be the first sign of immune-suppression and may signal a need for HIV counseling and testing in patients not known to be HIV infected (AIDS Education & Training Centers' National Resource Center, 2006).



(<http://lifestyle.iloveindia.com/lounge/tongue-ulcers-11050>.)

Figure 2.9: Herpes simplex ulcers on the tongue and lips



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.10: Herpes simplex on the lip, at an early stage of vesicle

2.3.2.3 HERPES ZOSTER

The reactivation of varicella zoster virus causes herpes zoster (shingles). The disease occurs in the elderly and the immunosuppressed. Oral herpes zoster causes skin lesions, followed by prodromal symptoms of pain, multiple vesicles on the facial skin, lips, and oral mucosa. Skin and oral lesions are often unilateral and follow the distribution of the maxillary and/or mandibular branches of the trigeminal nerve (Figure 2.11). The skin lesions form crusts and the oral lesions coalesce to form large ulcers (Figures 2.12 and 2.13). The ulcers frequently affect the gingival, so tooth pain may be an early complaint (American Academy of Dermatology, 2010).

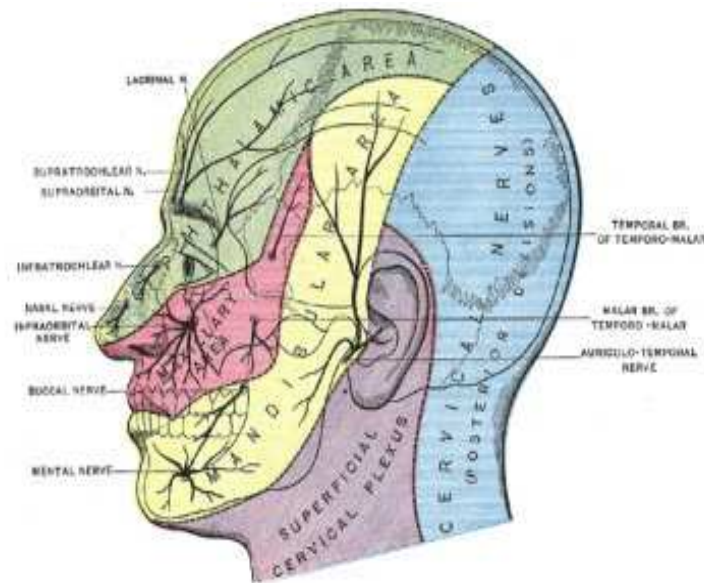


Figure 2.11: Diagram showing the three main branches of trigeminal nerve (Thomas & Habif, 2009)



© Elsevier 2004. Habif: Clinical Dermatology 4E - www.clinderm.com

Figure 2.12: Herpes zoster on one side of the face affecting the mandibular branch of trigeminal nerve (Bennington, 2006)



Herpes zoster ophthalmicus (www.health-res.com, 2010)

Figure 2.13: Herpes zoster affecting the ophthalmic branch of trigeminal nerve

2.3.2.4 HUMAN PAPILOMA VIRUS

The human papilloma virus, the virus associated with genital and other warts, is one of the most common sexually transmitted infections. Human papilloma virus associated lesions frequently occur in the oral cavity, including the lip and sides of the tongue (Figure 2.14). These lesions are usually raised, dull white and fleshy, smooth or rough, and may have a cauliflower-like appearance. Human papilloma virus lesions tend to be more serious and more difficult to treat in HIV-positive people. A few reports also suggest that these oral lesions may be more prevalent, or the number of lesions greater, in people with HIV (WHO, 2005).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.14: Oral warts on the lips

2.3.2.5 SALIVARY GLAND DISEASE ASSOCIATED WITH HIV INFECTION

Salivary gland involvement in children with HIV is well recognized and is much more common than involvement in adults (Figure 2.15). Characteristically, the gland is firm, non-tender and chronically enlarged (unilateral or bilateral) and usually causes few symptoms. Lymphoepithelial cysts are less common than in adults. Xerostomia with decreased salivary flow rates occurs in adults but is infrequent in children. The diagnosis of HIV parotitis is usually clinical with the typical findings. Other forms of chronic parotitis are rare in children (Jerry & Benjamin, 2009).



(HIV/AIDS Image Library (Oral), 2010)

Figure 2.15: Enlarged parotid salivary gland

The next discussion will be on the group 3 type of oral lesions.

2.3.3 GROUP 3

These lesions are rarer than those in groups 1 and 2. Lesions to be considered and to be discussed are drug reactions like the Stevens-Johnson syndrome, neurological disorders like Bell's palsy and squamous cell carcinoma.

d) 2.3.3.1 STEVENS-JOHNSON SYNDROME

Stevens-Johnson Syndrome is a life-threatening condition that starts to appear on the skin in which cell death causes the epidermis to break up from the dermis (Figure 2.16). The syndrome is an immune-complex mediated hypersensitivity reaction that is a severe expression of erythema multiform, due to a drug reaction. It is now known also as erythema multiform major. The Stevens-Johnson syndrome typically involves the skin and the mucous membranes. While minor presentations may occur, significant involvement of the oral, nasal, eye, vaginal, urethral, gastro-intestinal tract, and lower respiratory tract mucous membranes may develop in the course of the illness. Gastrointestinal and respiratory involvement may progress to necrosis. The Stevens-Johnson syndrome is a serious systemic disorder with the potential for severe morbidity and even death (Sulianti, 2010). According to the Mayo Clinic, the biggest factor for developing Stevens-Johnson syndrome is the use of certain medications. Such medications can include nonsteroidal anti-inflammatory drugs (NSAIDs), like ibuprofen, anti-gout medications, like allopurinol, as well as penicillin's, sulfonamides, and anticonvulsants. Infections from diseases such as

HIV, influenza, herpes, typhoid, diphtheria and hepatitis can also cause the disease (Mayo Foundation for Medical Education and Research, 2009).



(Steven Johnson syndrome image by flickr.com 2010)

Figure 2.16: Stevens-Johnson syndrome due to drug reaction affecting the mouth and neck

e) **2.3.3.2 BELL'S PALSY**

Bell's palsy (Figure 2.17) is a sudden, idiopathic, unilateral peripheral cranial V11 nerve palsy (Facial nerve). Symptoms are hemi facial paresis of the upper and lower face. There are no tests to confirm the diagnosis. Bell's palsy, being idiopathic, causes physicians to be circumspect about its origin. However, it is thought to have viral, bacterial, and autoimmune ties. Such ailments include nerve inflammation/muscular signal block from herpes simplex-virus 1 via unknown carriers, impaired immunity (stress, illness such as HIV, AIDS, trauma) or anything

directly or indirectly compromising the immune system. Examples here are for example, bacterial infections such as Lyme disease and middle ear infection (otitis media), or trauma, tumors and congenital defects. Anything that causes inflammation and swelling of cranial nerve VII can trigger Bell's palsy (Bruce Lo, 2010).



(Bruce Lo, 2010)

Figure 2.17: Bell's palsy depicting facial paralysis on the left side

f) 2.3.3.3 SQUAMOUS CELL CARCINOMA

The majority of malignancies arising in the head and neck among patients with HIV/AIDS are Kaposi sarcoma and non-Hodgkin lymphoma. Patients with HIV/AIDS are also at an increased risk of developing several carcinomas of the head and neck. They are also at an increased risk of developing mucosal squamous cell carcinoma, nasopharyngeal carcinoma, lymphoepithelial carcinoma of the salivary

gland, and Merkel cell carcinoma in this anatomic region. Data also suggest that HIV-positive patients with these cancers present at a younger age, with more aggressive diseases and worse prognosis compared to HIV-negative patients. The treatment involves surgical resection with or without radiation therapy and chemotherapy for locally advanced and metastatic diseases. AIDS patients, however, are more likely to suffer radiation treatment complications. Highly active antiretroviral therapy had not altered the incidence of these malignancies (Purgina, Pantanowitz & Seethala, 2011).

2.4 PREVALENCE OF ORAL MANIFESTATION OF HIV/AIDS

Studies from the Americas and Europe reported a decreased frequency of HIV-related oral manifestations of 10–50% following the introduction of highly active antiretroviral therapy. Evidence suggests that highly active antiretroviral therapy plays a crucial role in controlling the occurrence of oral candidiasis. The effect of highly active antiretroviral therapy in reducing the incidence of oral lesions other than oral candidiasis does not appear as significant, possibly as a result of low lesion prevalence in industrialized countries. In contrast to other oral manifestations of HIV, an increased prevalence of oral warts in patients on highly active antiretroviral therapy has been reported. HIV-related salivary gland diseases showed a rising prevalence in the USA and Europe. The emergence of HIV-related oral diseases may be indicative of failing therapy. In addition a range of orofacial iatrogenic consequences of HAART had been reported, and it is often difficult to distinguish between true HIV-related oral disease manifestations and the adverse effects of highly active antiretroviral

therapy. A possible association between an increased risk of oral squamous cell carcinoma and HIV infection had been suggested by at least three epidemiological studies, with reference to the lip and tongue. These substantial and intensive research efforts directed toward enhancing knowledge regarding the orofacial consequences of HIV infection in the industrialized nations require dissemination in the wider health care environment (Hodgson, Greenspan & Greenspan, 2006).

Furthermore, oral lesions in HIV infection have been well-documented in developed countries (see Table 2.1), but there are fewer reports on oral lesions from developing countries like in Namibia. Oral candidiasis is the most common opportunistic infection seen in all continents. Kaposi's sarcoma has been reported only from Africa and Latin America, while histoplasmosis and penicilliosis were reported in patients with advanced disease from Thailand. HIV-associated salivary gland disease has a high prevalence in Africa and Latin America, especially in the pediatric group. It is clear that there are considerable regional variations in the oral manifestations of HIV infection, depending both on the populations studied and on the clinical expertise available, among other factors. Well designed and documented studies are necessary for the correct assessment of the nature and magnitude of the problem in developing countries, if oral health measures are to be effectively formulated for the HIV-infected (Ranganathan & Hemalatha, 2006).

Table 2.1 Percentage prevalence of oral manifestations of HIV and oral candidiasis in different countries

Country	Percentage prevalence of oral manifestations of HIV/AIDS	Year	Country	Percentage prevalence of oral candidiasis	Year
Southern India	80.9%	2009	Uganda	70%	2007
Nigeria	84%	2008	Southern India	44.5%	2006
China	77.1%	2009	Southern India	43.1%	2008
Uganda	72%	2007	Nigeria	36.4%	2005
			Tanzania	23.5%	2006

Based on the above table, the prevalence of oral manifestations of HIV/AIDS is reported to be high in some areas, 72% in Uganda (Tirwomwe, Rwenyonyi, Muwazi, Besigye & Mboli, 2007) and 84.0% in Nigeria (Adedigba, Ogunbodede, Jeboda & Naidoo, 2008), and 77.1% in China (Hanil, Chen2, Ii1, Chen2, Zhao1, Iiu1, Iiu1, Ii2, Guo2, Zhao2, Zhang2, Wu2, Ili2 & Iiu1, 2009).

In a cohort study conducted in the southern part of India between 2004 and 2008, it was reported that the prevalence of oral lesions in HIV patients who are not on HAART was 80.9% (Ranganathan, 2009).

Candidiasis and its variants was the most commonly and prevalent reported oral lesion, the occurrence ranged from 23.5% in Tanzania (Matee, Hamza, Simon, Kikwilu, Moshi, Mugusi, Mikx, Verweij & Van der Ven, 2006), to 36.4% in Nigerian women (Taiwo, Okeke, Otoh & Danfillo, 2005). In South India in 2006 the prevalence was 44.5% (Sharma, Pai, Suhas, Ramapuram, Doshi & Anup, 2006) but dropped to 43.1% in 2008 (Sharma, Pai, Setty, Ramapuram & Nagpal, 2008). Research undertaken in Uganda reported an 70% prevalence rate (Tirwomwe, Rwenyonyi, Muwazi, Besigye & Mboli, 2007).

The discussion up to now focused on the disease processes and comparisons internationally. There is however a human side involved. The next discussion will therefore be on the effect of oral manifestations of HIV/AIDS on patients' lives.

2.5 THE EFFECT OF ORAL MANIFESTATIONS OF HIV/AIDS IN PATIENTS' LIVES

Patients with HIV/AIDS suffer from numerous complications, of which one is oral lesions that may lead to malnutrition. It is well established that HIV infection can lead to malnutrition, while poor diet can in turn speed the disease's progress. As AIDS treatment becomes increasingly available in the poorest parts of the world, critical questions are emerging about how well the drugs work in people who are short of food (WHO, 2005). One factor behind HIV-related weight loss is increased energy expenditure. Though no one knows quite why, many studies had found that

people with HIV tend to burn around 10% more calories while resting, compared to those who are uninfected (Batterham, 2005).

Faster metabolism is not the only problem. There are two other important reasons why people with HIV may lose weight or suffer childhood growth failure (Wanke, 2004). The first reason is a loss of appetite due to opportunistic infections, especially those that cause problems in eating and swallowing. For example, sores in the mouth or throat may cause pain when swallowing, while diarrhea or nausea may disturb normal eating patterns. The second reason is reduced absorption of nutrients due to diarrhea and direct damage to the intestinal mucosa by HIV. Moreover, someone who is ill may be less able to earn money, shop for food or prepare meals. Stress and psychological issues may also contribute to malnutrition.

Furthermore, oral lesions associated with HIV had been reported to cause a number of discomforts to patients. In a study done in Uganda it was reported that tooth brushing, chewing and swallowing were frequently associated with discomfort and the reported forms of discomfort were dry mouth, increased salivation and burning sensations, especially on taking salty and spicy foods or acidic drinks. Only 8.5% of the subjects were taking medications specifically for oral lesions, which included antifungal, antiviral, and antibacterial agents. However, despite the devastating oral lesions seen in HIV patients, antiretroviral drugs had played a significant role in lowering the prevalence hence prolonging patients' lives. A study, conducted among HIV positive adult and children in Tanzania, concluded that adult patients receiving HAART had a significantly lower prevalence of oral lesions, particularly oral

candidiasis and oral hairy leukoplakia. There was no significant change in occurrence of oral lesions in children receiving highly active antiretroviral therapy (HAART). In the mentioned study the occurrence of oral lesions, in both HAART and non-HAART patients, correlated with the WHO clinical staging and CD4⁺ of less than 200 cells/ μ l (Matee et al., 2006).

2.6 EFFECTS OF ORAL MANIFESTATIONS OF HIV/AIDS ON TAKING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY DRUGS

There is strong evidence that malnourished people are less likely to benefit from antiretroviral therapy compared to healthy ones. One study in Malawi found that patients with mild malnutrition (a low body weight for their height) were twice as likely to die in the first three months of treatment. For those with severe malnutrition the risk was six times greater than for those of healthy body weight (Zachariah, Rony, Fitzgerald, Margaret, Massaquoi, Moses, Pasulani, Ogles, Arnould, Line, Makombe, Simon, Harries & Anthony, 2006).

Without food or the right nutrition, taking antiretroviral drugs can be so painful that people simply do not take them. In a choice between taking pills with no immediate or obvious effect, and eating food to survive, food will almost certainly take priority every time. A health worker in Zimbabwe, where malnutrition is widespread, explained that taking antiretroviral drugs on an empty stomach is like digesting razor blades. The result is that many simply do not take them (David, 2009).

Since oral lesions can cause pain on food taking, early treatment is crucial to allow patients to adhere to antiretroviral treatment.

2.7 ASSOCIATION OF ORAL MANIFESTATIONS OF HIV/AIDS WITH CD4 COUNTS

Oral candidiasis lesions associated with HIV/AIDS may be a useful clinical indicator of early immune dysfunction mediated by HIV (Taiwo, Okeke, Otoh & Danfillo, 2005). Oral candidiasis can act as a marker for immunosuppression (Sharma et al., 2006). Concurrent oral manifestations were good predictors (80-100%) of severe immune suppression because in most resource poor countries where facilities for undertaking CD4⁺ counts were not available, the presence of concurrent oral manifestations may be used as an indicator of deteriorating immune status (Sharma, Pai, Setty, Ramapuram & Nagpal, 2008). Four or more concurrent oral lesions are statistically significant with low CD4⁺ counts <200 cells/ μ l. The highest and lowest mean CD4⁺ cell counts in these studies were seen in individuals with linear gingival erythema and pseudomembranous candidiasis, respectively. Patients with CD4⁺ counts < 200 cells/ μ l were associated with 15 times greater risk of pseudomembranous candidiasis and four times at greater risk for occurrence of any oral manifestation (Sharma, Pai, Setty, Ramapuram & Nagpal, 2008). In China it was reported that the prevalence of oral candidiasis and oral hairy leukoplakia increased as the CD4 decreased. Oral hairy leukoplakia was more closely correlated with CD4⁺ counts (Hani1 et al., 2009). There was also a significant association between the presence of oral lesions and CD4⁺ cell counts of < 200 cells/ μ l and with

the WHO clinical staging. Oral lesions were also associated with tobacco smoking and the occurrence of oral lesions in both HAART and non-HAART patients correlated with the WHO clinical staging and CD4⁺ less than 200 cells/ μ l (Matee et al., 2006).

2.8 SUMMARY

In chapter two the relevant literature was discussed and positioned to a certain extent within the framework of the study. The changes of the immune system provided the introduction to possible lesions to be identified. The chapter then presented a discussion of the prevalence of these oral lesions in HIV/AIDS patients. This was linked to the association with CD4 counts. The effect of oral HIV lesions in taking treatment was highlighted. In addition the aspect of nutrition was also briefly discussed. The next chapter addresses the research design and methodology.

CHAPTER THREE

RESEARCH DESIGN AND METHODOLOGY

3.1 INTRODUCTION

This chapter takes an in-depth look at both the methodology and study design of the study. The main purpose of the study was to explore and describe the magnitude of oral manifestations of HIV/AIDS and its association with CD4 counts among adult patients attending the *Centre for Disease Control* clinic at the Oshakati Hospital. The specific objectives were:

- To determine the prevalence and types of oral lesions among patients diagnosed with HIV/AIDS.
- To determine the association between CD4 counts and oral lesions among patients diagnosed with HIV/AIDS.

3.2 STUDY METHODOLOGY

The methodology is the approach to the entire process of the research study (Welman, Kruger & Mitchell, 2009, p. 13). In other words, the methodology is the research tool used to test the truth. In this study part of this truth is to assess the prevalence of oral manifestations of HIV/AIDS and its association with CD4 counts among adult patients in the pre-HAART *Centre for Disease Control* clinic at Oshakati Hospital.

3.2.1 STUDY DESIGN

The research design refers to the plan of action that links the philosophical assumptions to a specific method (Creswell, Vicki & Clark, 2007, p. 4). It seeks answers to the research question(s). A study design is thus a general plan or blueprint that describes how the research will be conducted. It focuses on the kind of study proposed and its desired results. It begins with a problem or question and in the context of the logic of the research, determines what kind of evidence will address the research question adequately (Mouton, 2002, p. 56). In this study a quantitative, cross sectional design, incorporating descriptive and explorative approaches was used.

A quantitative study is a positivist approach which is based on a philosophical approach known as logical positivism. It holds reasoning that research must be limited to what we can observe and measure objectively, namely that which exists independently of feelings and opinions of individuals (Welman, Kruger & Mitchel, 2009, p. 6). This study utilized cross-sectional design with a descriptive and explorative approach to answer the objectives of this study.

Cross-sectional studies provide a 'snapshot' of the outcome and the characteristics associated with it, at a specific point in time. That is, it entails collecting data *at* and *concerning* one point in time, where the results focus on finding relationships between variables at one moment in time by drawing inferences from existing differences between people, subjects, or phenomena. For this reason the design was

selected as the data collection was taken at a specific time of the year for academic purpose (University of Southern California Library, 2013).

Since cross-sectional designs provide only a snapshot of analysis so there is always the possibility that a study could have differing results if another time-frame had been chosen. This is most likely to be the case in this study, as the number of patients in pre HAART keeps on changing on a daily basis, since some move to the highly active antiretroviral therapy (HAART) clinic, some gets transfers, and some may die (University of Southern California Library, 2013).

Because cross-sectional designs generally use survey techniques to gather data, they are relatively inexpensive and take up little time to conduct. This was thought to be suitable for academic purpose as the program is time bound (University of Southern California Library, 2013).

In a descriptive approach, the researcher observes (i.e. clinical examination of patients), documents and describes a situation as it occurs naturally. This approach may also be used to collect, organize and summarize information about the situation being investigated (Capri & Egger, 2008). In this study the researcher sought to determine the prevalence of HIV related oral and peri-oral lesions and also to describe the association of these lesions in association with changes in CD4 counts.

Exploratory research is used to make preliminary investigations into relatively unknown areas (Blanche, Derrheim & Painter, 2006, p. 44). Exploratory research is conducted into an issue or problem where there are few or no earlier studies done to

refer to. In the context of this study, very little is known in Namibia about the prevalence of oral and peri-oral manifestations of HIV/AIDS in patients, thus an exploratory approach was deemed applicable.

3.2.1.1 STUDY POPULATION

This study was conducted at the Intermediate Hospital Oshakati pre-HAART *Centre for Disease Control* clinic in the Oshana Region. Oshana is one of the thirteen Regions of Namibia located in the northern part of the country. The town of Oshakati is the capital city for the Oshana Region (CIA World Fact Book, 2008).

After Windhoek, Oshakati is the second largest populated city in Namibia (CIA World Fact Book, 2008). The Intermediate Hospital Oshakati supports a number of clinics and is the largest referral hospital for the nearby northern regions (Absolute Astronomy.com, 2007)

A study population consists of individuals, organizations, human products and events. A research problem therefore relates to a specific population which encompasses the total collection of all units of analysis about which the researcher wishes to make specific conclusions (Welman, Kruger & Mitchel, 2009, p. 52). In this study the target populations was all HIV positive patients attending the pre-HAART *Centre for Disease Control* in the Oshakati Hospital from April to September 2012 were selected.

Inclusion criteria

- All HIV positive patients not on highly active antiretroviral therapy (HAART) who were willing to participate in the study by giving consent when attending the pre-HAART *Centre for Disease Control* clinic at Oshakati Hospital.
- Eighteen years and older.

Exclusion criteria

- All HIV positive patients on highly active antiretroviral therapy.
- Patients who were younger than eighteen years.
- All HIV positive patients not on highly active antiretroviral therapy, but who had received treatment for oral lesions in the last six months

3.2.1.2 SAMPLE SIZE AND SAMPLING PROCEDURE**SAMPLING SIZE**

A sample is a group of people or elements that form part of a study population. It is a small portion of the total set of the population. Together they comprise the subject of study (Welman, Kruger & Mitchel, 2009, p. 53). In this study the sample size was calculated as to be 303 based on the following formula:

$$n = \frac{t^2 \cdot p(1-p)}{m^2}$$

$$= \frac{1.96 \times 1.96 \times 0.73(1 - 0.73)}{0.05 \times 0.05}$$

$$= \frac{3.84 \times 0.1971}{0.0025}$$

$$n = 303$$

Explanation

n = required sample size

t = confidence level at 95% (standard value of 1.96)

p = estimated prevalence of oral manifestation of HIV from the neighboring country Lesotho 73% (0.73)

m = margin of error at 5% (standard value of 0.05)

SAMPLING PROCEDURE

The screening of newly enrolled HIV positive patients at Oshakati Hospital's Pre-HAART clinic was done from the 2nd April 2012 until the 10th September 2012. The time period of the study was selected based on the estimated number of newly enrolled patients per week at *Centre for Disease Control* clinic, and how long it would took to obtain the calculated sample size, namely a total of 303 patients. During this time period a total of 405 patients were screened. Three-hundred and

seventy five (375) patients met the inclusion criteria. Of the 375 who met the inclusion criteria, 360 consented to participate, and they were all included in the study, and thus became the sample of this study. This gave a participation rate of 96%.

3.3 DEVELOPMENT, REFINING AND CONFIRMATION OF THE CHECKLIST

The research instrument consisted of a checklist compiled by the researcher and is discussed under the following headings:

- The development and compilation of the checklist
- Refining the checklist
- Confirmation of the checklist (pilot phase)

3.3.1 THE DEVELOPMENT OF THE CHECKLIST

The checklist used was based on the clinical definition of oral manifestations of HIV/AIDS as presented by the WHO. It was divided into three sections as presented in Table 3.1 below (WHO, 2005).

Table 3.1 Framework used in the development of the checklist

Section of the Checklist	Format of items	Relationship to the framework of the study
Section A	Bibliographical information	Establishing a patient profile
Section B	Presence and type of oral Lesion	Assessment for the detections of oral lesions
Section C	CD4 count	Correlation of diagnosed oral lesion with CD ₄ count in cells per microlitre (cells/ μ l)

Section A included patients' social and demographic information such as age, sex, physical address, level of education and occupation. Section B covered clinical oral manifestations of HIV which were further classified as lesions strongly associated with HIV, lesions less commonly associated with HIV and lesions rarely seen in HIV. This classification is based on the European Community Clearing House (1993) and the WHO (2005), on oral problems related to HIV infection. Section C included the CD4 counts.

3.3.2 REFINING OF THE CHECKLIST

The refining of the instrument (checklist) included taking into account aspects such as validity, reliability and the pilot testing. These aspects will be discussed next.

3.3.2.1 VALIDITY

Validity refers to the degree in which the test or other measuring devices are truly measuring what the researcher intends to measure (AllPsych and Heffner Media Group, Inc, 2005).

In this study, the checklist was also analyzed for both face and content validity.

- **Face validity**

Face validity implies that the checklist (instrument) should be able to measure what it is intended to measure and also whether the measurement makes sense and is reasonable (Bell, 2006, p. 117). This checklist was presented to a professional colleague who agreed to the face validity of the checklist.

- **Content validity**

Content validity may be defined both as the adequacy of the content area being measured, as well as the representativeness or sampling adequacy of the content of an instrument. In this study the checklist used for the physical assessment of the oral cavity is based on the documented content from the WHO clinical case definition of oral manifestations of HIV/AIDS (WHO, 2005).

3.3.2.2 RELIABILITY

Reliability is the consistency of the research measurement, or the degree to which an instrument measures the same way each time it is used under the same condition with the same subjects. In short, it is the repeatability of a researcher's measurement. A measure is considered reliable if a person's score on the same test given twice is similar. It is important to remember that reliability is not measured, it is estimated (AllPsych and Heffner Media Group, Inc., 2005).

In this study an inter-rater reliability approach was followed, in which the five (5) patients selected for the pilot study, in which two had oral lesions, one was afflicted with cheilitis and the second one had oral Kaposi's sarcoma and three of them did not have lesions. These patients were again assessed for a second time by a different (second) dentist and the results were compared. Both the researcher and the second dentist derived at similar diagnoses for these five patients (see also the discussion in section 3.4, which deals with the pilot testing of the checklist).

3.4 PILOT TESTING OF THE INSTRUMENT

A pilot study is a small-scale methodological test intended to ensure that the proposed methods and procedures will work in practice before being applied in a large expensive investigation. Pilot studies provide an opportunity to make adjustments and revisions before investing in, and incurring the heavy costs associated with a large study (Ruxton & Colegrave, 2006). In this study a pilot

testing was conducted during March 2010 at the pre-HAART clinic used in this study in order to pre-test the checklist before starting data collection. The pilot testing of the checklist was conducted on five (5) patients who were not included in the main study of the current research. Inter-rater reliability of the instrument was established and minor mistakes that were encountered, for example the sequence followed during the assessment, were also corrected (Annexure 1).

3.5 DATA COLLECTION

The data collection was done using a checklist instrument which was divided into two parts, namely a structured interview, which was used to collect demographic data, and a structured observational schedule which was used to collect data for the oral lesions and CD4 counts (cells/ul).

Data collection was done in coordination with the personnel of the Centre for Disease Control at the pre-HAART clinic, who identified the patients and communicated with the researcher during the visits of patients to the study site (*Centre for Disease Control* clinic) from the 2nd April 2012 up to the 10th September 2012.

This liaison between the nursing manager and the researcher during this phase did present a possibility of a breach of anonymity and confidentiality. This gray area was addressed by the nursing manager by asking permission from the patients if she could refer them to the researcher who is also their resident dentist. This request

involved also requesting their permission for their HIV status to be revealed to the dentist.

During the subsequent meetings, the researcher then completed the consent forms and explained her role as well as all relevant ethical considerations that she would adhere to. These considerations are discussed under “Ethical Issues”.

All HIV positive patients that were identified and who accepted to participate in the study, were invited one by one in the examination room, and under the direct sunlight sitting on the chair in an upright position, the researcher used a mouth mirror and a dental explorer (probe) to undertake a physical dental examinations of peri-oral and oral structures. Simultaneously, the most recent CD4 count results were recorded from the patient’s respective health passports. Thus those who did not have CD4 counts or old CD4 counts on their health passports had the relevant tests done.

3.6 DATA ANALYSIS

Descriptive as well as inferential statistics was utilized. Data entry and analysis were done using the Epi Info programme, version 3.0 software. For descriptive statistics the percentages and proportions were calculated as well as frequency distributions.

In addition chi-square tests and odds ratios were calculated to establish the associations. A statistician provided inputs from the outset of the study, for example, during the compilation of the data collection instrument.

3.7 ETHICAL ISSUES

Ethical issues are very important in research, as it is imperative that a study does not interfere with patients' rights. It included the right to decide whether to participate, not be subjected to possible harm, deception or embarrassment. To ensure that all ethical issues pertaining to the research were addressed, the proposal was submitted to be approved by a biomedical ethics committee prior to commencement of this study, ethics approval was obtained from the University of Namibia Post Graduate Studies Committee (Annexure 2) and the Ministry of Health and Social Services (MOHSS) research committee (Annexure 3), where the written proposal was reviewed by the committee to ensure that it conformed to ethical standards of scientific research. In addition, permission to commence data collection was requested, and obtained, from the Oshakati Hospital management at the health facility selected for this study (Annexure 4). Finally, informal verbal consent was obtained from the patients before individuals were recruited as participants.

The patients were informed about all aspects of the research, specifically with regards to the nature and purpose. Informed consent is a legal condition whereby a person can be said to have given consent based upon a clear appreciation and understanding of the facts, implications and future consequences of an action. In order to give informed consent, the individual concerned must have adequate information on what to give consent for, in other words, being informed is an important part of decision making of the participants to take part in a research or not

which depend on the quality of information they received about the research to be able to make educated/ informed decisions (Welman, Kruger & Mitchel, 2009, p. 346).

All the participants who met the inclusion criteria were informed that they had a right to withdraw from the research at any time and were assured of confidentiality, anonymity and privacy during demographic data collection as well as the physical oral examination. In addition to obtaining consent for the oral examination, informed consent was also obtained from the patient/client to allow their CD4 counts results from the health passport to be used. They were ensured that the results will be kept confidential and never to be revealed. Information about the purpose, methods, benefits and possible outcomes of the research was given to the patients before data collection and they were requested to ask questions which were answered to ensure that informed decision were made.

When people agree to participate in research, they are expected to provide personal information and researchers must commit to respecting and maintaining the confidentiality of their subjects. When people disclose private information for any public health purpose it is expected that the information will be held in confidence. Only with this trust can public health programmes succeed (Encyclopedia of Public Health, 2005). All the patients in this study were assured that the information and opinions they shared would be treated with strict confidentiality. They were assured that data would only be used for the stated purpose of the research and that no other person would have access to the data collected.

Special consideration was given to protection of the privacy of patients during the observation phase, namely the physical oral examination. Each patient was examined in a closed room by the researcher who used the assistance of a nurse for language translation. No other person was allowed to enter the room during this period. It was made clear to the patients that they had the right to refuse to participate in the research if they wish so.

Anonymity of information collected from research patients means that there was no way to ascertain personal information of the participants or to link responses to them. A study should not collect identifying information of research participants unless it is essential to the study protocol (William & Trochim, 2006). In this study the patients responses were anonymous as their personal details, such as names and addresses were not recorded on the questionnaires, only their areas of residence. To ensure anonymity each patient/client was given a number that was recorded on the questionnaire.

All the patients with oral lesions in this study received appropriate care and treatment according to national guidelines on care and treatment of HIV infected individuals with the help of doctors and a dentist (including myself) at the selected research site and referrals to other specialists, disciplines and even other hospitals as per need identified at that particular time was done.

3.8 SUMMARY

In this chapter, the methods used to select the study population, sampling, research design, including the development of the checklist used, the pilot study and validity and reliability were discussed. The data collection process and analysis to be utilize were also highlighted, as well as the ethical considerations. The next chapter deals with the data analysis and presentations of the research findings.

CHAPTER FOUR

DATA ANALYSIS AND PRESENTATION AND DISCUSSION OF THE FINDINGS

4.1 INTRODUCTION

This chapter presents the findings and discussion of the study on the prevalence of oral and peri-oral lesions of HIV/AIDS, and its association with CD4 counts in adult patients attending the *Centre for Disease Control* clinic at the Oshakati Hospital.

The objectives were:

- *To determine the prevalence and types of oral lesions among patients diagnosed with HIV/AIDS.*
- *To determine the association between CD4 counts and oral lesions among patients diagnosed with HIV/AIDS.*

Before the prevalence and types of peri-oral lesions will be discussed, the demographic profile will first be described.

4.2 THE DEMOGRAPHIC PROFILE OF THE PATIENTS

The demographic profile included five items (see Annexure 1). The presentation on the demographic data is inclusive as no distinction as yet is made between patients with oral lesions and those without any lesions. They were:

- Gender (sex)
- Age
- Place of residence
- Employment status, and
- Education.

The first discussion will be on gender.

- **Gender**

A total of three hundred and sixty patients met the inclusion criteria and was examined. The results in this study indicated that the majority of the patients were females, namely 221 (61.4%) and only 139 (38.6 %) were male (See Table 4.1)

The findings in this study appeared to support similar statistics on gender distribution and the prevalence of HIV/AIDS in Namibia. The estimated HIV prevalence in Namibia during 2012 was indicated as 10.3% among 15- 24 year old females, and 3.4% among 15- 24year old males (De Beer, Gelderblom, Schelleken, Gaeb, Van Rooy, McNally, Wit & Tobias, 2012).

The next discussion will be on the age distribution of the patients.

- **Age Distribution**

In this study the ages ranged between 18 years to more than 61 years. The mean age was 35 years. One patient was 81 years of age (see Table 4.1).

The mean age of 35 concur to a degree to the available information about the age distribution nationally. In Namibia, young people aged 20 to 34 years constitute one of the groups at highest risk of HIV infection (De Beer, Gelderblom, Schelleken, Gaeb, Van Rooy, McNally, Wit & Tobias, 2012).

- **Employment Status**

From the findings in this study it emerged that 131 (36.4 %) were self-employed, 125 (34.7%) were employed in a more employer/employee relation, and 39 (10.8%) were students (see Table 4.1).

- **Education Status**

There were two patients (0.6%) who had a minimum of a Bachelors degree with a total of 168 (46.7%) who indicated that they had completed their secondary school education (see Table 4.1).

These results indicated to a substantial group of patients who had completed their secondary school education. Descriptively these findings compared well with the current information available in Namibia. According to the last demographic and health survey in 2006/2007 on HIV/AIDS patients, more than half of the 20- to 34-year-old group attained a secondary level at school and up to 10% reached a higher educational level (De Beer, Gelderblom, Schelleken, Gaeb, Van Rooy, McNally, Wit & Tobias, 2012).

Table 4.1 Demographic characteristics of patients in the study sample (n=360)

Characteristics	Categories	Frequency	Percentage (%)
Sex	Male	139	38.6
	Female	221	61.4
	Total	360	
Age	18-20	30	8.3
	21-29	28	7.8
	30-39	166	46.1
	40-49	67	18.6
	50-59	39	10.8
	61 +	10	2.8
	Total	360	
Employment	Student	39	10.8
	Not employed	65	18.1
	Employed	125	34.7
	Self employment	131	36.4
	Total	360	
Education	No formal education	40	11.1
	Primary	91	25.3
	Secondary	168	46.7
	Vocational Training College	29	8.1
	Diploma	28	7.8
	Degree +	2	0.6
	Total	360	

Four of the five items that dealt with biographical information of the patients in this study, thus appeared to correlate at least descriptively with the biographical information available about HIV/AIDS patients in Namibia in general.

The next discussion will be on the first objective of the study, which is to determine the prevalence and types of oral and peri-oral lesions among newly diagnosed HIV/AIDS patients.

This discussion will be presented in the following order:

- The prevalence of oral lesions in general in the study group (patients).
- The prevalence of oral lesions based on types of lesions.
- The prevalence of oral lesions based on their strength of associations with HIV/AIDS, as well as with possible demographic characteristics.

The first discussion will be on the prevalence of oral lesions in general.

4.3 THE PREVALENCE OF ORAL LESIONS IN GENERAL

The findings that emerged indicated that out of the 360 patients examined, 197 (55%) had oral lesions associated with HIV/AIDS [95% CI (1.52-3.67)] (see Figure 4.1).

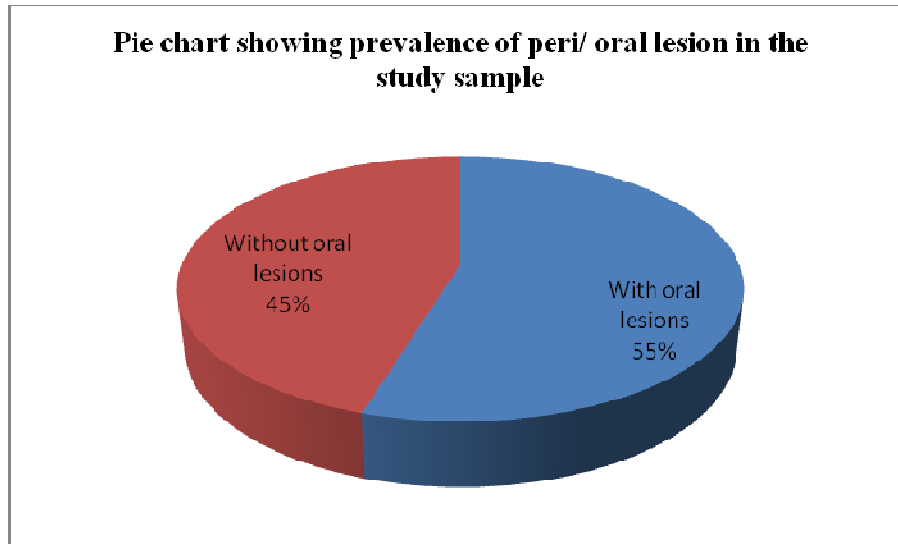


Figure: 4.1 Pie chart on prevalence of oral and peri-oral lesions in the study sample (n=360)

This prevalence (55%) of oral lesions in this region, namely Oshakati, is lower than that reported by Tirwomwe, Rwenyonyi, Muwazi, Besigye and Mboli (2007), who found that 72% of the 370 patients examined in a study in Uganda had oral and peri-oral lesions. In another study in Nigeria, Adedigba, Ogunbodede, Jeboda and Naidoo (2008) reported that 84% of 225 patients examined had oral and peri-oral lesions.

The researcher could not find any applicable Namibian literature for comparison purposes. The conclusion that was drawn from this finding is thus descriptive only, meaning that in this study the prevalence of oral lesions was lower than the prevalence reported in studies from two major developing countries in Africa.

The different types of oral and peri-oral lesions identified in this study will be presented next.

4.4 TYPES OF ORAL LESIONS IDENTIFIED

The types of oral and peri-oral lesions are indicated in Table 4.2. Although only 197 patients manifested with these lesions, some presented with more than one lesion, thus increasing the number of lesions to a total of 207. Table 4.2 presents the results on the distribution and prevalence of the different types of oral and peri-oral lesion identified.

Table 4.2 Percentage distribution of the different types of oral lesions identified**(n=207)**

Type of oral lesions	Number	Percentage (%)
Group I lesions : Strongly associated with HIV AIDS	128	61.8
Cheilitis	43	20.9
Pseudomembranous candidiasis	32	15.5
Erythematous candidiasis	15	7.3
Kaposi's sarcoma :	15	7.3
Linear gingival erythema	15	7.3
Angular cheilitis	4	1.9
Hairy leukoplakia	4	1.9
Group 2 lesions: Less commonly associated with HIV/AIDS	47	22.8
Parotitis	20	9.7
Oral warts	9	4,4
Herpes Zoster	9	4,4
Ranular	8	3.9
Herpes simplex lesions	1	0.6
Group 3 lesions: Rarely seen in HIV/ AIDS	32	15.5
Bell's palsy	9	5.5
Oral ulcers	11	5.3
Trigeminal neuralgia	8	3.9
Drug reaction	4	1.9
All groups Total	207	100.0

The information presented in table 4.2 will be discussed as three subsections. These three subsections are:

- Lesions strongly associated with HIV/AIDS;
- Lesions less commonly associated with HIV/AIDS; and
- Lesions rarely seen in HIV/AIDS.

NOTE: The percentages were calculated out of 207 since, table 4.2 are referring to lesions and not to patients.

- **Lesions strongly associated with HIV/AIDS**

From table 4.2 it is evident that 61.8% (n=128) out of all 207 lesions are of the type classified as being “*strongly associated*” with HIV/AIDS. These findings were found to be similar to a study done in South Africa where it was reported that group one oral lesions, namely those strongly associated with HIV, were found to have a higher prevalence than others.

Thus such lesions were found to be useful markers of HIV infections, especially with regard to this study, as these lesions may be identified without any conformational CD4 counts. The options for earlier interventions become thus available. In addition multiple lesions were also regarded as highly predictive of HIV infections (Bhayat, Yengopal, Rudolph & Nmutandani, 2008). This finding will again be referred to when presenting the conclusions of the study.

In this study cheilitis was the most prevalent oral and peri-oral lesion as it was identified in 43 (20.9%) of the patients. This finding should however be placed in context. From the literature it emerged that this type of lesion was typical in people over the age of 59, and who also had many years of sun exposure (NDRI.com, 2013). Namibia, and specifically Oshakati where this study had been conducted, is noted for high sun intensity during most of the year as well as scourging temperatures.

Pseudomembranous candidiasis was the second most prevalent lesion in this study, with a prevalence of 32 (15.5%). This prevalence can be attributed to the opportunistic nature of the *Candida* species. These findings concurred also well with the findings of Adedigba, Ogunbodede, Jeboda and Naidoo (2008). They reported about the findings of a study conducted in Nigeria. In this mentioned study the commonest HIV lesion was pseudomembranous candidiasis (43.1%), followed by erythematous candidiasis (28.7%). Except for Nigeria, this high prevalence of candidiasis and its variants found in this study is also similar to other developing countries namely, Tanzania, Uganda, Nigeria and Southern India (Tirwomwe, Rwenyonyi, Muwazi, Besigye & Mboli, 2007; Matee et al., 2006; Ranganathan & Hemalatha, 2006; Sharma, Pai, Suhas, Ramapuram, Doshi & Anup, 2006; Taiwo, Okeke, Otoh & Danfillo, 2005).

The descriptive statistical evidence that emerged from this item was the possible strength of candidiasis and its variants as indicators of HIV/AIDS and therefore the possibility of early antiretroviral therapy, even in the absence of confirmation CD4 counts.

The next discussion covers lesions less commonly associated with HIV/AIDS (see Table 4.2).

- **Lesions less commonly associated with HIV/AIDS**

From the findings as depicted in Table 4.2, it is noted that parotitis was the most commonly encountered oral lesion in this category, namely, twenty (20). This finding was in agreement with a study done by Hodgson, Greenspan and Greenspan (2006) who reported a high prevalence of salivary gland lesions in Africa and Latin America, especially in children. The high prevalence of salivary gland disease had been reported as a challenge both in HIV patients on highly active antiretroviral therapy (HAART) and pre-HAART. Furthermore, it was noted that in a study done in Brazil, the prevalence of oral manifestations decreased following implementation of highly active antiretroviral therapy, but there was an increase in the prevalence of oral warts and HIV-associated salivary gland disease (Ferreira, Noce, Júnior, Gonçalves, Torres, Meeks, Luiz & Dias, 2007).

The emerging conclusion for this finding is that parotitis could be an easily identifiable lesion, with the option of early intervention and not to unnecessarily delay any treatment to wait for a CD4 confirmation.

The next discussion covers lesions rarely seen in HIV/AIDS.

- **Lesions rarely seen in HIV/AIDS**

Of the rarely seen oral lesions associated with HIV/AIDS, oral ulcers were the most encountered in this category, namely eleven (11) as is evident in Table 4.2. The conclusion in this study, and based on descriptive statistics only, was that ulcers in the mouth could alert dentists to possible HIV/AIDS afflicted patient, and thus could provide the option for early antiretroviral therapy. Unfortunately the researcher was not able to compare such data as no relevant literature was found.

The next discussion, still addressing the first objective, will focus on the prevalence of oral lesions with possible associations with selected demographic characteristics.

4.5 THE PREVALENCE OF ORAL LESIONS WITH A POSSIBLE ASSOCIATION WITH SELECTED DEMOGRAPHIC CHARACTERISTICS

Table 4.3 A statistical comparison on the prevalence of oral lesions in binary groups of selected demographic characteristics

Factor	Patients with lesion	Patients without lesion	Odds Ratio	95% CI	Chi square	p-value
Sex						
Female	124	97	1.16	0.74-1.81	0.44	0.505
Male	73	66				
Total	197	163				
Education						
Secondary and higher	126	103	1.03	0.66-1.63	0.08	0.88
Primary and lower	71	60				
Total	197	163				
Employment						
Not employed	36	29	1.17	0.65-2.09	0.30	0.58
Employed	132	124				
Total	168	153				
Age						
Young (≤ 50)	171	140	1.07	0.43-1.21	7.703	0.103
Old (>50)	26	23				
Total	197	163				

****NOTE:**

The 39 students were excluded from the analysis with regard to employment and oral lesions, and employment also encapsulated “*self employed.*”

From table 4.3, the prevalence ratio of developing oral lesions in female versus males was found to be 1.1 [124/221/73/139 =1.1]. Since the prevalence ratio was > than 1, the probability of developing oral lesions in females was 10% higher than in males. Despite the higher prevalence of developing oral lesions in females, this could be by chance, since there is no statistical significant difference between males and females. (Chi square =1.36, df =1,P=0.51). These findings were found to be similar to a study done in the USA where gender did not correlate with a higher prevalence in oral lesions (Sroussi, Villines, Epstein, Alves & Alves, 2007).

In Table 4.3 the patients’ ages were arranged into two categories with the purpose of identifying any possible statistical significant associations as depicted in table 4.3, the majority of the oral lesions were seen in patients younger than 50 years, namely 87%. Despite this high prevalence, the results were not regarded as statistically significant (p=0.103). In this study no significant association was found between age and the development of oral lesions. No comparable literature was found.

As can be seen in table 4.3, none of the variables reached statistical significance of a $p < 0.05$. The study sample did not provide evidence of statistically significant

differences in the prevalence of oral lesions across sex, education, age and employment status. No study was found to compare the results.

The next discussion will present the findings as they relate to the second objective, namely:

- To determine the association between CD4 counts and oral lesions among newly diagnosed HIV/AIDS patients.

4.6 POSSIBLE ASSOCIATIONS BETWEEN THE DETECTED ORAL LESIONS AND CD4 COUNTS

In the literature review in chapter two, an overview of the connection or association between CD4 counts and opportunistic infections was presented (see for example point 2.3.1). Since it was well established in the literature that associations between CD4 counts and opportunistic infections or some oral lesions did exist, it was necessary to rather contextualize the findings of this current study since such a study had not been done in Namibia. The rationale was that, when oral lesions eventually did manifest, it then became more difficult for patients to maintain an optimal nutritional status which could lead to a rapid deterioration in their health due to inadequate nutrition even if their CD4 counts seemed acceptable at that moment. This information was regarded as crucial to assist the Namibian Ministry of Health and Social Services in planning and budgeting for these oral lesions.

The associations between the oral lesions and the accompanying CD4 counts are presented in Table 4.4 to follow.

Table 4.4 The level of risk (probability) of developing oral lesions with decreasing CD4 counts

CD4	Oral lesion present		No oral lesions present		Prevalence Ratio	95% confidence interval
	Number	%	Number	%		
500+	23	37.7	38	62.3	0.6	0.48-0.73
350-499	29	44.6	36	55.4	0.8	0.68-0.90
200-349	58	49.2	60	50.8	0.9	0.85-0.99
<200	87	75.7	29	25.2	3.0	2.55-3.45

NOTE: 500+ is the reference CD4 group

Chi-square for linear trend=25.324; p-value = 0.0000

As is evident in table 4.4, a high number of oral lesions were seen at CD4 counts of <200 cells/ul, namely 75.7% (n=87). These findings were statistically significant (Chi-square =30.7920, df=4, and p=0.0000). The findings from this study were found to be similar to a study done in Tanzania, where there was also a significant association between the presence of oral lesions and CD4 cell counts of < 200 cell/ul

and with the WHO clinical staging (Matee et al., 2006). The prevalence ratio (PR) of developing oral lesion at CD4 counts of < 200 cells/ul versus CD4 counts of >500 cells/ul is 2.0.

Since the PR is >1 , then the probability of developing oral lesions at CD4 counts of <200 cells/ul is 2.0 (20%) higher than with CD4 counts of >500 cells/ul.

The strong positive association between the occurrence of oral lesions and low CD4 cell count found in this study was an important result in light of the need for inexpensive surrogate markers of HIV disease progression in resource-poor countries, where the measurement of CD4 cell counts is expensive and in some areas not available in nearby clinics. Consistent and accurate diagnosis of oral lesions by the oral surgeon (dentist) is of paramount importance if oral lesions are to be used as indicator of CD4 counts. Furthermore, visual inspection of the mouth is quick (<5 minutes), noninvasive, and inexpensive, and it may be used in combination with other clinical indicators in the decision-making process of when to initiate antiretroviral therapy or prophylactic regimens.

4.7 SUMMARY

In this chapter the findings were discussed and some were interpreted analytically. However, for some findings it was only possible to do so descriptively. The next chapter, chapter five addresses the conclusion, limitations and recommendations for future studies.

CHAPTER FIVE

CONCLUSIONS, STUDY LIMITATIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

The previous chapter dealt with the data analyses and presentation of the findings. This chapter focuses on the conclusions drawn from the study, limitations encountered during the study and the presentation of applicable recommendations.

The presentation in this chapter is sequenced on the stated objectives. The objectives of this study were:

- To determine the prevalence and types of oral lesions among newly diagnosed HIV/AIDS patients.
- To determine the association between CD4 counts and oral lesions among newly diagnosed HIV/AIDS patients.

5.2 THE FIRST OBJECTIVE: To determine the prevalence and types of oral lesions among patients diagnosed with HIV/AIDS

5.2.1 CONCLUSION WITH REGARD TO THE FIRST OBJECTIVE

Based on the number of oral lesions in HIV/AIDS patients in this study, it was concluded that the prevalence was lower compared to other studies in third world

countries as indicated in chapter four. Although the lesions were more prevalent in females than males and mostly affecting those in the 21-29 year age group, none of these two findings were statistically significant. In addition, the most prevalent oral lesions were cheilitis, pseudomembranous candidiasis, erythematous candidiasis and parotitis (in descending order of prevalence). The study also did not provide evidence of statistically significant differences in the prevalence of oral lesions across gender (sex), education and employment status.

5.2.2 RECOMMENDATIONS WITH REGARD TO THE FIRST OBJECTIVE

More emphasis should be placed on health education to HIV patients, especially in “Preventing Mother To Child”-programmes to target more women since they are more prone to develop the lesions. This could be done by giving education on:

- Implementing good oral hygiene practice to facilitate healing of the lesions.
- Providing education on the importance of proper nutrition to HIV/AIDS patients.
- Involvement of dental personnel in HIV training and research to ensure total patient management.
- Printing and distributing leaflets in vernacular languages on the importance of oral hygiene.
- Practical demonstrations on oral hygiene during counseling sessions to HIV/AIDS patients.

- Incorporating family members to assist patients on oral hygiene.
- Establishing a comparative relationship with community leaders with assistance in the food supply to patients with specific needs.
- Establishing/liaising with private specific food manufactures for special offers for foods that are manufactured for critical ill patients with specific nutritional needs. Some common used spices like garlic have shown to have a number of antimicrobial properties and has been shown to inhibit the growth of candida in the laboratory (Iwalokun, Ogunledun, Ogbolu, Bamiro & Jimi-Omojola, 2004). As oral candidiasis was the most prevalent oral lesion, attention should be focused on its treatment. Laboratory studies revealed that candida is especially sensitive to a purified extract of garlic known as allyl alcohol, which produces oxidative stress inside the yeast organism and inhibits its growth (Lemar, Muller, Plummer & Lloyd, 2005). Other studies have demonstrated that garlic extracts begin exerting their anticandidal effect within one hour of ingestion (Hronek , Vachtlova , Kudlackova & Jilek, 2005).

5.3 THE SECOND OBJECTIVE: To determine the association between CD4 counts and oral lesions among patients diagnosed with HIV/AIDS

5.3.1 CONCLUSION WITH REGARD TO THE SECOND OBJECTIVE

There was a strong association between oral lesions in group one, namely the lesions strongly associated with HIV/AIDS with CD₄ Count < 200 cells/ul. It was also noted that some lesions were seen even at CD4 counts >500 cells/ul.

5.3.2 RECOMMENDATIONS WITH REGARD TO THE SECOND OBJECTIVE

More emphasis as to why there is a need of routine dental examination on HIV patients as part of general examination regardless of their CD4 counts is highly recommended. Therefore, the prevention, diagnosis, treatment and control of these oral manifestations should be part of the objectives of every dental health professional by:

- Giving oral health education on the oral manifestations of HIV/AIDS for patients to seek treatment early.
- Educating patients on the importance of keeping professional appointments with a dental professional at least twice a year. This may be more frequent if oral complications or abnormalities in the mouth arise compared to those who do not have oral lesions.

- Placing more emphasis for health workers to be on the lookout for the oral lesions as they may appear even with acceptable counts.
- In addition, the researcher proposes earlier commencement with antiretroviral therapy, motivated by strong positive association between the occurrence of oral lesions and low CD4 cell counts found in this study. It could be used as inexpensive surrogate markers of HIV disease progression in resource-poor countries, where the measurement of CD4 cell counts is expensive and in some areas not available.

5.4 THE RELATIONSHIP BETWEEN THE STUDY AND THE FRAMEWORK OF THE STUDY

It was confirmed that there is an association between oral lesions and CD4 counts, although this confirmation had not been formally documented in Namibian studies. It was however evident that some lesions may also be clinical visible, without the corresponding decrease in CD4 counts. The confirmation phase, as depicted in the framework, might thus not in all cases support the clinical evidence. The implication in this study for dentists is therefore to consider recommendation for initiation of treatment in certain cases based on physical assessment alone.

5.5 RECOMMENDATION FOR FUTURE STUDIES

- A bigger study needed to be done to know the reality in the whole country. Few studies have been done on oral hygiene status and HIV worldwide and none in Namibia hence these calls for studies in this area.
- In terms of HIV and drug reaction, there was no study that states clearly the direct association of drug reaction in HIV with low CD4 count. This calls for more research on oral health diseases associated with HIV.
- There is a need to conduct research on dental problems in Namibia, so as to have local need assessments of dental problems in the country. Oral health services and professionals can contribute effectively to the control of HIV/AIDS through health education and health promotion, patient care, effective infection control, and surveillance.
- Multidisciplinary studies with a common theme, addressing the pathogenesis of the oral manifestations associated with AIDS is crucial for increasing the understanding of these disorders. The information gained can provide the basis for the development of novel diagnostic, preventive and therapeutic strategies for HIV-related oral disorders.
- Research on alternative therapies for treatment of oral candidiasis and other opportunistic infections should be considered and their efficacy assessed in randomized controlled trials.
- Further research to assess the impact of oral disease on the quality of life, and on access to oral care is needed and it is necessary to integrate oral health research into other health care research programmes.

- Research to assess the impact of oral diseases by being treated by antiretroviral medication
- Investigation of the factors that lead to late initiation of highly active antiretroviral therapy in patients with oral lesion is crucial so as to fulfill the overall aim, which is to prolong patients' lives.
- A number of oral ulcers were seen in this study. However, history of oral lesion as when did they occur, treatments given and response were not included, as any ulcer which does not respond to treatment after two weeks is treated as cancer unless proven otherwise. In this case, a follow-up study to include proper history taking of the oral ulcers and tissue biopsy from those oral ulcers would be of help to rule out cancer from these oral ulcers.

5.6 LIMITATIONS OF THE STUDY

The limitation(s) of this study were methodological in nature. This was due to a relative small assessable population. Also, due to the sensitivity of the health problem/diagnosis, some patients did not want to participate.

The researcher acknowledges also the possibility that some false positive or false negative identifications might have occurred.

The researcher also acknowledges that, although strict adherence to the checklist was observed at all times, the assessments could have subjective interpretations, as some lesions were difficult to classify.

5.7 CONCLUSION

Oral manifestations of HIV and AIDS are among the health challenges to HIV patients in this study. Although the overall prevalence was low, the problem exists and the lesions were found to be more in females than males, although not statistically proven to be significant. Cheilitis was the most prevalent oral lesion seen, followed by pseudomembranous candidiasis. The already worldwide proven association between CD4 counts and the prevalence of oral had also been proven in this contextualized study.

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ANNEXURE 1

DATA COLLECTION TOOL/CHECK LIST**CHECK LIST FOR DATA COLLECTION ON THE PREVALENCE OF ORAL MANIFESTATIONS OF HIV/AIDS AMONG ADULT PATIENT WHO ARE NOT ON HAART IN OSHAKATI NAMIBIA.**

I am DR R.T. Muro, a dentist working in oshakati hospital, i am conducting a resaech to determine prevalence of oral manifaستاions of hiv/aids among hiv partints in pre haart.

Section A: Identification information

1	Name of study site	
2	Name (code) of data collector	
3	Serial No of study participant	
4	Date of data collection/examination	

Section B: Identification and demographic information of study participant.

I am going to ask you general questions about yourself, is it ok? YES / NO

5	Sex (Please tick with √)	Male		Female			
6	Age (Years)						
7	Place of residence						
8	Employment						
9	Education (Please tick with √)	No formal educ	Primary	Secondary	VTC	Diploma	Degree

Section C: History of illness of the oral cavity

I am going to ask you general questions about your illness involving the oral cavity and surrounding tissues, is it ok? YES / NO

10	Do you currently have any complaint of illness/lesion of the oral cavity? (current or less that one month) Please tick with √	Yes		No	
11	If yes, what is the complaint				
12	Did you receive or are you receiving treatment for the complaint? Please tick with √	Yes		No	

13	Did you experience any oral illness/lesion of the oral cavity in the last six months? Please tick with √	Yes		No	
14	If yes, what is the type of the complaint				
15	Are you using dental prosthesis? Please tick with √	Yes		No	

Section D: Examination of the oral cavity for the presence and type of oral lesions.

I am going to examine your mouth and the surrounding tissues, is it ok? YES / NO

Lesions strongly associated with HIV/AIDS			Lesions less commonly associated with HIV/AIDS			Lesions rarely associated with HIV/AIDS		
		Tick with a √ if present			Tick with a √ if present			Tick with a √ if present
16	creamy white, removable plaques on the oral mucosa (PC)		22	Enlargement parotid salivary gland. (Parotitis)		28	Painful red or purplish rash that spreads and blisters, eventually causing the top layer of your skin to die and shed (Drug reactions)	
17	Flat, red patches of varying size(EC)		23	enlargement sublingual salivary gland (Ranular)		29	Sudden weakness or paralysis on one side of the face that causes it to droop. Drooling, Loss of ability to taste and numbness in the affected side of your face (bell's palsy)	

18	Redness, ulceration, and fissuring, either unilaterally or bilaterally at the corners of the mouth(AC)		24	Small vesicles at the vermilion border of the lips or intraoral clusters of painful small vesicles or ulcers on keratinized mucosa palate and gingival or sometimes tongue.(HS)		30	Sharp, stabbing, electric-shocks. Pain that comes and go, unilateral side of the face. (TN)	
19	Nonmovable, corrugated or "hairy" white lesion on the lateral margins of the tongue(HL)		25	Solitary or multiple nodules. sessile or pedunculated or multiple, small papilliferous or cauliflower-like projections (HPV)-warts		31	Oral ulcers	
20	Red, blue, or purplish lesion (KS)		26	Oral cavity ulcers which appear necrotic with a white halo (CMV).		32	Lip ulcers	
21	Clean mouths with very little plaque or calculus, with red band gingival margin and edematous. (LGE).		27	Pain, multiple vesicles on the facial skin, lips, and oral mucosa, unilateral following maxillary and/or mandibular branches of the trigeminal nerve (Varicella zoster)				

Section E: Medical and laboratory information

	Code number of hospital record number	
33	CD4 count	
34	WHO Stage	

ANNEXURE 2

UNIVERSITY OF NAMIBIA

Private Bag 13301, 340 Mandume Ndemufayo Avenue, Pionierspark, Windhoek, Namibia



FACULTY OF MEDICAL AND HEALTH SCIENCES

**Letter of permission:
Post graduate students**

Date: 12 October 2009

Dear Student: Dr Muro

The post graduate studies committee has approved your research proposal.

Title: Prevalence of oral manifestations of human immunodeficiency virus and its association with CD4 counts in adult patients attending Oshakati Hospital Namibia

You may now proceed with your study and data collection and formal registration for the degree.

It may be required that you need to apply for additional permission to utilize your target population. If so, please submit this letter to the relevant organizations involved. It is stressed that you should not proceed with data collection and fieldwork before you have received this letter and got permission from the other institutions to conduct the study. It may also be expected that these organizations may require additional information from you.

Please contact your supervisors on a regular basis.

Faculty Representative Post Graduate Studies Committee


Prof A van Dyk



REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

**Private Bag 13198
Windhoek
Namibia**

Enquiries: A. Muheua

**Ministerial Building
Harvey Street
Windhoek**

Ref.: 17/1/1

Tel: (061) 2032125

Fax: (061) 272286

E-mail: amuheua@mhss.gov.na

Date: 02 January 2010

OFFICE OF THE PERMANENT SECRETARY

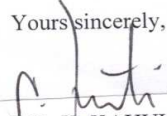
Dear Dr. Muro

Re: Study – Prevalence of oral manifestation of HIV/AIDS and its association with CD4 count in adult patient attending Oshakati hospital, Namibia

1. Reference is made to your application to conduct the above-mentioned study.
2. The proposal has been evaluated and found to be of great importance.
3. Kindly be informed that approval has been granted under the following conditions:
 - 3.1. The data collected is only to be used for academic purposes;
 - 3.2. A quarterly progress report is to be submitted to the Ministry's Research Unit;
 - 3.3. Preliminary findings are to be submitted to the Ministry before the final report;
 - 3.4. Final report to be submitted upon completion of the study;
 - 3.5. Separate permission to be sought from the Ministry for the publication of the findings.

Wishing you success with your project.

Yours sincerely,


MR. K. KAHUURU
PERMANENT SECRETARY



ANNEXURE 4

		
REPUBLIC OF NAMIBIA MINISTRY OF HEALTH & SOCIAL SERVICES OSHANA REGION DIRECTORATE OF HEALTH		Private Bag X5501 Oshakati Phones: +264(65)2233000 +264(65) 221 380 Faxes: +264(65) 224564 +264(65) 221 390 E-mail: supt.ihosh@weay.na
INTERMEDIATE HOSPITAL OSHAKATI		
Enquiries:	Ref:	Date: 24 February, 2010
Dr. RT. Muro Dental Clinic IHO		
<p>REQUEST TO CONDUCT STUDY—PREVALENCE OF ORAL MANIFESTATION OF HIV/AIDS AND ITS ASSOCIATION WITH CD4 COUNT IN ADULT PATIENTS ATTENDING OSHAKATI HOSPITAL.</p> <p>Your letter on the above issue refers.</p> <p>The Intermediate Hospital Oshakati Management granted you a permission to conduct study, on condition that you must adhere to the rules and regulations of the institution.</p> <p>During your study period, you must be under the supervision of the Medical Officer and Registered Nurse in charge of the section concern.</p> <p>Yours Sincerely</p> <p style="text-align: center;">  MEDICAL SUPERINTENDENT OSHAKATI HOSPITAL MINISTRY OF HEALTH AND SOCIAL SERVICES NAMIBIA DR SHANNON KAKUNGULU MEDICAL SUPERINTENDENT </p> <p>Cc: CCRN</p> <p>Registered Nurse in charge of the Section</p>		

Medical Superintendent: Dr. Shannon Kakungulu

Chief Control Registered Nurse: Ms. Kashupi Hilma

Chief Control Officer: Mr. Ihweula Ben