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HIV and Its Periodontal Influence - An Overview

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ABSTRACT:
Human Immunodeficiency virus results in severe immunodeficiency resulting in susceptibility to a number of infections. Periodontitis is an inflammatory disease of the supporting structures of the tooth that is seen as manifestation in severe immunodeficiency. The oral and periodontal condition closely associated with HIV includes oral candidiasis, Kaposis sarcoma, oral hairy leukoplakia, Linear gingival erythema and necrotizing periodontal diseases.Periodontal disease in HIV patients shows an increasing prevalence rate of upto 76% when the patients suffers from AIDS. The present review focuses on the structure of HIV, pathogenesis of the disease and in detail on the oral and periodontal manifestations and treatment aspects.
Key words- Human Immunodeficiency virus, Periodontitis, Linear Gingival Erythema, Kaposis Sarcoma

I. INTRODUCTION

A **virus** is an infectious particle that reproduces by "commandeering" a host cell and using its machinery to make more viruses.

The **human immunodeficiency viruses** (**HIV**) are two species of Lentivirus (a subgroup of retrovirus) that infect humans. Over time, they cause AIDS, a chronic, potentially life-threatening condition, without treatment the average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype.

II.EPIDEMIOLOGY[(1)]

Clinically, AIDS was first recognized in the United States, including the State of Washington, in 1981. In 1983 HIV was discovered to be the cause of AIDS. Since then, the number of AIDS cases has continued to increase, both in the United States and in other countries.

EVENTS IN THE CHRONOLOGY OF HIV EPIDEMIC

- 1981- First case reported of pneumocystis carinii pneumonia associated with unexplained immune deficiency
- 1983-84 Identification of HIV as ablood borne virus that causes AIDS.
- 1984- Identification of oral hairy leukoplakia which was later recognized as an oral marker of symptomatic HIV infection and immune suppression.
- 1985- Approval of the first HIV antibody test by FDA.
- 1987- AZT (zidovudine)becomes the 1st anti-HIV drug to be approved.
- 1992- CDC reports the 1st and only dentist to patient HIV transmission.
- 1993- CDC redefines AIDS by including immunesuppression and additional opportunistic infections
- 1995-first HIV protease inhibitor drug Saquinavir was approved
- 1995-96 Introduction of HAART (highly active antiretroviral therapy)
- 1998-99 Failures of HAART attributed to developing HIV drug resistance pattern.

The HIV prevalence rate is the number of persons living with HIV per 100,000 population. The HIV incidence rate represents the number of persons who newly acquired HIV during a fixed time period (typically 1 year) per 100,000 population.

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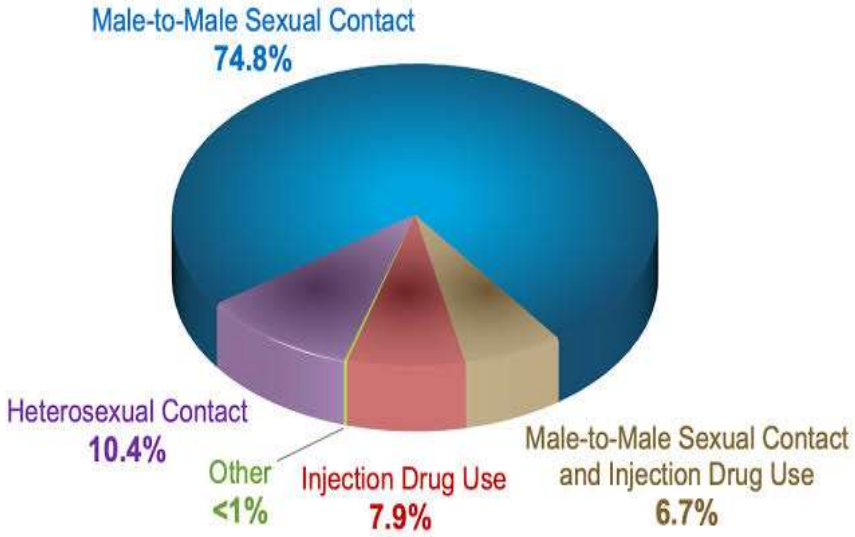

The above chart represents the epidermiology of HIV ,

Male to male sexual contact	74.8%
Heterosexual contact	10.4%
Injection drug use	7.9%

Male to male sexual contact & injection drug use 6.7%

This pie chart shows transmission categories for HIV acquisition for males >13 years old with diagnosed or undiagnosed HIV in united states in 2019 . other =perinatal ,hemophilia ,blood transfusion and risk factors not reported or identified[2]

III.STRUCTURE OF HIV[3]

Gp120

The 120 in its name comes from its molecular weight. It is essential for virus entry into the cells as it plays vital role in attachment to specific cell surface receptors.

GP41

It is a subunit of the envelope protein complex of retroviruses including human immunodeficiencies virus. It is family of enveloped viruses that replicate in host cell through process of reverse transcriptase. It targets a host cell.

Viral envelope

It is envelope through which virus binds.

P17

Viral core is made from protein. It is bullet shaped. Three enzymes required for HIV replication are reverse transcription, integrase and protease.

P24

P24 is component of HIV capsid.

PROTEASE

It is a retroviral aspartyl protease that is essential for life cycle of HIV, the retrovirus that caused AIDS. This enzyme cleaves newly synthesized polyproteins at appropriate place to create nature protein components of infectious HIV virion.

Integrase

Enzyme produce by retrovirus that enables its genetic material to be integrated into the DNA of infected cell.

RNA

All organisms including most viruses store their genetic material on long strands of DNA. Retrovirus is exception because their genes are composed of RNA

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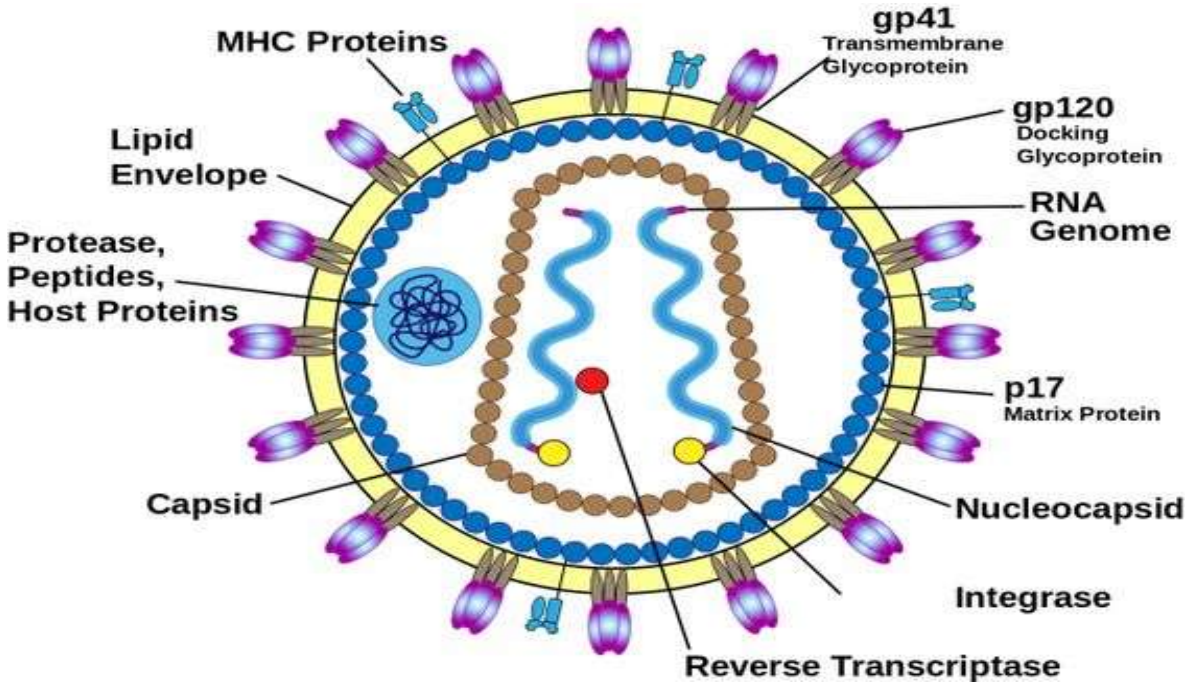

IV.LIFE CYCLE OF HIV INFECTION[4]

- BINDING (also called Attachments): HIV binds to the receptor on the surface of the CD4 cells.
- FUSION: The HIV envelope and the CD4 cell membrane fuse, which allows HIV to enter the CD4 cells.
- REVERSE TRANSCRIPTION: inside the CD4 cells, HIV releases and uses reverse transcriptase to convert its genetic material- HIV RNA-into HIV DNA. The conversion of HIV RNA to HIV DNA allows HIV to enter the CD4 cells nucleus combined with the cell genetic material- cell DNA
- INTEGRATION: inside the CD4 cell nucleus, HIV release integrase.HIV uses integrase to insert its viral DNA into the DNA of the CD4 cell.
- REPLICATION: once integrated into the CD4 cell DNA. HIV use the machinery of the CD4 cell to make the long chain of HIV proteins. The protein chain are the building blocks for more HIV.
- ASSEMBLY: The new HIV protein and HIV RNA move to the surface of the cell and assemble into the immature HIV.
- BUDDING: Newly formed immature HIV pushes itself out of the host CD4 cell. The new HIV releases protease. Protease breaks up the long protein chain in the immature virus creating the mature virus.

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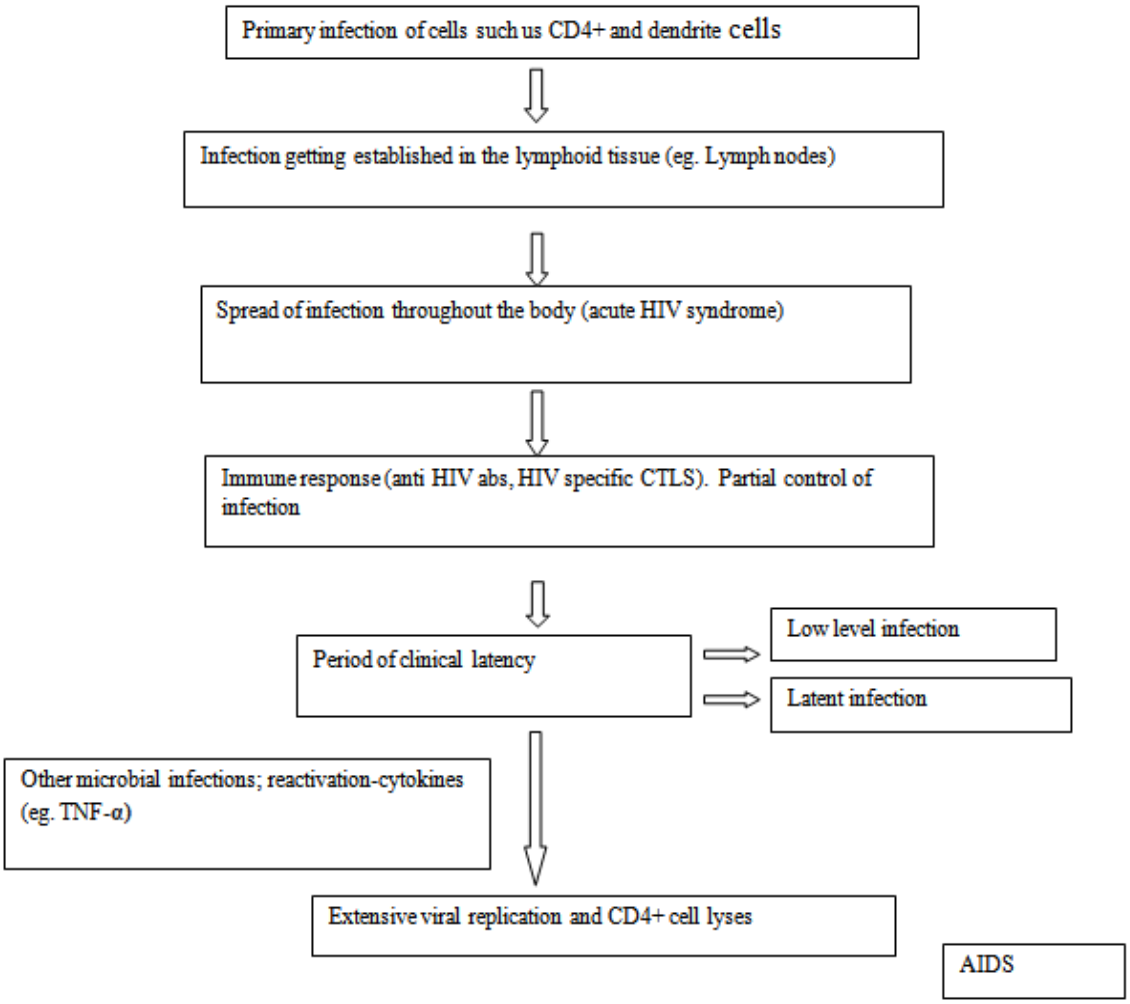
V.PATHOGENESIS[5]



VI. CLINICAL STAGING:[6]

STAGE I	STAGE II	STAGE III	STAGE IV
ASYMPTOMATIC	MODERATE UNEXPECTED WEIGHT LOSS	UNEXPECTED SEVERE WEIGHT LOSS	HIV WASTING SYNDROME
PERSISTENT GENERALIZED LYMPHADENOPATHY	RECURRENT RESPIRATORY TRACT INFECTION	PERSISTENT ORAL CANDIDIASIS	PNEUMOCYTIC PNEUMONIA
	HERPES ZOSTER	PULMONARY TUBERCULOSIS	KAPOSI'S SARCOMA
	ANGULAR CHEILITIS		EXTRA PULMONARY TUBERCULOSIS

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VII. CDC SURVEILLANCE CLASSIFICATION (1993)

	CATEGORY-A	CATEGORY-B	CATEGORY-C
CD4+ Tcell categories (cells / cu mm)	Asymptomatic acute (primary) HIV or PGL with or without malaise	Symptomatic, oropharyngeal or valvovaginal candidiasis , fatigue or low grade fever	AIDS indicator or herpes zoster oral hairy leukoplakia , ITP
(1)>=500	A1	B1	C1
(2) 200-499	A2	B2	C2
(3)<200	A3	B3	C3

Persons in categories A3,B3,C1,C2 and C3 have AIDS under the 1993 surveillance case definition.
PGL = persistent generalized lymphadenopathy. clinical category A includes acute (primary) HIV infection[7]

VIII. AIDS:

Acquired immunodeficiency syndrome.

AIDS is a chronic immune system disease caused by the human immunodeficiency virus (HIV).

HIV damages the immune system and interferes with the body's ability to fight infection and disease. HIV can be spread through contact with infected blood, semen, or vaginal fluids. There's no cure for HIV/AIDS, but medications can control the infection and prevent disease progression.

Worlds AIDS day is celebrated on 1st December of every year.[8].

IX. ORAL MANIFESTATION:

CLASSIFICATION OF ORAL MANIFESTATION:[9]

GROUP-1 lesions; strongly associated with HIV infection.

- ❖ Candidiasis
  - Pseudomembraneous
  - Atropic or erythematous
  - Angular chelitis
- ❖ Hairy leukoplakia
- ❖ Kaposi's sarcoma
- ❖ Non- hodgkins lymphoma
- ❖ Periodontal diseases-
  - LGE- Linear gingival erythema
  - NUS- Necrotizing ulcerative gingivitis
  - NUP-necrotizing ulcerative periodontitis

GROUP 2 LESIONS: lesions less commonly associated with HIV infection

- ❖ Bacterial infection
  - Mycobacterium avium/intracellulae
  - Mycobacterium tuberculosis
- ❖ Melanotic Hyperpigmentation
- ❖ Salivary Gland Disease
  - Dry mouth due to decreased salivary flow rate
  - Unilateral or bilateral swelling of major salivary glands
- ❖ Thrombocytopenic purpura
- ❖ Viral Infections
  - Herpes simplex virus
  - Human papiloma virus(warty like lesion)
  - Varicella zoster virus

GROUP 3 LESIONS: lesions seen in HIV infection

- ❖ Bacterial infections
  - Actinomyces israeli
  - Escherichia coli
- ❖ Drug reactions (ulcerative,Erythema multiforme,Lichenoid,Toxic epidermolysis)
- ❖ Fungal infections other than Candidiasis
  - Cryptococcus neoformans
  - Geotrichum
  - Histoplasma capsulatum
  - Mucormycosis,Zygomycosis
  - Aspergillus flarus
- ❖ Neurologic disturbances
  - Facial palsy
  - Trigeminal neuralgia
  - Recurrent Aphthous stomatitis
- ❖ Viral infections
  - Cytomegalo virus
  - Molluscum contagiosum

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X. PERIODONTAL INVOL VEMENT[10]

Periodontal manifestation of HIV infection

- Linear gingival erythema
- Necrotizing ulcerative periodontitis
- Chronic Periodontitis
- Necrotizing ulcerative gingivitis

LINEAR GINGIVAL ERYTHEMA

Linear gingival erythema is a condition that is related to a fungal infection of the gums. It appears as a red line along the gum line and causes pain and sometimes bleeding. This condition is one of the most common oral complications of HIV.

NECROTIZING ULCERATIVE PERIODONTITIS

A necrotizing,ulcerative,rapidly progressive form of periodontitis occurs more frequently among HIV positive individuals.NUP appears to represent an extension of NUG in which bone loss and periodontal attachment loss occurs .

NUP is characterized by soft tissue necrosis , rapid periodontal destruction and interproximal bone loss.lesions may occur anywhere in the dental arch;they are usually localized to the few teeth,although generalized NUP is sometimes present after marked CD4+ cell depletion. Bone is often exposed

CHRONIC PERIODONTITIS

The presence of preexisting gingivitis, poor diet, the age of the patient, smoking, other periodontal disease risk factors leads to chronic periodontitis.

This indicates that HIV infected patients are potential candidates for conventional periodontal treatment procedures, including surgery and implant placement.

NECROTISING ULCERATIVE GINGIVITIS

Necrotizing ulcerative gingivitis is a microbial disease of the gingiva with the impaired host response and it manifests with the characteristic clinical signs of necrosis and sloughing of the gingival tissues and may be accompanied by systemic symptoms.

Some reports have been described an increased incidence of NUG among HIV infected individuals. There is no consensus regarding whether the incidence of NUG increases in HIV positive patients.

XII. DIAGNOSIS:

Tests used for the diagnosis of HIV infection in a particular person require a high

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degree of both sensitivity and specificity.Blood tests are the most common way to diagnose the human immunodeficiency virus (HIV)

TYPES OF TEST:

- HIV serological testing. Antibodies to HIV-1 and HIV-2 are detected by enzyme-linked immunosorbent assay (ELISA), simple/rapid test devices, and western blot (WB) tests. However, because maternal HIV antibodies (immunoglobulin G [IgG]) are passively transferred across the placenta, HIV serological assays in infants are difficult to interpret. Infants born to HIV-infected women may therefore initially test seropositive, irrespective of their own infection status.[11]
- HIV antibody testing: An HIV antibody test measures the presence of antibodies in response to the presence of HIV. The most common HIV antibody tests are

A. ELISA (EIA) and
B. Western Blot.

These tests can now be performed on samples of oral (mouth) fluid.

ANTI HIV ANTIBODY

1. **The ELISA test** is used to detect the HIV antibody. It checks for certain proteins that the body makes in response to HIV.The blood sample will be added to a cassette that contains the viral protein, called antigen.If the blood contains antibodies to HIV, it will bind with the antigen and cause the cassette's contents to change color. This very sensitive test was the first one widely used to check for HIV.
2. **The Western blot test** was previously used to confirm the result of the ELISA, but it is no longer recommended, as other tests are now more reliable and enable a faster diagnosis.

In the Western blot test, the blood is taken in the same way, but the sample is separated with an electrical current and transferred onto a piece of blotting paper. Here, an enzyme is added to cause color changes that signal the presence of HIV antibodies.[12]

ASSAY TO DIRECTLY DETECT HIV INFECTIONS:

1. **Detect p24 antigen**: **An antigen test checks your blood for an HIV antigen, called p24**. When you're first infected with HIV, and before your body has a chance to make antibodies to the virus, your blood has a high level of p24. The p24 antigen test is accurate 11 days to 1 month after getting infected.
2. **HIV culture:** HIV culture tests are used to detect the presence of the human immunodeficiency virus in serum, saliva, or urine. Such tests may detect HIV antibodies, antigens, or RNA.
3. **The HIV RNA test**: It is used for early detection of HIV. Compared to standard HIV tests which measure antibodies your body produces to fight HIV, the HIV RNA test detects the genetic material of the virus itself. The HIV RNA test determines if you are reactive (indicating a positive result) or non-reactive (indicating a negative result).[13]

XIII. TREATMENT:[14]

Dental management of HIV infected patients does not differ from that of non-HIV infected patients. Most treatment can be performed by general practitioners.

Many HIV -infected persons suffer from periodontal disease.
In HIV -positive patients, periodontal disease is often severe, aggressive and difficult to manage.

- No special facility or equipment is required. "Standard/Universal Precautions" are followed.
- HIV infected patients who require specialist care should be appropriately referred according to the same referral protocol as for the non-HIV infected patient e.g. oral medicine, oral pathology, oral surgery, endodontics, periodontal therapy, orthodontics, pedodontics, prosthodontics.
- A comprehensive medical and oral health assessment is an essential component for safe and appropriate oral health care.
- HIV infected persons often present with medical problems resulting from HIV-related immune suppression and comorbid conditions

HIV MEDICINES IN SEVEN DRUG CLASSES STOP(#) HIV AT DIFFERENT STAGES IN THE HIV LIFE STYLE[15]

- BINDING (also called Attachments): HIV binds to the receptor on the surface of the CD4 cells.

#CCRS antagonist
#post attachment inhibitors

- FUSION: The HIV envelope and the CD4 cell membrane fuse, which allows HIV to enter the CD4 cells.

#fusion inhibitors

- REVERSE TRANSCRIPTION: inside the CD4 cells, HIV releases and uses reverse transcriptase to convert its genetic material- HIV RNA-into HIV DNA. The conversion of HIV RNA to HIV DNA allows HIV to enter the CD4 cells nucleus combined with the cell genetic material- cell DNA

#non nucleoside reverse transcriptase inhibitors(NNRTI's)
#nucleoside reverse transcriptase inhibitors(NRTI's)

- INTEGRATION: inside the CD4 cell nucleus, HIV release integrase.HIV uses integrase to insert its viral DNA into the DNA of the CD4 cell.

#integrase inhibitors

- REPLICATION: once integrated into the CD4 cell DNA. HIV use the machinery of the CD4 cell to make the long chain of HIV proteins. The protein chain are the building blocks for more HIV.
- ASSEMBLY: The new HIV protein and HIV RNA move to the surface of the cell and assemble into the immature HIV.
- BUDDING: Newly formed immature HIV pushes itself out of the host CD4 cell. The new HIV releases protease. Protease breaks up the long protein chain in the immature virus creating the mature virus.

#protease inhibitors

HAART THERAPY:

HIGHLY ACTIVE ANTI RETROVIRAL THERAPY(HAART)is a medication regime used to manage and treat human immunodeficiency virus type 1 (HIV 1). It is composed several drugs in the antiretroviral classes of medication

It blocks reverse transcriptase to disrupt of coping HIV genetic code (NRTIs, NNRTIs) block proteases enzyme , preventing maturation of new virion and prevent fusion of HIV with cell membrane.(16)

XIV. CONCLUSION:

A tremendous change has been noted in the past few years in diagnosis and treatment aspects of HIV infection. Althoughmany clinical and research challenges remain in addressing the nature of the disease the newer treatment options led to drastic influence in the treatment outcome.As the pathogenesis of periodontal disease in HIV positive individuals is due to alteration in the microbial flora and host response, these factors need to be taken into consideration in treatment and prevention of periodontal disease in HIV patients.

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