INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
eISSN:2320-3137
Earthjournals Publisher
www.earthjournals.in

REVIEW ARTICLE

KNOWING AND UNDERSTANDING THE HIV PEDIATRIC PATIENTS

Lavinder Kaur Gill[1], JN Jaiswal[2], Gunjan Yadav[2], Alok Avinash[1], Manpreet Singh[3], Neelam Dewani[1]

1. Department of Pedodontics and Preventive Dentistry, Rungta college of Dental Sciences and Research Centre, Kohka Kurud Road, Bhilai, Chhattisgarh, India.

2.Department of Pedodontics and Preventive Dentistry, Sardar Patel Post Graduate Institute of Dental and Medical Sciences, Lucknow, U.P, India

3.Department of Pedodontics and Preventive Dentistry, Saraswati Dental College,

Lucknow, U.P, India

Corresponding author: Dr. Lavinder Kaur Gill,Senior Lecturer,Department of Pedodontics and Preventive Dentistry, Rungta college of Dental Sciences and Research Centre, Kohka Kurud Road, Bhilai, Chhattisgarh, India.

Publication history: Received on 2/1/2017, Published online 15/01/2017

ABSTRACT:

Along with the evolution of modern-day society, infectious diseases are changing to become more resistant to standard treatment regimens and new diseases are constantly emerging. A weakened immune system allows the development of a number of different infections and cancers, and it is these diseases which cause illness and death in people. The acquired immunodeficiency syndrome (AIDS) was first recognised in 1981, although the earliest documented case has been traced to a blood sample from 1959. It is caused by the human immunodeficiency virus (HIV-1), which has evolved a number of mechanisms to elude immune control and has there by prevented effective control of the epidemic. HIV-2 causes a similar illness to HIV-1 but is less aggressive and restricted mainly to western Africa. Highly active retroviral therapy (HAART) with three or more drugs has improved life expectancy to near normal in the majority of patients receiving it, with an 80% reduction of mortality since its introduction. HIV also infects and causes direct damage to other types of cells: for example, damage to the lining of the intestine can contribute to wasting (severe weight loss); damage to nerve cells can cause neurological problems. This review article provides a detailed overview of HIV in children with the diagnosis and management.
Keywords: Immunodeficiency, HIV-AIDS.

INTRODUCTION

Immunodeficiency is a disorder or a condition where the immune response is reduced or absent. It can be traced to the failure of one or more parts of immune system. The immune system is composed of variety of different cell types and proteins. Each component performs a special task aimed at recognizing foreign material (antigens) and/or reacting against foreign material.

Extrinsic factor can adversely affect immune responses producing states of secondary immunodeficiency and consequent increased risk of infections. Acquired Immunodeficiency Syndrome (AIDS) resulting from infection by Human Immunodeficiency Syndrome (HIV) is the best known secondary immunodeficiency largely because of its prevalence and its high mortality rate if not treated.

The Centers for Disease Control and Prevention (the CDC) has defined AIDS (1993) as "HIV infection and a specific group of diseases or conditions which are indicative of severe immunosuppression related to infection with the human immunodeficiency virus (HIV)".[1]

AIDS is characterized by profound immunosuppression associated with opportunistic infections, secondary neoplasms, and neurologic manifestations.[2] It is caused by a virus called HIV (Human Immunodeficiency Virus). This virus infects certain types of white blood cells, principally CD4 cells (also called helper cells or T4-cells) and monocytes/macrophages. CD4 cells and macrophages both have important functions in the immune system.[1]

History

- **Pre-1981-** While 1981 is generally referred to as the beginning of the HIV/AIDS epidemic, scientists believe that HIV was present years before the first case was brought to public attention
- **1983-**Dr. Luc Montagnier of the Pasteur Institute in France isolated lymphadenopathy-associated virus (LAV)-which he believed to be related to AIDS-and published findings. That same year, Dr. Robert Gallo of the National Cancer Institute in the United States successfully cultivates LAV (which he identified as HTLV-III) in laboratory and submits paper for publication proposing that a retrovirus causes AIDS.
- **1984**- Dr. Gallo and Dr. Luc Montagnier held joint press conference in June announcing discovery that a retrovirus and later named Human Immunodeficiency Virus (HIV)-causes AIDS.
- **1987** - First antiretroviral drug - Zidovudine or AZT (a nucleoside analog) - approved by U.S. FDA.
- **1988** - World AIDS Day first declared by World Health Organization (WHO) on December 1.[3]

Epidemiology of HIV/AIDS

WHO estimated that in 2009, 2.5 million children were living with HIV-1 infection, 90% of who were from Sub Sahara Africa while between 2004 and 2009 the global number of children born with HIV decreased by 24% and death from AIDS-related illness among children who are less than 15 years of age declined by 19%, still 370,000 were newly infected with HIV in 2009 alone.A greater proportion of female adolescents have AIDS (male: female ratio 1.5: 1) than do female adults more than 25 years of age (male: female ratio 2.9: 1).[2]

Etiology and Pathogenesis

HIV-1 and HIV-2 are the members of the Retroviridae family and belong to *Lentivirus* genus, which includes cytopathic viruses causing diverse diseases in several animal species. The HIV-1 genome contains two copies of single-stranded RNA. The genome includes three major sections: the **GAG** region, which encodes the viral core proteins (p24, p17, p9 and p6 which are derived from precursor p55), the **POL** region, which encodes the viral enzymes i.e., reverse transcriptase [p51], protease [p10], and integrase

[p32]); and the **ENV** region, which encodes the viral envelope proteins, (gp120 and gp41, which are derived from the precursor gp160).[4]Each mature virion is spherical and has a lipid membrane lined by a matrix protein that is studded with glycoprotein (gp) gp120 and gp41 spikes surrounding a cone shaped protein core.[5] gp41 is very immunogenic and is used to detect HIV-1 antibodies in diagnostic assays; gp120 is a complex molecule that includes the highly variable **V3 loop**. It also carries the binding site for CD4 molecule, the most common host cell surface receptor of T lymphocytes.[4]

The virus infects the CD4 cells in a complicated sequence of events (**Figure 1**):

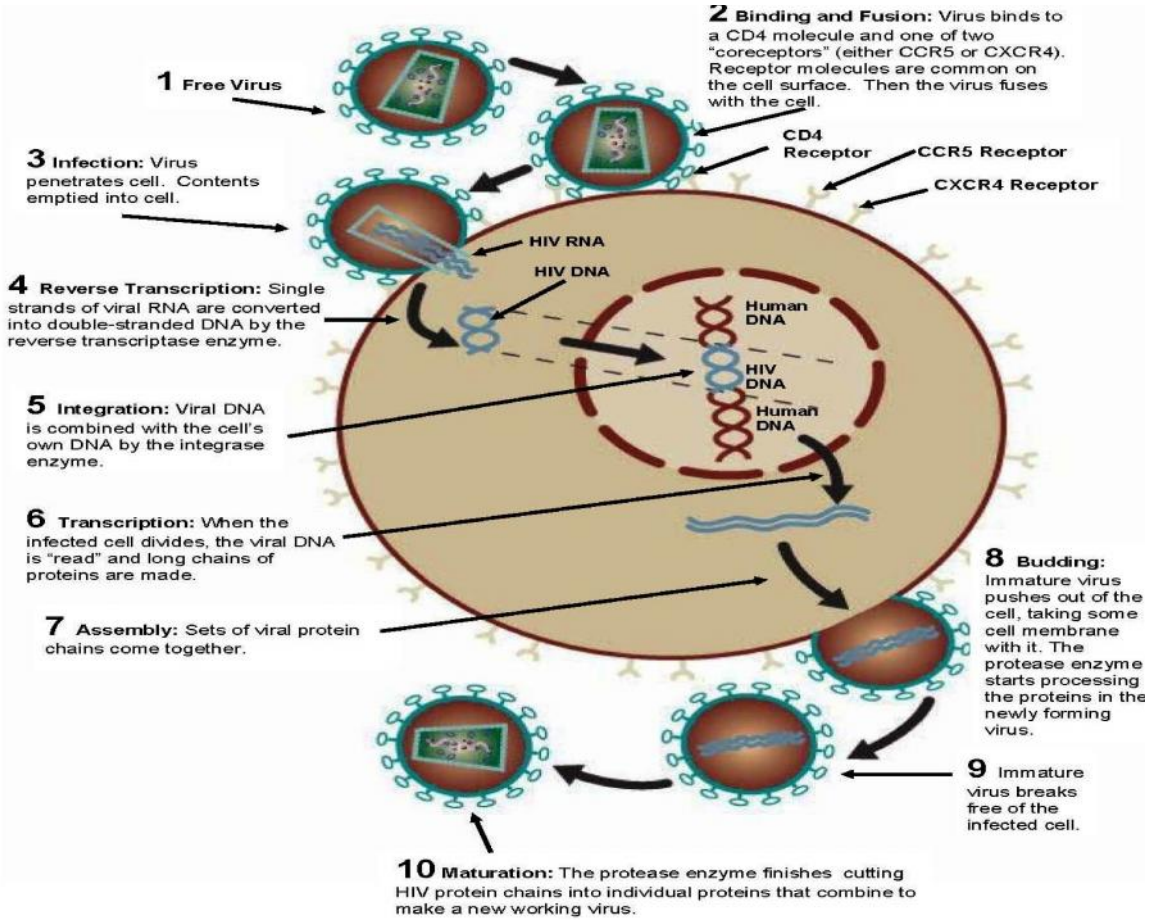

Figure 1

Transmission of HIV

- Sexual contact
- Injection drug use (IDU)
- Mother to child
  - Perinatal
  - Breast feeding
- Exposure to blood / blood products

- Blood / blood products transfusion or infusion
- Organ transplantation
- Occupational exposure.[6]

The primary route of infection in the pediatric population is vertical transmission. **Vertical transmission** of HIV can occur before (**intrauterine**), during (**intrapartum**), or after delivery (**throughbreast-feeding**).[4]

Risk of HIV transmission to and from the dental community

There is a high possibility that dentists treat HIV-infected patients unknowingly because most patients are probably unaware of their HIV status. The undiagnosed, untreated patient may unknowingly be a hazard to dentists, dental staff and other patients, especially because everyday dental practices involve invasive procedures and instrument reuse. Failure to adequately clean, disinfect and/or sterilize dental instruments contaminated with HIV from previous patients will endanger subsequent patients. If adequate precaution is not taken to prevent blood and body fluid contamination, the risk of HIV transmission increases tremendously.[7]The risk of HIV transmission to dental health care workers is extremely small when proper dental management and universal precautions are practised.

The possibility of transmission of blood-borne infections from dental health care workers to patients is very small. Currently most states and provinces have established expert panels to determine the limitations of practice of HIV-infected health care workers.[2]

The impact of HIV/AIDS on children and young adults

One of the most serious consequences of the AIDS epidemic has been the death of parents.[8]In India, according to the Human Rights Watch (2004), there were 1.2 million children under age fifteen orphaned by AIDS.[9]

The main impact of HIV/AIDS on children can be divided into three main areas, as follows:-

- **Loss of social / family support, or 'psycho-emotional impact'**
- **Stigma and discrimination, or 'social impact'**
- **Decreased access to education, health care and social services, or 'material impact'.**[9]

Clinical Manifestations

The HIV classification system is used to categorize the stage of pediatric disease by using 2 parameters: **clinical status** and **degree of immunologic impairment.**

1. Clinical Status

Category A: Mild symptomatic

Lymphadenopathy ≥0.5 cm at more than 2 sites; bilateral at 1 site)

Hepatomegaly

Splenomegaly

Dermatitis

Parotitis

Recurrent or persistent upper respiratory tract infection, sinusitis, or otitis media

Category B: Moderately symptomatic

- Anemia (hemoglobin <8 g/dL [<80 g/L]), neutropenia (white blood cell count <1,000/iL [<1.0 × 109/L]), and/or thrombocytopenia (platelet count <100 × 103/iL [<100 × 109/L]) persisting for ≥30 days
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Candidiasis, oropharyngeal (thrush), persisting (>2 mo) in children older than 6 mo of age
- Cardiomyopathy
- Cytomegalovirus infection, with onset before 1 mo of age
- Diarrhea, recurrent or chronic
- Hepatitis
- Herpes simplex virus (HSV) stomatitis, recurrent (>2 episodes within 1 year)
- HSV bronchitis, pneumonitis, or esophagitis with onset before 1 mo of age
- Herpes zoster (shingles) involving at least 2 distinct episodes or more than 1 dermatome
- Leiomyosarcoma
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex
- Nephropathy
- Nocardiosis
- Persistent fever (lasting >1 mo)
- Toxoplasmosis, onset before 1 mo of age
- Varicella, disseminated (complicated chickenpox)

Category C: Severely symptomatic

- Candidiasis, esophageal or pulmonary (bronchi, trachea, lungs)
- Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis or isosporiasis with diarrhea persisting >1 mo
- Cytomegalovirus disease with onset of symptoms after 1 mo of age (at a site other than liver, spleen, or lymph nodes)
- Encephalopathy (at least 1 of the following progressive findings present for at least 2 mo in the absence of a concurrent illness other than HIV infection that could explain the .ndings): (1) failure to attain or loss of developmental milestones or loss of intellectual ability, veri.ed by standard developmental scale or neuropsychologic tests; (2) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by CT or MRI (serial imaging required for children younger than 2 yr of age); or (3) acquired symmetric motor deficit manifested by 2 or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbance

- HSV infection causing a mucocutaneous ulcer that persists for greater than 1 mo or bronchitis, pneumonitis or esophagitis for any duration affecting a child older than 1 mo of age
- Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
- Kaposi sarcoma
- Lymphoma, primary, in brain
- Lymphoma, small, noncleaved cell (Burkitt), or immunoblastic; or large-cell lymphoma of B-lymphocyte or unknown immunologic phenotype
- Mycobacterium tuberculosis infection, disseminated or extrapulmonary
- Mycobacterium, other species or unidenti.ed species infection, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)

- Pneumocystis jiroveci pneumonia
- Progressivemultifocal leukoencephalopathy
- Salmonella (nontyphoid) septicemia, recurrent
- Toxoplasmosis of the brain with onset at after 1 mo of age
- Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following .ndings: (1) persistent weight loss >10% of baseline; (2) downward crossing of at least 2 of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child 1 yr of age or older; OR (3) <5th percentile on weight-for-height chart on 2 consecutive measurements,≥30 days apart; PLUS (1) chronic diarrhea (i.e., at least 2 loose stools per day for >30 days); OR (2) documented fever (for >30 days, intermittent or constant).4

2. Degree of immunologic impairment

The immune classification is based on the absolute CD4 lymphocyte count or the percentageof CD4 cells. Age adjustment of the absolute CD4 count is necessary because counts that are relatively high in normal infants decline steadily until 6 years of age, when they reach adult norms. If there is a discrepancy between the CD4 count and percentage, the disease is classified into the more severe category.

The WHO Clinical Staging System for HIV/AIDS: adults and adolescents 15 years-of-age and older.

Four Clinical Stages

Stage1. Patients who are asymptomatic or have persistent generalized lymphadenopathy

Stage2.Unexplained weight loss of less than 10 percent of total body weight and recurrent respiratory infections, dermatological conditions including herpes zoster flares, angular cheilitis, recurrent oral ulcerations, papular pruritic eruptions, seborrhoeic dermatitis and fungal nail infections.

Stage3. Weight loss of greater than 10 percent of total body weight, prolonged (more than 1 month) unexplained diarrhea, pulmonary tuberculosis, and severe systemic bacterial infections including pneumonia, pyelonephritis, empyema, pyomyositis, meningitis, bone and joint infections and bacteremia. Mucocutaneous conditions, including recurrent oral

candidiasis, oral hairy leukoplakia and acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis may also occur at this stage**.**

Stage 4.Wasting Syndrome, *Pneumocystis pneumonia* (PCP), recurrent severe or radiological bacterial pneumonia, extrapulmonary tuberculosis, HIV encephalopathy, CNS toxoplasmosis, chronic (more than 1 month) or orolabial herpes simplex infection, esophageal candidiasis and Kaposi's Sarcoma, cerebral or B cell Non-Hodgkin Lymphoma, progressive multifocal leukoencephalopathy (PML) and HIV associated cardiomyopathy or nephropathy.[10]

Oral Health Consideration in Paediatric patients

Group 1: Oral Lesions Commonly Associated With Paediatric HIV Infection

- Candidiasis-
  - Pseudomembranous
  - Erythematous
  - Angular cheilitis
- Herpes simplex viral infection
- Linear gingival erythema
- Major salivary gland enlargement
- Recurrent aphthous ulcers-
  - Minor, major and herpetiform

Group 2: Oral lesions less commonly associated with paediatric HIV infection

- Bacterial infections
- Periodontal diseases
  - Necrotizing ulcerative gingivitis (NUG)
  - Necrotizing ulcerative periodontitis (NUP)
  - Necrotizing stomatitis (NS)
- Viral infections (cytomegalovirus, human papilloma virus, varicella zoster virus)
- Xerostomia

Group 3: Oral lesions strongly associated with HIV infection but rare in children

- Kaposi's sarcoma
- Non-Hodgkin's lymphoma
- Oral Hairy Leukoplakia

Group 4: Oral conditions with increased severity in paediatric HIV infection

- Gingivitis and Periodontitis (increased gingival and plaque indices)
- Primary dentition caries
- Delayed eruption of primary and permanent teeth [11]

Diagnosis

Confirmation of HIV infection can be made by viral culture or by detection of HIV antibodies or antigens. The standard screening tool is the enzyme immunoassay (EIA) for antibodies to HIV. This test can have false positive results or cross-reactions; therefore, it should be repeated radioimmunoprecipitation (RIPA), rapid latex agglutination assay and dot-blot immunobinding assay.

The diagnosis of AIDS is indicated if the patient has laboratory evidence of HIV infection combined with documentation of less than 200 CD4+T lymphocytes per microliter.[12]

Table 1:

	IMMUNOLOGIC CATEGORIES									
	AGE-SPECIFIC CD4+ T-LYMPHOCYTE COUNT PERCENTAGE OF TOTAL LYMPHOCYTES						CLINICAL CLASSIFICATIONS			
	<12 mo		1–5 yr		6–12 yr					
IMMUNOLOGIC DEFINITIONS	**µ**	**%**	**M**	**%**	**µ**	**%**	**N: No Signs or Symptoms**	**A: Mild Signs and Symptoms**	**B: Moderate Signs and Symptoms**	**C: Severe Signs and Symptoms**
1: No evidence of suppression	≥1500	≥25	≥1000	≥25	≥500	≥25	N1	A1	B1	C1
2: Evidence of moderate suppression	750–1499	15–24	500–999	15–24	200–499	15–24	N2	A2	B1	C2
3: Severe suppression	<750	<15	<500	<15	<200	<15	N3	A3	B3	C3

Treatment and Prognosis of HIV infection

Antiretroviral therapy is recommended for any patient with a history of an AIDS-defining illness, regardless of $CD4^+$ counts or any asymptomatic patient with a $CD4^+$ count <200 cells/mm.[13]

Antiretroviral drugs are

1) Fusion inhibitors
2) Nucleoside reverse transcriptase inhibitors (NRTIs)
3) Non- Nucleoside reverse transcriptase inhibitors (NNRTIs)
4) Protease inhibitors (PIs)

The treatment of HIV infection requires combination therapy known as highly active antiretroviral therapy (HAART). HAART usually results in improved $CD4^+$ counts and decreased viral load.[14]

Antiretroviral therapy (ART) should be initiated in HIV-infected children aged ≥1 year with minimal or no symptoms with the following CD4 values:

- **Aged 1 to <3 years:**
  - With CD4 cell count <500 cells/mm^3 or CD4 percentage <75%
- **Aged 3 to <5 years:**
  - With CD4 cell count <750 cells/mm^3 or CD4 percentage <75%
- **Aged ≥5 years:**
  - With CD4 cell count ≤500 cells/mm^3

ART should be considered for HIV-infected children aged ≥1 year with minimal or no symptoms with the following CD4 values:

- **Aged 1 to <3 years:**
  - With CD4 cell count ≥500 cells/mm^3 or CD4 percentage ≥75%
- **Aged 3 to <5 years:**
  - With CD4 cell count ≥750 cells/mm^3 or CD4 percentage ≥75%
- **Aged ≥5 years:**
  - With CD4 cell count >500 cells/mm^3.[15]

Management of Newborns Exposed to Maternal HIV Infection

The management of infants whose mothers are infected with the human immunodeficiency virus (HIV) involves ***minimizing the risk of vertical transmission of HIV, recognizing neonatal HIV infection early, preventing opportunistic infections, and addressing psychosocial issues.*** Maternal antiretroviral drug therapy during pregnancy and labor, followed by six weeks of neonatal zidovudine therapy, can significantly decrease the risk of vertical transmission.[16]

CONCLUSION

More than 25 years have passed since the first report of AIDS was published in 1981. Although tremendous progress has been made in reducing the morbidity and mortality of HIV/AIDS, the pandemic, short of a major scientific breakthrough is expected to persist well into the future. Providers of oral health care should be expect to see more patients infected with HIV and should be familiar with the pathogenesis, management and infection control procedures necessary to provide oral/dental care to this population.

HIV/AIDS is a deadly disease that spreads in conditions of ignorance and silence. The consequences of it are borne by individuals and communities affected by it, again in silence and shame. Only by shedding more light on the dynamics of vulnerability to the epidemic, by researching appropriate ways of dealing with its impact, and by seriously upscaling human and financial resourses available for battling the epidemic can we stand a chance of overcoming a global catastrophe.

REFERENCES

1. Martin B. Investigating the origin of AIDS: some ethical dimensions. Journal of Medical Ethics 2003; 29(4): 253-256.
2. Wood NK, Sawyer DR.Acquired Immunodeficiency Syndrome. In: Alex Weldon, editor.Differential Diagnosis of Oral and Maxillofacial Lesions, 5th ed. Texas: Mosby Elsevier; 2009.p. 596-610.
3. Anand KP, Satapathy Y, Kashyap AS. Luc Montagnier-Discoverer of HIV Virus. Journal of the Association of Physicians of India 2015; 63(1): 126.
4. Kliegman RM, Stanton BF, St.Geme JW, Schor NF, Behram RE. Acquired Immunodeficiency Syndrome. In:Judith Fletcher, editor. Nelson Textbook of Pediatrics, 19thed. Philadelphia: Elsevier Saunders; 2012.p.1041-1141
5. Wilkins EGL. HIV infection and AIDS. In: Colledge NR, editor. Davidson's Principles and Practise of Medicine, 21st ed. China: Churchchill Livingstone Elsevier; 2010.p.383-408.
6. DePaola LG, Meeks VL. Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome, and Related Infections. In Hauber M, editor. Cottone's Practical Infection Control In Dentistry, 3rd ed. Philadelphia: Wolters Kluwer, Lippincott Williams & Wilkins; 2010.p.32-44.
7. Azodo CC, Ehizele AO, Umoh A, Ogbebor G. Preventing HIV Transmission in Nigeria: Role of the Dentists. *Malaysian Journal of Medical Sciences*2010; 17(2): 10-17.
8. Jacobson MA, Mills J.Serious cytomegalovirus disease in the acquired immunodeficiency syndrome (AIDS). Clinical findings, diagnosis, and treatment.Annals of Internal Medicine 1988; 108(4): 585-594.

9. Jaffe HW, Bregman DJ, Selik RM. Acquired immune deficiency syndrome in the United States: the first 1,000 cases. The Journal of Infectious Diseases 1983; 148(2): 339-345.
10. Weinberg JL, Kovarik CL. The WHO Clinical Staging System for HIV/AIDS. Virtual Mentor2010; 12(3): 202-206.
11. Adebola AR, Adeleke SI, Mukhtar M, Osunde OD, Akhiwu BI, Ladeinde A. Oral manifestation of HIV/AIDS infections in paediatric Nigerian patients. Nigerian Medical Journal 2012; 53(3): 150-154.
12. Neville, Damm, Allen, Bouquet.Viral Infections. In: Neville, editor. Oral and Maxillofacial Pathology, 2nd ed. Philadelphia: ElsevierSanduers; 2007.p.213-52
13. Greenberg MS, Glick M, Ship JA.Immunologic Diseases. In: Petrice Custance, editor. Burket's Oral Medicine, 11thed. Ontario: BC Decker Inc; 2008.p.435-60.
14. Gunthard HF, Aberg JA, Eron JJ, Hoy JF, Telenti A, Benson CA*et al.* Antiretroviral treatment of adult HIV infection: 2014 recommendations of theInternational Antiviral Society-USA Panel. The Journal of the American Medical Association2014; 312(4): 410-425.
15. Maron G, Gaur AH, Flynn PM. Antiretroviral therapy in HIV-infected infants and children. The Pediatric Infectious Disease Journal 2010; 29(4): 360-363.
16. Krist AH, Crawford-Faucher A.Management of newborns exposed to maternal HIV infection. American Academy of Family Physicians 2002; 65(10): 2049-2056.

Paper cited as: Lavinder Kaur Gill, JN Jaiswal, Gunjan Yadav, Alok Avinash, Manpreet Singh, Neelam Dewani. KNOWING AND UNDERSTANDING THE HIV PEDIATRIC PATIENTS. International Journal of Medical and Applied Sciences, 5(4), 2016, pp.37-46.