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Eradication of Pediatric HIV-1 Infection: A Review on Progress and Challenges

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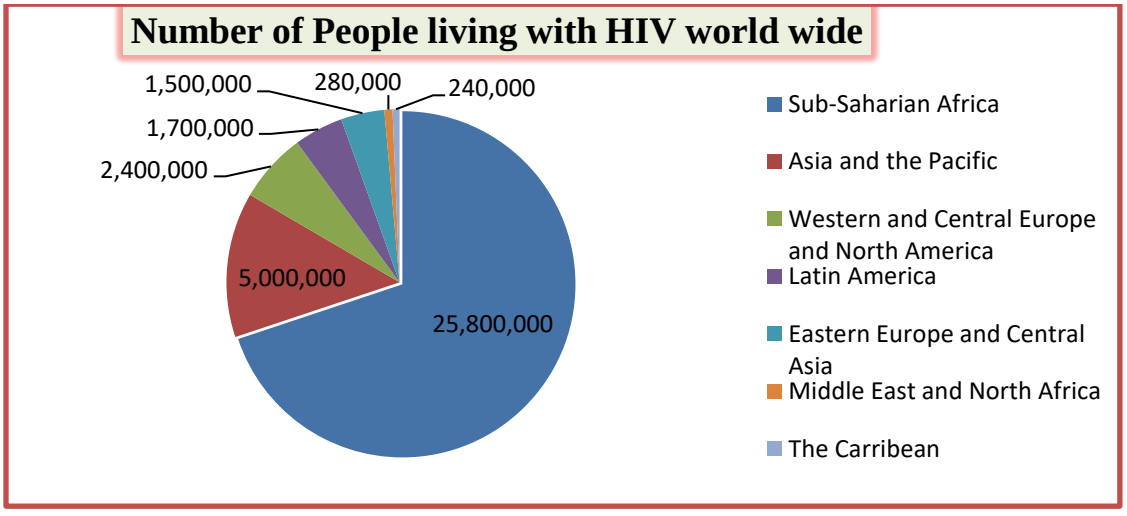
Abstract

Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome has a tremendous impact on society as well as also has large economic impacts. HIV infection by mother to child transference is increasing in the world because of the increase in infected mother that she has not receiving appropriate antiretroviral therapy. There are several barriers to efficient management like delayed infant diagnosis, lack of appropriate pediatric dosage form, inadequate skilled health professionals, etc. Underdeveloped immunity allows large spreading throughout various organs of the body. There is an increased rate of occurrence of lack of proper nutrition and infections that may be more tenacious, severe and less responsive to treatment. Early diagnosis and therapy are required to prevent the development of AIDS. New therapies are also becoming available but absolute prevention of infection, through maternal therapy during pregnancy, is the most fruitful measure in preventing this infection. During pregnancy, labor and delivery successfully reduces intrauterine and intrapartum HIV-1 transmission by the use of antiretroviral drugs.

Key Words: HIV/AIDS, mother to child transference, antiretroviral therapy, pediatric dosage form etc.

1. INTRODUCTION:

The crowd of Human Immunodeficiency Virus infected people is tremendously increasing worldwide (Steinbrook, 2004). In 2014 about 3.69 million people were living with HIV (containing 2.6 million children) – a global HIV prevalence of 0.8 %(UNAIDS, 2015). Above 90% of HIV-infected children got the infection from their mother, either before or around the time of birth and about 230,000 children die.



Most of the remaining subjected to contaminated blood or blood products. A few cases are the outcome of sexual abuse. Programs generated to convey antiretroviral therapy (ART) to pregnant women and children has minimizes the annual number of new childhood infections and deaths by 10 to 15% in the last few years. But, most of the infected children quite do not receive ART nearly like adults; only about 28% of children with manifestation for therapy receive ART vs. 57% of adults (Steven, Zeichner & Jennifer, 2005). Vertical transmission has reduced from about 25% by using wide ranging serologic screening and treating the infected pregnant women during pregnancy and delivery. Obstructing vertical transmission and giving treatment to HIV-infected children remain the two most vital objects of global pediatric HIV medicine (Coll, Hernandez, Boucher, et al. 1997). Available effective preventive measures include therapy applied during pregnancy, at delivery and in the post-partum period. If no antiretroviral therapy is applied infections in children are increasing and mortality remains very high (Rongkavilit & Asmar, 2004). Many questions are still to be resolved regarding susceptibility to infection containing measures for immune protection in different populations and different circumstances (Coutsoudis, et al.2004). However, it has been very clearly indicated that viral load at delivery are prognostic of viral transmission (Dunn, 2003). Besides, the very good results obtained with antiretroviral therapy (AR) in pregnant women with low viral load at delivery confirm that viral transmission is almost nil (Connor et al.1994).

2. CLASSIFICATION:

HIV is a constituent member of the genus Lentivirus part of the family Retroviridae (WHO, 2007). There are two types of HIV have been categorized like HIV-1 and HIV-2. Virus structure has shown in fig.2 and Phylogenetic Tree of the SIV and HIV viruses *(*Yamaguchi et al. (2006) shown in Fig.1. HIV-1 infection causes a broad spectrum of disease, of which AIDS is the most severe. HIV-1 is the most common pathogenic strain of the virus.

2.1 Researchers categorized HIV-1 into a major group (Group M) and two or more minor groups, namely Group N, O and group P.

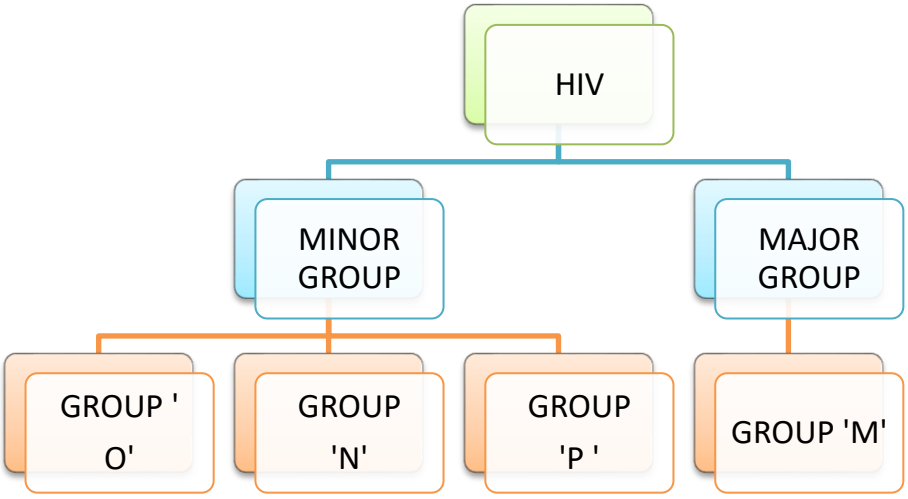


Fig.1. Classification of HIV-1.

2.1.1 Group M

With 'M' for "major", is mainly the common type of HIV, with above 90% of HIV/AIDS cases acquiring from infection with HIV-1 group M. The M group is also further subdivided into species, called subtypes, which are also given a letter (Sharp & Hahn, 2011).

Subtype A is common in West Africa.

Subtype B is the presiding form in Europe, America, Japan, Thailand, and Australia.

Subtype C is the most presiding form in Southern and Eastern Africa, India, Nepal, and parts of China.

Subtype D is generally only seen in Eastern and central Africa.

Subtype E has infrequently been identified as a non recombinant and only recombined among subtype A as CRF01 AE.

Subtype F has been available in central Africa, South America and Eastern Europe (Dhar, Amit & Kumar, 2012).

Subtype G (and the CRF02 AG) have been originate in Africa and central Europe.

Subtype H is limited to central Africa (Bobkov, Kazennova, Selimova, et al. 2004).

Subtype I was originally used to narrate a strain that is now accustomed for as CRF04 cpx, with the cpx for a "complex" recombination of various subtypes.

Subtype J is fundamentally originates in North, Central and West Africa, and the Caribbean.

Subtype K is limited to the Democratic Republic of Congo and Cameroon.

These subtypes are periodically divided into sub-subtypes likes A1 and A2 or C1 and C2. In 2015, in Cuba the strain CRF19, a recombinant of subtype A, D and G, with a D protease, was found to be strongly incorporated with rapid development to AIDS.

This is not considerably a complete or final list, and besides types is likely to be found (Hemelaar, Gouws, Ghys, et al. 2006).

2.1.2 Group N

The 'N' denotes "non-M, non-O". This group was ascertained in 1998 and it has only found in Cameroon. As in 2006, only 10 Group N infections had been identified (Yamaguchi, Coffey, Vallari, Ngansop, et al.2006).

2.1.3 Group O

The O ("Outlier") group is not often seen outside of West-central Africa. It is most common in Cameroon, where a survey of 1997 found that up to 2% of HIV-positive samples were from Group O (Yamaguchi, Coffey, Vallari, Ngansop, et al.2006).

The group caused to be pertinent because it cannot be diagnosed by early forms of the HIV-1 test kits. Recently most advanced HIV tests have now been developed to identify both Group O and N.

2.1.4 Group P

In 2009, a latest analyzed HIV sequence was investigated to have much similarity to a simian immunodeficiency virus recently detected in wild gorillas (SIVgor) than to SIVs from chimpanzees (SIVcpz). The virus was isolated from a Cameroonian woman lived in France who was detected with HIV-

1 infection in 2004. The researchers reporting this sequence placed it in a Group P "pending the recognition of in addition human cases.

2.2 Classification demonstrated by the Centers for Disease Control and Prevention (CDC):

2.2.1 Clinical categories- In children < 13 year described by presence/ absence of explicit common opportunistic infections or cancers. These categories are

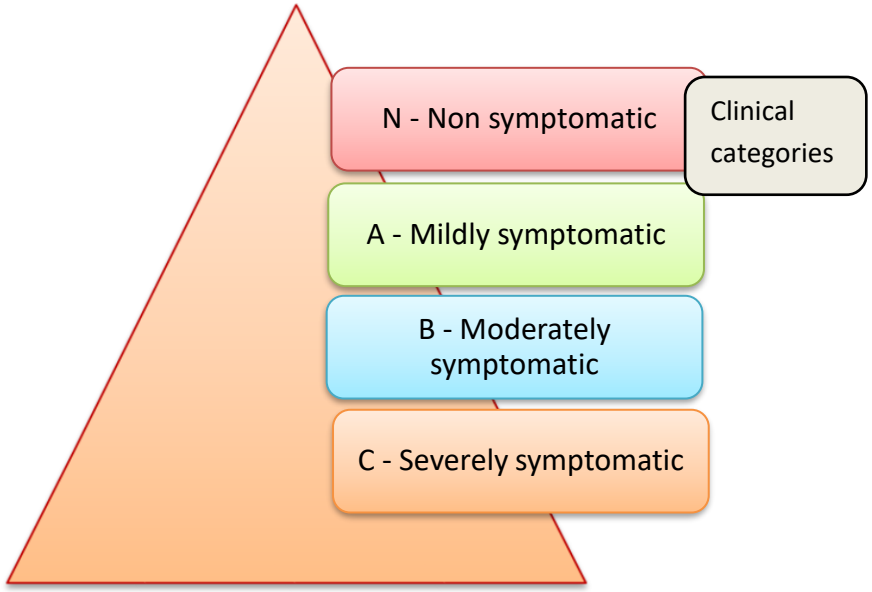


Fig.2. Clinical categories

2.2.2 Immunologic categories- In children < 13 year indicate the stage of immune extinction based on the CD4+ T-cell count (as % of total lymphocyte counts)

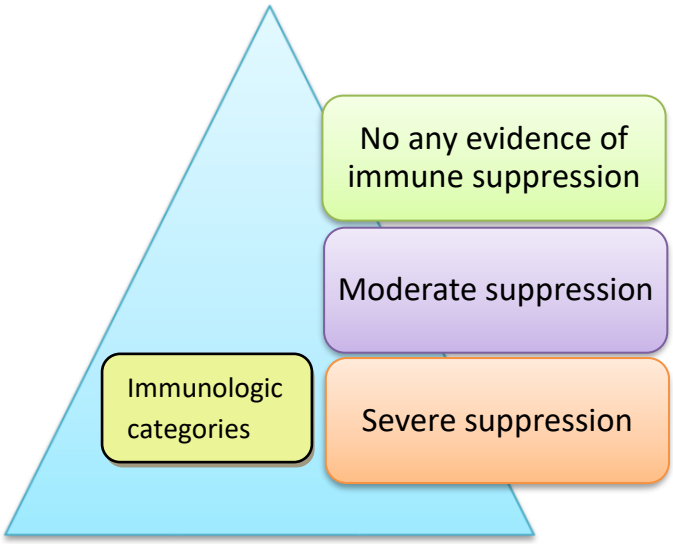


Fig.3. Immunological categories

These clinical and immunologic categories are becoming less important in the period of combination ART, which, when taken as prescribed, without fail leads to reduce in symptoms and a rise in CD4+ T-cell counts shown in (Table. 1). The categories are most helpful for clinical research and for narrate the severity of illness at the time of detection (Espanol, Caragol, Soler, & Manuel, 2004).

Types of Immunologic Categories	**< 12 month**		**1 to 5 year**		**6 to 12 year**	
	Cells/µL	**%**	**Cells/µL**	**%**	**Cells/µL**	**%**
No evidence of immune suppression	More than 1500	More than 25	More than 1000	More than 25	More than 500	More than 25
Evidence of moderate immune suppression	750 to 1499	15 to 24	500 to 999	15to 24	200 to 499	15to 24
Severe immune suppression	Less than 750	Less than 15	Less than 500	Less than 15	Less than 200	Less than 15

Table. 1. Immunologic categories for children 13 yr with HIV infection based on Age-Specific Cd4+ T-Cell counts and % of total lymphocytes count

3. VIRUS STRUCTURE AND REPLICATION CYCLE :

HIV progressively destroys the immune system by attacking and killing CD4 cells. CD4 cells are a kind of white blood cell that plays a vital part in shielding the body from contamination. HIV utilizes the machinery of the CD4 cells to proliferate and broaden all over the body. The mechanism of viral entrance comprises diverse phases like

3.1 Preliminary contact involving gp120 and CD4.

3.2 Conformational alteration in gp120 permits for secondary contact with CCR5.

3.3 The distal tips of gp41 are introduced in to the cellular membrane

3.4 Gp41 endures considerable conformational change; breakdown in half and forming coiled-coils (Thomas Splettstoesser, 2014)

This progression pulls the viral and cellular membranes jointly, fusing them. (Françoise, Anna Laura, & Jean-François, 2013). Following HIV has bound to the target cell; the HIV RNA and a variety of enzymes, together with reverse transcriptase, protease, ribonuclease, integrase are inserted into the cell shown in fig. 3 and fig.4

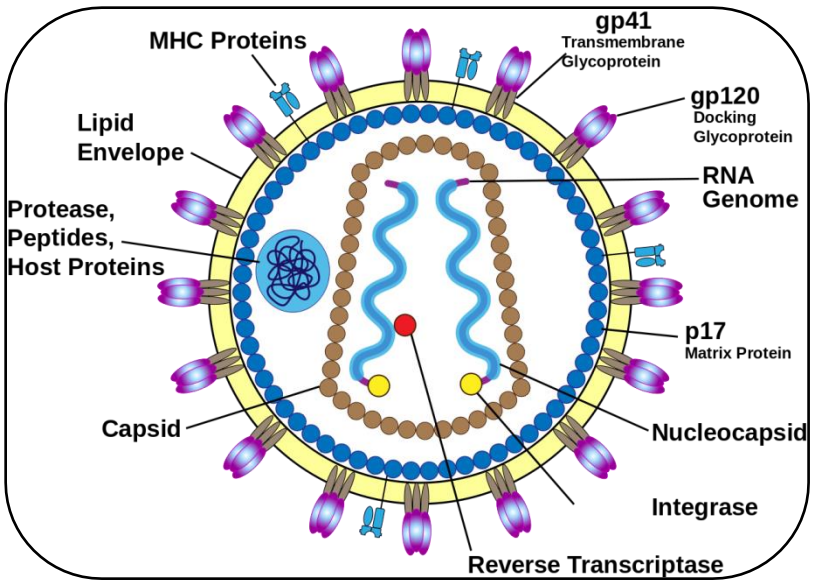


Fig.4. Structure of Virus

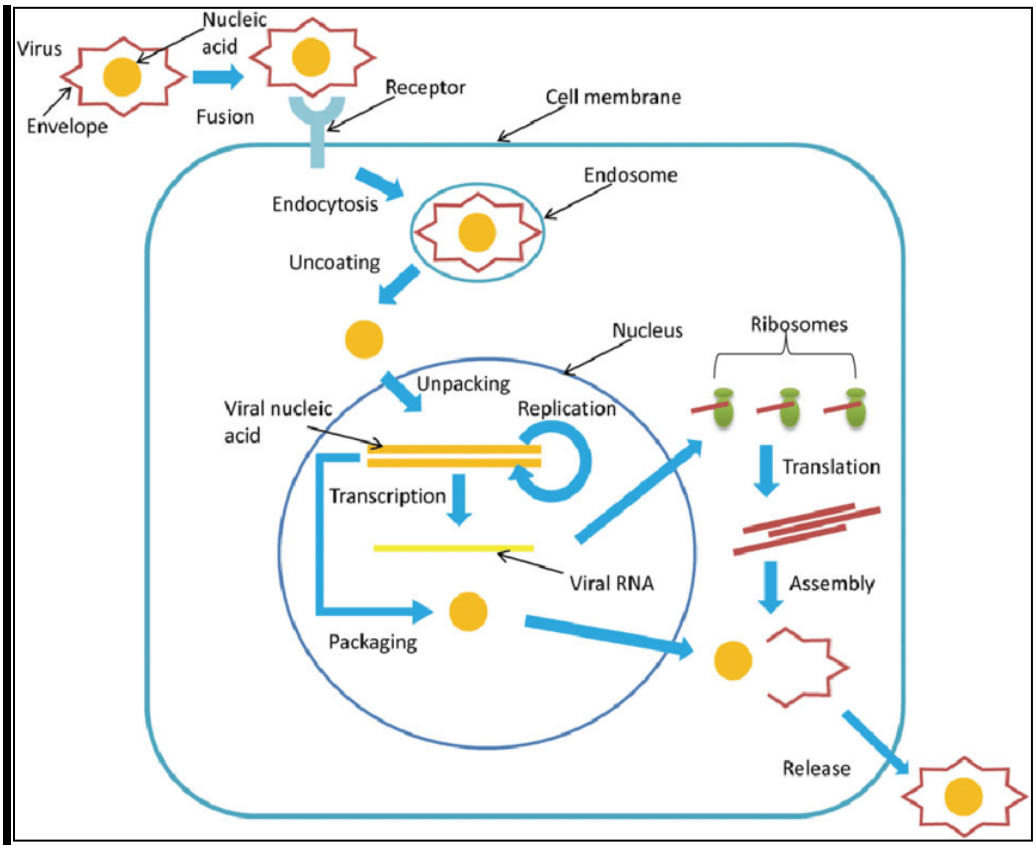


Fig.5. Replication cycle of Virus cell.

4. TRANSMISSION:

The infection probability for a new born from an HIV-positive mother who did not be given ART during pregnancy is approximate at 25% (range 13 to 39%). Probability factors for vertical transmission incorporate

- High plasma viral RNA concentrations (major risk)
- Seroconversion during pregnancy or breastfeeding (major risk)
- Advanced disease
- Low peripheral CD4+ T-cell counts
- Prolonged rupture of membranes

In vaginal births, a 1st-born twin is at higher possibility than a 2nd born twin, however this relationship may not bear true in developing countries. Cesarean delivery before arrival of active labor minimizes the possibility of mother-to-child transmission (MTCT) (Buchanan, Cunningham, 2009). Although, it is clear that MTCT is minimized most notably by giving combination ART, usually containing zidovudine (ZDV), to the mother and baby. ZDV monotherapy minimizes MTCT from 25% to around 8%, and current combination ART minimizes it to 1%.

HIV has been identifying in both the cellular plus cell-free portions of human breast milk. The occurrence of transmission by breastfeeding is around 6/100 breastfeed children/year. Evaluation of the overall risk of transmission through breastfeeding is 12 to 14%, demonstrate changeable extents of breastfeeding. Spread by breastfeeding is highest in mothers with high plasma viral RNA concentrations (e.g. women who become infected while pregnancy or throughout the period of breastfeeding) (WHO, 2011).

5. SIGNS AND SYMPTOMS:

- Abnormal recurrent and extreme occurrences of usual childhood bacterial infections, like otitis media, sinusitis, and pneumonia
- Recurrent fungal infections, like as candidiasis, which do not react to standard antifungal agents: Indicate lymphocytic dysfunction
- Frequent and severe viral infections, like recurrent or disseminated herpes zoster infection ; observe with moderate to severe cellular immune deficiency
- Growth failure
- Failure to thrive
- Wasting
- Failure to accomplish typical objectives: Recommends a developmental delay; such delays, distinctly diminished in the development of expressive language, may designate HIV encephalopathy
- Behavioral deformity (in older children), like loss of concentration and memory, may also shows HIV encephalopathy

Infants infected perinatally generally are asymptomatic during the first few months of life, even if no combination ART is start. However the median age at symptom arrival is about 3 yr, some children endure asymptomatic for > 5 yr and, with proper ART, are expected to exist to adulthood. In the pre-ART period, up to 10 to 15% of children had fast disease development, with symptoms appearing in the first year of life and death appearing by 18 to 36 months; these children were about to have acquired HIV infection earlier in utero. Although, most children certainly obtain infection at or near birth and have slower disease development that remain alive beyond 5 yr even before ART was used regularly(Lynne, & Mofenson, 2010).

The far typical appearance of HIV infection in children not receiving ART contain generalized lymphadenopathy, hepatomegaly, nephropathy hypertrophy, failure to thrive, oral thrush, lymphoid interstitial pneumonitis, hepatitis, repetitive

bacteremia, opportunistic infections, frequent diarrhea, parotitis, CNS disease cardiomyopathy, and cancers(Abuzaitoun, & Hanson, 2000).

5 COMPLICATIONS:

When complications observe, they generally contain opportunistic infections and hardly cancer. Combination ART has made such infections rare, and they nowadays observe mostly in undiagnosed children who have not still been given ART.

When opportunistic infections observed, *Pneumocystis jirovecii* pneumonia is the likely common and critical and has high mortality. Pneumocystis pneumonia occurs in the early age of 4 to 6 wk but occurs largely in infants aged 3 to 6 months who get infection before or at birth. Infants and older children with Pneumocystis pneumonia notably develop a sub acute; diffuse pneumonitis with breathlessness at rest, nonproductive cough, tachypnea, Oxygen desaturation, and fever.

Other opportunistic infections in immune suppressed children contain disseminated infection of varicella-zoster, cytomegalo virus and herpes simplex virus. Candida esophagitis, chronic enteritis due to Cryptosporidium or other organisms and disseminated or Toxoplasma gondii, CNS cryptococcal infection. Cancers in immune compromised children with HIV infection are mostly uncommon, but certain lymphomas and leiomyosarcomas, including non-Hodgkin B-cell lymphomas (Burkitt type) and CNS lymphomas, observe most often than in immune competent children. Kaposi sarcoma is mostly rare in HIV-infected children(Montessori, Press, Harris, et al. 2004).

6 DIAGNOSIS:

HIV/AIDS is diagnosed by laboratory testing and then staged based on the occurrence of definite signs or symptoms(WHO, 2007). HIV-1 testing is at first done by:

1. Serum antibody tests
2. Virologic nucleic acid tests (NATs; includes HIV DNA PCR or HIV RNA assays)

7.1 HIV-specific tests

In **children > 18 months,** the diagnosis is made using serum antibody tests (e.g, enzyme immunoassay [EIA] and confirmatory Western blot) as in adults. Recently, a new diagnostic algorithm of a 4th-generation HIV-1/2 antigen/antibody combination immunoassay done after a 2nd generation HIV-1/2 antibody differentiation assay and if needed, an HIV-1 qualitative RNA assay has been used in adults and may likely be used in children. Only very hardly an older HIV-infected child has of lack HIV antibody because of notably hypogammaglobulinemia (Barbaro, & Barbarini, 2011).

In **Children < 18 months,** preserve maternal antibody, generate false-positive results on EIA, so determination is done by HIV virological assays like qualitative RNA assays or DNA PCR assays, which can detect around 30% of cases at birth and up to 100% by 4 to 6 months of age. HIV viral culture has adequate sensitivity and specificity but is technically more demanding and dangerous and has been

supersedes by NATs in various laboratories (Shah, 2006).

Other type of NAT, the quantitative HIV RNA assay is recently most often utilized in infants for diagnostic testing. Moreover, care should be taken while using RNA assays for infant diagnosis because test specificity is unclear at very low RNA concentrations (< 5,000 copies/mL) and sensitivity is unknown in newborns in which mothers given complete treatment at the time of delivery.

Firstly within the first 2 wk of life a virologic test (a NAT) should be carried out, at about 1 month of age, and between 4 month and 6 month. A positive test should be confirmed promptly using the similar or other virologic test. If the serial HIV virologic tests are negative at ≥ 2 wk and ≥ 4 wk, the infant is considered uninfected with > 95% accuracy. If HIV virologic tests are also negative at ≥ 4 wk and ≥ 4 month, the infant is accounted as non infected with up to 100% accuracy. However, many experts continue to suggest follow-up antibody tests. If an infant < 18 mo with a positive antibody test but negative virologic tests develops an AIDS-defining illness (category C, HIV infection is diagnosed(WHO, 2010).

Rapid tests for detection of HIV antibody are derivatives of EIAs that furnish results within minutes to some hours. These tests can be done as point-of-care tests on whole blood, or serum and oral secretions. In US, these tests are very useful in labor and delivery suites to test women of unknown HIV serostatus, thus permit counseling, initiation of ART to eradicate MTCT, and testing of the infant to be organized at the time of birth visit. Rapid assays generally need confirmatory tests, like second EIA, HIV-1/2 antibody differentiation assay/ Western blot. These confirmatory tests are very important because in areas where the supposed HIV prevalence is minimum, albeit a specific rapid assay gives largely false positives. Moreover, if the expected probability of HIV is maximum, the positive prognostic value increases.

Before HIV determination test of a child is done, the mother or primary caregiver and the child, if old enough should be counseled regarding the possible psychosocial dangers and advantages of testing. Written or oral consent should be acquired and recorded in the patient's chart, undeviating the state, local, and hospital laws and regulations. Counseling and consent constraints should not prevent testing if it is medically suggested; non-acceptance of a patient or their guardian present with consent does not mitigate physicians of their professional and legal responsibilities, and many times authorization for testing must be procured by other means like court order. Test results should be discussed with the family members, the main caregiver, and if old sufficient, the child. If the child is HIV-positive, proper counseling and successive follow-up care must be provided. Maintaining confidentiality is very essential in all cases. Children and adolescents meeting the standards that for HIV infection or AIDS must be reported to the suitable public health department(WHO, 2013).

7.2 Other tests:

When infection is diagnosed, other tests are required to be done:

7.2.1 The CD4+ T-cell count

7.2.2 The CD8+ T-cell count
7.2.3 Plasma viral RNA concentration

Infected children needs determination of CD4+ and CD8+ T-cell counts and the plasma viral RNA concentration to help in measurement of their degree of illness, prognosis, and the outcome of therapy. CD4+ counts may be normal but reduced eventually. CD8+ counts generally increase initially and do not decrease until late in the infection. These changes in cell populations gives in a decrease in the CD4+:CD8+ cell ratio, a characteristic of HIV infection. Less expensive alternative surrogate markers for instance total lymphocyte counts and serum albumin altitudes may also forecast AIDS mortality in children, which possibly helpful in developing countries.

Although not routinely determined, serum immunoglobulin concentration, especially IgG and IgA, often are distinctly eminent, but intermittently utmost children evolve pan hypogammaglobulinemia. Patients may be energic to skin test antigens (WHO, 2013).

8 TREATMENT:

The only and the best treatment for human immunodeficiency virus (HIV) as well as the most serious viral infections is prevention. Successful management of HIV among children is crucial for affected children. With the appearance of ART, HIV has begin a chronic controllable disease from what was considered as fatal disease. However ART is very expensive (Chauhan, & Chaudhary, 2015).

8.1 Antiretroviral (ARV) drugs: Combination ART most commonly contains 2 nucleoside reverse transcriptase inhibitors (NRTIs) in addition either a protease inhibitor (PI) or a non nucleoside reverse transcriptase inhibitor (NNRTI); many times an integrase inhibitor specified with 2 NRTIs. Mainly there are > 2 dozen ARV drugs, containing multidrug combination products, obtainable in the US, and in various countries each of which may have side effects and drug interactions with other ARV drugs or generally used antibiotics, sedatives and anticonvulsants. Novel ARV drugs, immunomodulators as well as vaccines are under evaluation. Consultation about ART, principally for issues containing HIV post exposure prophylaxis and eradication of HIV mother to child transference, are too accessible through the National HIV/AIDS Clinicians. Standard treatment is with combination ART to increase viral suppression and minimize selection of drug-resistant strains. Perhaps mostly, ART consists of a foundation of 2NRTIs like zidovudine with lamivudine or emtricitabine, abacavir with lamivudine or emtricitabine, and for adolescents, tenofovir with emtricitabine or l amivudine specified in combination with a ritonavir-boosted PI (i.e. lopinavir or ritonavir or ritonavir-boosted atazanavir) or NNRTI (efavirenz or, in some situations, nevirapine). Other combinations generally sometimes used (like as 2 NRTIs with raltegravir), but only fewer data are available to support their use as first-line regimens. Tenofovir is functionally grouped within the NRTIs but is actually a nucleotide reverse transcriptase inhibitor by chemical structure.

8.2 Supportive care: Due to the success of combination ART, appreciable of the current attention is on the management of HIV infection as a persistent disease, specifying

social and medical issues together. Most important long-term medical issues contain the requirement to manage HIV-related and drug-related metabolic circumstances and rationalize age-related changes in drug pharmacokinetics and pharmacodynamics.

8.3 Indications

Commencement of ART for children is similar but not identical to that in adults; for children, initiation of therapy mainly depends on immunologic and clinical basis with additional features of age and, in some conditions, plasma HIV viral load. The objective of therapy is identical to that in adults: to prevent HIV replication and maintain or attain age-normal CD4+ counts and percentages with the minimum amount of drug toxicity(Mothi, et.al. 2011).

8.4 Adherence

Treatment will be accomplished only if the family and child are able to closely follow to a possibly complex medical regimen. Non adherence not only causes to failure to control HIV but also selects drug-resistant HIV strains, which decreases future therapeutic alternatives. Obstacle to adherence should be addressed before starting treatment. Obstacles containing availability and palatability of pills or suspensions, side effects that including those due to drug interactions with current therapy, pharmacokinetic factors like the need to take some drugs with food or in a fasted state, and a child's dependence on others to give drugs and also HIV-infected parents may have problems with memorizing to take their own medicines. Advanced once- or twice-daily combination regimens and more palatable pediatric formulations may assist to improve adherence.

9. CHILDREN PRESENTED WITH COMBINATION ANTIRETROVIRAL THERAPY:

Combination ART has notably changed the clinical manifestations of pediatric HIV infection. Along with of bacterial pneumonia and other bacterial infections like bacteremia, recurrent otitis media quite appear more often in HIV-infected children; opportunistic infections and growth retardation are substantially less persistent than in the pre-ART periods(WHO, 2007). New problems, like alterations in serum lipids, fat mal distribution, hyperglycemia, osteonecrosis, and nephropathy are reported; moreover, the frequency is lower in children than in HIV-infected adults.

Although the combination ART clearly boosts neuro developmental outcome, there seems to be an increased frequency of behavioral, developmental, and cognitive complications in treated HIV-infected children. It is not clear that these problems are generated by HIV infection itself, medicinal drugs, and other biopsychosocial factors among HIV-infected children. It is not actually known that whether any further effects of HIV infection or ART between the severely periods of growth and development will inarguable later in life because the first wave of perinatally infected children is right now attain adulthood. To identify such side effects, providers will require observing HIV-infected children over time(WHO, 2013).

10. MONITORING AND FOLLOW UP OF CHILDREN ON ART:

After beginning an infant or child on ART it is very important for regular clinical monitoring at 2 wk after commencement and every 4 wks after that. These visits are to estimate growth and improvement immunization condition and provide nutrition counseling. There is also an opportunity to educate the parents and care providers on unfavorable drug reactions (Mothi, et.al. (2011).

10.1 ARV drug toxicities

The majority of common toxicities comprise the following:

10.1.1 Hematological: with AZT (anemia, neutropenia and thrombocytopenia).

10.1.2 Mitochondrial dysfunction: along with other NRTI drugs: consists of lactic acidosis, hepatic toxicity, pancreatitis and peripheral neuropathy.

10.1.3 Lipodystrophy along with other metabolic abnormalities: More common among the stavudine (d4T) and protease inhibitors, and to a slighter extent among other NRTI drugs. Abnormalities incorporate fat maldistribution and hyperglycemia, hyperlipidaemia, diabetes mellitus, insulin resistance, body habits changes, osteoporosis osteopenia and osteonecrosis.

10.1.4 Allergic reactions: As well as skin rashes and hypersensitivity reactions. These are more ordinary among the NNRTI drugs, but also seen with certain NRTI drugs, for example abacavir (ABC).

10.1.5 Hepatic impairment: In children with hepatic dysfunction of any etiology NVP requires careful consideration as a result of its probable life threatening hepatotoxicity.

10.1.6 Discontinuation and drug substitution: As a common principle mild toxicities do not necessitate discontinuation of treatment or drug replacement, and indicative treatment might be specified (e.g. antihistamines for a mild rash). Moderate or severe toxicities may have need of replacement with a drug in the same ARV class although with a dissimilar toxicity profile, or with a drug from a different class. These do not necessitate discontinuation of all ART. Rigorous life-threatening toxicities necessitate discontinuation of all ARV drugs, and the commencement of suitable supportive therapy until the patient is stabilized and the toxicity is resolved(Draft Guidelines for Care of HIV Exposed Infants and Children less than 18 months January 2010).

10.2 ART regimen failure: Poor adherence, inadequate drug levels or primary drug resistance can all cause to ARV treatment failure. Genetic variations in drug metabolism may also be important. When treatment failure is confirmed, changing to a new second-line regimen becomes essential. Prior to switching therapy, it is essential to assess and address adherence issues(Bhattacharyya Mukherjee, 2006).

10.3 Additional issues

10.3.1 Psychosocial management of pediatric HIV: HIV is a social ailment and its management needs every aspects of physical, psychological, spiritual and social support.

10.3.2 Immunization: HIV-infected children are more prone to diseases caused by infectious agents and are further liable to develop severe complications when evaluated to immune-proficient children.

Therefore it becomes crucial to vaccinate them against all vaccine-avoidable diseases. HIV-infected infants and children can safely be given the majority childhood vaccines even though effective response depends on the extent of immune-suppression. NACO suggests regular immunization to all HIV exposed infants and children.

Overall, it is preferable to circumvent live-virus vaccines if a substitute inactivated vaccine is

obtainable such as polio, influenza. In addition, live attenuated vaccines are commonly not recommended with the exclusion of measles, mumps, rubella vaccine and varicella vaccines which can be specified to children who are not thoroughly immune-compromised. The recent WHO recommendation is that for infants born to HIV-infected mothers where early HIV diagnostic testing can be performed, BCG can be delayed until diagnostic testing outcome are available, in view of the significantly elevated possibility of disseminated BCG disease in ill infants. Inactivated vaccines are intended for diphtheria, tetanus, and pertussis and hence are unlikely to pose significant risk to patients with HIV infection. Invasive pneumococcal disease stays a source of significant morbidity and mortality amongst HIV-infected individuals, therefore pneumococcal vaccination will help to diminish invasive pneumococcal disease; similarly Haemophilus influenza and meningococcal vaccines will facilitate to diminish invasive diseases.

All additional vaccines beneath the (EPI) Expanded Programme of Immunization, in conjunction with Haemophilus influenza type B and pneumococcal vaccine supposed to be presented. Human papilloma virus vaccine is suggested for young girls between 9 to 26 yr, as this virus is coupled with an increased risk of anogenital cancers in HIV infection(Bhattacharyya Mukherjee, 2006).

10.3.3 Nutrition: Micro- and macronutrients insufficiency are common in HIV infected children impacting on the succession of the disease leading to growth retardation and improved risk of morbidity and mortality. Energy needs increase by 10 % still in asymptomatic children, up to 25-30 % among chronic or persistent infections and TB, and increasing additional to a greatest of 50-100 % increase throughout periods of severe malnutrition. Common sources for insufficient nourishment are persistent illness, deficiency, lack of awareness, insufficient access to food, parental illness, psychosocial problems and undesirable effects of drugs.

Even though the possibility of transmission throughout breast feeding is about 14 %, the decision on policy to breastfeed or not is left to national health authorities taking into concern socio-economic circumstances, worth of health services, local epidemiology, sources of infant and child mortality. NACO suggests restricted breast feeding for the first six months(Bhattacharyya Mukherjee, 2006).

11. PREVENTION:

Numerous measures are to be executed in order to reduce extremely significant the occurrence of MTCT:

11.1. Prevention of perinatal transmission: Suitable prenatal ART efforts to optimize maternal health, disrupt MTCT, and decrease in utero drug toxicity. In the US

and other countries wherever ARV drugs and HIV testing are readily obtainable, treatment with ARV drugs is standard for all HIV-infected pregnant women. Rapid HIV testing of pregnant women who present in labor with no documentation of their HIV serostatus may allow instantaneous institution of such measures. All HIV-infected pregnant women should commence combination ART to avoid MTCT, in addition to their own health, beginning at 14 to 34 wk gestation(Buchanan, Cunningham, 2009).

11.2. Caesarean section: It has been shown to reduce transmission of the infection by circumventing the entry of blood cells from the mother into the fetus´s blood during labor and delivery(Chauhan & Chaudhary, 2015).

11.3. Avoiding breastfeeding: The danger of HIV transmission to infants through breast milk outweighs the dangers coupled with other nursing methods [21].

11.4. Prevention of adolescent transmission: Since adolescents are at greater possibility of HIV infection, they should receive education, have access to HIV testing, and know their serostatus. Education should incorporate information about transmission, implications of infection, and strategies for avoidance, including abstaining from high-risk behaviors(Buchanan, Cunningham, 2009).

11.5. Prevention of opportunistic infections: Prophylactic drug treatment is suggested in certain HIV-infected children for avoidance of Pneumocystis pneumonia and *M. avium* complex infections. Information is insufficient on the use of prophylaxis for opportunistic contamination by other organisms, such as cytomegalovirus, fungi, and toxoplasma (Bhattacharyya & Mukherjee, 2006).

12. CURRENT STATUS OF HIV VACCINES:

The question for an effective vaccine to prevent HIV transmission, which is likely to be the most effective approach to stop the progress of the epidemic, has been and continues to be an undefeatable challenge. Traditional vaccine strategies that have been helpful for other vaccines have confirmed ineffective or unusable for HIV for the reason of safety concerns. However, significant pains have been intended for the development as well as clinical testing of HIV vaccines throughout the past two decades. Four most important HIV vaccine effectiveness trials carried out by VaxGen Inc (AIDSVAX 003 and AIDSVAX 004) and the NIH-supported HIV Vaccine Trials Network (HVTN 502 and HVTN 503) unsuccessful to reveal effectiveness; though, a current trial carried out in Thailand (RV144 trial) confirmed a low level of efficacy, resulting in several improved hopefulness. Scrutinizing the roots for vaccine disappointment and, more importantly, for the some degree of efficacy observed in the RV144 trial be supposed to present significant assistance to the field(Bansal, Malaspina, & Flores, 2010).

13. CHALLENGES AND APPROACHES IN FOREFRONT OF PEDIATRIC HIV/AIDS:

To sort out the multi-factorial issues that revolve around HIV/AIDS in children, there is an imperative need for a concerted, sustainable and multi-pronged national and global response:

- Enhanced Antenatal care(ANC) exposure
- Elasticity of Prevention of Mother-to-child transmission of HIV (PMTCT) protocol in diverse health care situations.
- Eminence care to keep mother and child alive and healthy.
- Ensuring breast milk safer by extended ARV prophylaxis during lactation.
- Improve follow up of mother - infant pair and early infant diagnosis leading to early initiation of ART in children <2 yr of age.
- Periodic RNA-PCR assay (viral load) in children on ART for early diagnosis of failing course of therapy and commencement of 2nd line ART.
- Build up availability and accessibility of 2nd line ART.
- Update policies and authorized documents pertaining to privacy, consent and status disclosure in children and adolescents.
- Need for a wide-ranging supplementary nutrition programme to be immediately implemented (micro & macro nutrients).
- Inclusion of a pediatrician as vital part of care continuum of children living with HIV/AIDS.
- Recognize areas of need based research in pediatric AIDS[33].

CONCLUSION:

With more access to antiretroviral therapy in conjunction with good nutrition there is hope that more and more HIV positive children would cross adolescence phase to adulthood. Regular clinical follow up in conjunction with enhanced understanding of HIV among doctors and society will bring rays of hope for these untoward innocent sufferers of a deadly virus.

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