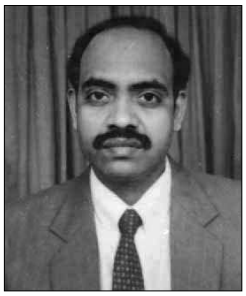

Pregnancy and HIV

NK Singh

Consultant Physician, Dhanbad 826 001, Jharkhand

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ABSTRACT

Recent advances, together with a growing understanding of the mechanism of perinatal transmission of HIV infection, have provided tremendous opportunity for the management of pregnant women who are infected with the HIV, but they have also greatly complicated their care. Adverse pregnancy outcomes that have been reported in HIV positive women in developing countries include increased rates of spontaneous early abortion, low birth weight babies, and stillbirths, preterm labour, preterm rupture of membranes, other sexually transmitted diseases, bacterial pneumonia, urinary tract infections and other infectious complications.

HIV testing in pregnancy has a number of benefits, but this must be balanced against the possible risks of stigmatisation, discrimination and violence.

The management of pregnancy in HIV-positive women should be seen as part of the holistic and long-term care of the woman. The medical care of HIV positive women should be tailored to the individual needs of the woman. Obstetric management will be similar to that for uninfected women in most instances, although invasive diagnostic procedures should be avoided, and iron, folate and other vitamin supplementation should be considered. Careful management of women infected with HIV is also important during labor and at delivery in order to minimize risk of vertical transmission and reduce the potential for maternal and neonatal complications. The HIV-infected woman should be provided with the most up-to-date information on the use of antiretroviral therapy, mode of delivery, and other issues, such as whether to undergo cesarean delivery, and then should be encouraged to make her own decisions.

The use of antiretroviral drugs in pregnancy for the prevention of mother-to-child transmission of HIV should be encouraged and provided as widely as possible. In settings where this cannot be implemented in the short-term, other interventions including modifications of obstetric practice should be considered.

Since 1994, the results of the Pediatric AIDS Clinical Trials Group (PACTG) Protocol 076 revolutionized the care of pregnant women infected with human immunodeficiency virus (HIV). The care of people infected with HIV has also dramatically changed from one of supportive care of individuals with a terminal illness to aggressive care of an often manageable chronic disease. Goals of therapy during pregnancy are two-fold: (1) to provide appropriate care for the woman's HIV infection, and (2) to attempt to reduce the risk of vertical transmission to the neonate. Choice of antiretroviral medications has to be made not only with these considerations in mind, but also with care taken not to jeopardize maternal or fetal health. For the pregnant woman, the issues surrounding the management of her HIV infection and pregnancy are also complex. HIV infection in pregnancy has become the most common complication of pregnancy in some developing countries. This has major implications for the management of pregnancy and birth. With an estimated one and a half million HIV-positive women becoming pregnant each year, almost 600 000 children will be infected by mother-to-child transmission annually: over 1600 each day.[1,2] Maternity services in areas of high HIV prevalence have several responsibilities. Firstly, to enable women to be tested and to use these results to maintain their health in an optimal manner; secondly, to utilize appropriate interventions to reduce the rate of mother-to-child (MTC) transmission of HIV; and thirdly, to train staff and provide equipment to prevent nosocomial transmission of HIV and other pathogens in developing countries where heterosexual transmission is the predominant mode of spread.[3]

SUSCEPTIBILITY OF WOMEN TO HIV INFECTION

Women in the developing world are at higher risk of HIV infection than their male counterparts for a number of reasons, biological and sociological. The rate of transmission of HIV from male to female is two to three higher than that from female to male.[4,5] But women are essentially at more risk because of the conditions

Table 1: Benefits of VCT

Where a woman is found to be infected, this knowledge can facilitate early counseling and treatment.
A diagnosis in the mother allows appropriate treatment and follow-up of her child.
Knowledge of her HIV status enables the woman to take decisions on continuation of the pregnancy and on future fertility.
Testing allows an opportunity to implement strategies to attempt to prevent transmission to the child.
Knowledge of HIV status enables the woman to take precautions to help prevent transmission to sexual partners.
Women diagnosed as HIV positive can tell their sexual partners and enable partners to be counseled and tested.
If the test result is negative, women can be guided in appropriate HIV prevention measures and risk reduction behavior.

in cultures and communities that remove their control over their own bodies.

EFFECT OF PREGNANCY ON THE NATURAL HISTORY OF HIV INFECTION

In pregnancy, immune function is suppressed in both HIV-infected and uninfected women but studies in the United States and Europe have shown no effect of pregnancy on the progression of HIV disease.[6-8] Reports from developing countries suggest that progression accelerates with pregnancy, but it is difficult to interpret such reports because the samples are small and the studies are subject to selection bias related to the presence of indications for testing.[9,10]

EFFECT OF HIV INFECTION ON PREGNANCY

Studies in developing countries have shown greater frequencies of preterm birth, low birth weight, intrauterine growth restriction, and stillbirth among the infants of HIV-infected women than among those of similar groups of women who were HIV-negative.[11,12] Higher rates of adverse outcomes were seen among women with more advanced HIV infection.[11,12] Increased mortality, primarily related to HIV infection in the infant, has been reported among infants born to HIV-infected women in developing countries.[11] No studies have indicated that there is an increase in the frequency of birth defects related to HIV infection, and the theory that there is a syndrome of malformation related to HIV infection has been disproved.[11-13] The rates of factors related to preterm birth and low birth weight are similar among HIV-infected and HIV-negative pregnant women; these factors include previous adverse outcomes, hypertension, multiple gestation, smoking, bleeding during pregnancy and *Trichomonas vaginalis* infection.[15,16] In the absence of antiretroviral therapy, a low percentage of CD4+ cells was an additional risk factor for adverse outcomes;[15] but with zidovudine therapy, maternal HIV RNA levels and CD4+ cell counts were not directly correlated with adverse outcomes.[16] Studies conducted in industrialized countries before antiretroviral agents became available did not show an increase in the frequency of prematurity, low birth weight, or intrauterine growth restriction associated with HIV infection.[11,13]

Table 2: Issues in counseling HIV-positive pregnant women

The effect of pregnancy on HIV infection
The effect of HIV infection on pregnancy outcome: risks of adverse pregnancy events
The risk of transmission to the fetus during pregnancy, delivery and breastfeeding
Termination of pregnancy options
Treatment options during pregnancy
Interventions available to attempt to prevent mother-to-child transmission
Infant feeding options: the advantages and disadvantages of breastfeeding
Disclosure of results to male partners and/or to other significant family or community members: advantages and risks
The need for follow-up of both mother and child
Future fertility and contraceptive options

VOLUNTARY HIV COUNSELING AND TESTING OF PREGNANT WOMEN [TABLES 1, 2]

Voluntary counseling and testing (VCT) for HIV infection among pregnant women is a public health priority given the ability of potent antiretroviral therapy to prevent HIV infection in infants and preserve the mother's health during pregnancy.[17-20] New recommendations represent a philosophical departure from previous policy, as formal, informed consent and pre- and post-test counseling sessions would no longer be required.[6] Recently, investigators have demonstrated that the implementation of an opt-out, prenatal HIV-testing strategy resulted in a dramatic increase in the number of women being tested for HIV[21,22] under the CDC interpretation of opt out, pretest counseling would be replaced by written information on HIV transmission to newborns and its prevention. Pregnant women would be notified that they will be tested for HIV as part of the routine battery of prenatal blood tests and that the HIV test may be refused.[21] There are, however, a number of potential benefits to women of voluntary HIV testing prior to or during pregnancy. This is the case even in the absence of expensive interventions such as long-course antiretroviral therapy. Balanced against these advantages are the possible disadvantages of HIV testing in pregnancy. These will vary from community to community, but reports have described an increase in the risk of violence against women; the possibility that the woman may be stigmatised within her community and by health workers; higher levels of anxiety and psychological sequelae; and concerns about the additional workload for maternity services.[23-26]

MOTHER-TO-CHILD TRANSMISSION [TABLE 3]

Estimates of the rate of MTCT (Mother to Child Transmission) of HIV in cohorts of women who have not received any preventive treatment (such as antiretrovirals) range from 15-25% in industrialized countries to 25-45% in developing countries.[27]

HIV can be transmitted from mother to infant in three ways 1. In utero-infection - Direct infection may occur in utero, via transplacental passage. 2 Intrapartum Infection - During the time of delivery, by breaks in the skin and subsequent direct exposure to infected blood or secretions, or by ingestion of maternal blood or other fluids. Recent data indicate that as much as 62% to 85% of perinatal transmission may occur in the intrapartum or

Table 3 : Risk factors associated with increased overall risk of mother-to-child transmission

Strong Evidence	Limited Evidence
Maternal	• Vitamin A deficiency
• High viral load	• Anaemia
• Viral characteristics	• Sexually transmitted diseases
• Advanced disease	• Chorioamnionitis
• Immune deficiency	• Frequent unprotected sexual intercourse^
• HIV infection acquired during pregnancy or breastfeeding period	• Multiple sex partners
	• Smoking
	• Injecting drug use
Obstetric	
Vaginal delivery (compared with cesarean section)	Invasive procedures
Prolonged rupture of membranes	Episiotomy
Infant	
Prematurity	Lesions of skin and/or mucus membranes
Breastfeeding	

^ — Probably due to acquisition of further virus or minor trauma
[Source-UNICEF-UNAIDS-WHO HIV and infant feeding, 1998].

neonatal period. 3. Breast feeding- HIV is known to be present in breast milk from HIV-infected mother, and transmission of HIV-1 via breast feeding has been demonstrated in a number of studies.[29-31]

Risk factors for perinatal transmission:

Maternal factors

Maternal HIV viral load

Multiple studies have confirmed the importance of maternal viral load in predicting the risk of HIV transmission to the infant.[32-34] More than half of the women with viral loads of >50,000 RNA copies per ml. at the time of delivery have been shown to transmit the virus.[32,35] Maternal viral load is an important determinant of perinatal transmission, but transmission may occur even with undetectable levels of HIV-RNA.[36-38]

Other maternal risk factors

Aside from more advanced HIV disease, additional maternal factors have been associated with an increased chance of perinatal transmission like higher concordance rates in class 1 HLA type between mother and child,[39] decreased CD 4 + cell counts,[40] lower serum vitamin A levels in HIV-1 positive mothers,[41] maternal cigarette smoking with low CD 4 + cell count,[42] unprotected sexual intercourse, the presence of sexually transmitted diseases, use of illicit drug use during pregnancy and chorioamnionitis.

Placental factors

Placental infection and non-placental conditions such as abruptio placentae have been also implicated. An association between increased transmission and presence of chorioamnionitis is well known.[43] Placental *P. falciparum* infestation has been associated with poorer survival in infants born to HIV-1 positive mothers, which may represent increased transmission rates[44] and with higher rates of transmission from mother to child in Kenya.[45]

Obstetrical factors

With the majority of mother-to-child transmission occurring at the time of labour and delivery, obstetric factors are important determinants of transmission. Suggested mechanisms of intrapartum transmission of HIV-1 include direct skin and mucus membrane contact between the infant and maternal cervico-vaginal secretions during labour, ingestion of virus from these secretions, and ascending infection to amniotic fluid.

Premature rupture of membranes

It has been shown to be a significant factor in predicting perinatal transmission independent of maternal CD_4 + cell count and also mode of delivery.[46,47] The impact of membrane rupture over 4 hours is also evident among women who have been treated with antiretroviral agents during pregnancy.[47,48]

Role of elective cesarean section

During 1999, results from a meta-analysis of 15 prospective cohort studies[49] and a randomized clinical trial[50] became available to show that cesarean delivery performed before labour and membrane rupture reduces perinatal HIV-1 transmission by 50-87% in women receiving either no antiretroviral therapy or zidovudine prophylaxis. In a study of French Cohort patients benefit of this procedure was only found if it was performed in conjunction with antiretroviral treatment of mother.[51] Although current data do demonstrate significant advantage of elective cesarean section delivery in HIV-infected mother, there are few important considerations. At present no conclusions can be drawn about what additional benefit, if any, an elective cesarean section would have in preventing perinatal transmission from mothers with undetectable plasma levels of virus. Recent data on the rate of infectious complications after surgical deliveries in HIV-infected women are conflicting. Cesarean section does not prevent against in utero infection, although intrauterine acquisition of infection is rare.[52] At best in the present context, on an individual basis, elective cesarean section should now be seen as part of a package to be put as an option to HIV-1 positive pregnant women where related circumstances are favorable. In situations of social and economic deprivation, it cannot be recommended as such. Its role resides in more developed countries only. In terms of vaginally delivered infants, rates of transmission are increased in deliveries in which episiotomy, scalp electrodes, forceps, or vacuum extractors are used, but only in those centres where procedures are not routinely performed.[53]

Fetal factors

A low birth weight of less than 2500 gm[32,54] and /or gestational age less than 34 weeks[54] or less than 38 weeks[32,54] and the birth order of twins[35] have been associated with increased risk of perinatal transmission. A significantly increased risk of HIV-1 infection is also apparent among first-born as opposed to second-born twins, independent of mode of delivery.

ANTIRETROVIRAL THERAPY

Antiretroviral therapy is recommended during pregnancy to reduce the risk of perinatal transmission of human immunodeficiency virus type 1 (HIV-1) infection and to improve maternal health. The most important recent studies in this regard which showed remarkable reduction in perinatal transmission are :Pediatric AIDS Clinical Trials Group (PACTG) Protocol 076 study,[17] a

Table 4 : Recent Antiretroviral Interventions

Trial	Regimen	Transmission
ACTG 076[17]	Antenatal: ZDV 100 mg 5 times/day	ZDV 8%
	Peripartum: ZDV 2 mg/kg stat,1 mg/kg/hr iv	Placebo 26% (68%)*
	Infant: ZDV 2 mg/kg/ hrly x 6 wk	
	No breast feeding	
Thai Trial[55]	Antenatal: ZDV 300 mg bid at 36 weeks	ZDV 9%
	Peripartum: ZDV 300 3 hrly	Placebo 19% (51%)*
	Infant: None	
	No breast feeding	
Ivory Coast[58]	Antenatal: ZDV 300 mg bid at 36 weeks	ZDV 16%
	Peripartum: ZDV 300 3 hrly	Placebo 25% (37%)*
	Infant: None	
	Breast feeding allowed	
Petra[60]	G-1 Antenatal: ZDV/3TC at 36 weeks	G-1 9% (42)*
	Postpartum and Infant ZDV/3TC x 1 week	G-2 11% (37)*
	G-2 Labour: ZDV/3TC	G-3 18%
	Postpartum and Infant ZDV/3TC X 1 week	G-4 17%
	G-3 Labour: ZDV/3TC	
	G-3 Placebo	
HIVNET 12[61]	G-1 Labour: NVP 200 mg at onset	G-1 13% (47%)*
	Infant: breastfed, NVP 2mg single dose	G-2 25%
	G-2 Labour 600 mg at onset, 300 mg 3 hrly till delivery	
	Infant: breastfed, 4 mg bid x 1 week	

*Efficacy of each trial

ZDV= zidovudine, NVP=nevirapine, G = group

short-course zidovudine study in Thailand (Thai Short),[55] the Perinatal HIV Prevention Trial in Thailand (Thai 4-Group),[56] PACTG 316,[57] a short-course zidovudine trial in the Ivory Coast and Burkina Faso,[58,59] the Perinatal Transmission (PETRA) trial,[60] the HIV Network for Prevention Trials (HIVNET) 012 Trial,[61] and the South African Intrapartum Nevirapine Trial (SAINT).[62] Details of these studies are given in Table-4.

Safety Issues of ART (Table 5)

In 1998, a retrospective Swiss study of 30 women with HIV-1 who had received combination antiretroviral therapy during pregnancy (with protease inhibitors in 13 women and without protease inhibitors in 17) showed that such treatment was associated with a 33 percent risk of premature delivery.[63] As compared with no antiretroviral therapy or monotherapy, combination therapy for HIV-1 infection in pregnant women is not associated with increased rates of premature delivery or with low birth weight, low Apgar scores, or stillbirth in their infants in a recent study.[64]

Nucleoside & Nucleotide Analogue Reverse Transcriptase Inhibitors

The nucleoside reverse-transcriptase inhibitors are generally well tolerated and cross the placenta. These agents have not been shown to be teratogenic in animals in concentrations similar to those used in humans. There are currently seven approved nucleoside analogue reverse transcriptase inhibitors. Data are available from clinical trials in human pregnancy for zidovudine, lamivudine, didanosine, and stavudine. Abacavir, emtricitabine, and zalcitabine have not been studied in pregnant women. Tenofovir disoproxil fumarate is the first nucleotide analogue reverse transcriptase inhibitor. Data on use of nonnucleoside reverse-transcriptase inhibitors during pregnancy are limited, but nevirapine and efavirenz readily cross the placenta in primates.[65] Use of efavirenz in the early stages of pregnancy is not recommended because birth defects (anencephaly, anophthalmia, or cleft palate) have been reported.

Clinical disorders linked to mitochondrial toxicity include neuropathy, myopathy, cardiomyopathy, pancreatitis, hepatic steatosis, and lactic acidosis. Among these disorders, symptomatic lactic acidosis and hepatic steatosis may have a female preponderance. These syndromes have similarities to the rare but life-threatening syndromes of acute fatty liver of pregnancy and hemolysis, elevated liver enzymes and low platelets (the HELLP syndrome) that occur during non-nucleoside reverse transcriptase inhibitors.

Protease Inhibitors

Protease inhibitors are increasingly being used during pregnancy. There appears to be minimal transplacental passage in humans.[66] No specific teratogenic effects have been noted in animals. Optimal dosing of protease inhibitors during pregnancy remains under study. Lower serum concentrations of protease inhibitors have been observed in pregnant patients than in nonpregnant

Table 5: FDA classification of antiretroviral drugs for use in pregnancy [Modified]

Drug	FDA Category
Nucleoside Reverse Transcriptase	C
Zidovudine (ZDV, AZT)	C
Zalcitabine (ddC)	B
Didanosine (ddI)	C
Stavudine (d4T)	C
Lamivudine (3TC)	C
Abacavir	B
Emtricitabine	B
Tenofovir	B
Non-nucleoside Reverse Transcriptase Inhibitor	
Nevirapine	C
Delavirdine	C
Efavirenz	C
Protease Inhibitors	
Indinavir	C
Ritonavir	B
Saquinavir	B
Nelfinavir	B
Amprenavir	C
Atazanavir	B
Fosamprenavir	C
Fusion Inhibitors	
Enfuvirtide	B

A: Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk during later trimesters)

B: Animal reproduction studies fail to demonstrate a risk to the fetus but well controlled studies of pregnant women have not been conducted

C: Safety in human pregnancy has not been determined, animal studies are either positive for fetal risk or have not been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the fetus

D: Positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks

X: Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit

patients, although in most cases, the HIV RNA levels in pregnant women have been suppressed. The toxic effects among pregnant women appear to be similar to those among nonpregnant women. There are insufficient data to support the recommendation of a specific protease inhibitor during pregnancy, although nelfinavir has been used most commonly.

Indications for Antiretroviral Therapy during Pregnancy

Although therapy is recommended for nonpregnant persons with a CD4+ lymphocyte count below 350 per cubic millimeter or an HIV RNA level above 55,000 copies per millimeter,[51] antiretroviral therapy should be offered to all HIV -infected pregnant women in order to reduce the risk of perinatal transmission.[67] Women with a new diagnosis of HIV infection during pregnancy should be fully evaluated to determine the stage of the HIV infection and to identify any coexisting conditions. If therapy is indicated for maternal health (CD4+ lymphocyte count <350 cells per cubic millimeter; or HIV RNA level >55,000 copies per milliliter), the clinician and the patient should discuss these indications, potential regimens, and the need for strict adherence in order to prevent the development of resistance. Even without maternal indications for therapy, initiation of highly active antiretroviral therapy should be considered for the prevention of HIV transmission when the HIV RNA level is above 1000 copies per milliliter.[67] If the pregnancy is discovered after the first trimester, therapy should be continued. A detailed ultrasonographic examination should be performed at 18 to 20 weeks of gestation to confirm the gestational age of the fetus and to screen for detectable anomalies. Options during the first trimester include continuing the regimen; changing the regimen if it includes specific drugs that carry an increased risk, such as efavirenz or delavirdine; or discontinuing all antiretroviral drugs and reinstituting them after the first trimester. This last strategy has the potential to cause viral rebound and might increase the risk of transmission. Decisions should depend on the clinical circumstances and the treatment history. Hydroxyurea should be discontinued during pregnancy, since it is teratogenic in animals and its value in the treatment of HIV is unclear. If antiretroviral therapy must be interrupted during the first trimester, all agents should be discontinued and reinstated simultaneously in order to prevent the development of resistance.[64]

PREVENTION AND TREATMENT OF OPPORTUNISTIC INFECTIONS DURING PREGNANCY

Recommendations for prophylaxis against and treatment of opportunistic infections in nonpregnant adults should be followed with slight modification during pregnancy.[68] Prophylaxis against and treatment of *Mycobacterium tuberculosis, Pneumocystis carinii, M. avium* complex, and *Toxoplasma gondii* infections during pregnancy are similar to prophylaxis and treatment in nonpregnant adults. Primary prophylaxis against cytomegalovirus infection, mucosal candida infections, and invasive fungal infections is not recommended routinely for nonpregnant persons because of drug toxicity. Treatment of serious infections should not be withheld because of pregnancy; regimens should be chosen in consultation between the obstetrician and a specialist in infectious diseases. Hepatitis B, influenza, and pneumococcal vaccines may be given during pregnancy for the usual indications but should be administered after HIV RNA has been suppressed to undetectable levels with antiretroviral therapy, in order to prevent the increase in the risk of transmission that theoretically accompanies the transient increase in HIV RNA after immunization.[64]

OTHER ASPECTS OF CARE FOR HIV-INFECTED PREGNANT WOMEN

Antepartum Care

Most HIV positive women will be asymptomatic and have no major obstetrical problems during their pregnancies They should receive similar obstetric antenatal care to that given to HIV-negative women, unless indicated by the need to provide specific HIV-related treatment.[69,70] The schedule of testing for toxic effects of antiretroviral drugs depends on which drugs are chosen. In general, frequent evaluation (every two to four weeks) for new symptoms and laboratory abnormalities is indicated during the first one to two months of therapy, with less frequent testing thereafter. HIV RNA levels should be monitored as in nonpregnant adults — that is, 4 weeks after a change or initiation of therapy, then monthly until undetectable, then every 3 months while therapy remains stable, and at 34 to 36 weeks of gestation for the planning of delivery. If an invasive prenatal procedure is planned for an HIV -infected woman, she should be receiving optimal antiretroviral therapy and have undetectable HIV RNA before the procedure.[71-73]

Intrapartum Care

The potential mode of delivery should be discussed throughout the pregnancy, and the final decision should be based on the HIV RNA level at 34 to 36 weeks of gestation. Infusion of zidovudine should be begun as soon as possible after the onset of labor or the rupture of the membranes (or at least three hours before a scheduled cesarean delivery), at a dose of 2 mg per kilogram of body weight given over the course of one hour, followed by a continuous infusion of 1 mg per kilogram per hour until delivery.[17] The use of other antiretroviral medications should be continued on schedule during labor or preoperatively. Stavudine may antagonize the effects of zidovudine and should therefore be given orally without zidovudine or discontinued before intravenous zidovudine is administered. Artificially induced rupture of the membranes should be avoided, and the interval between rupture and delivery should be minimized by augmenting labor as needed after spontaneous rupture has occurred. Fetal-scalp electrodes, scalp blood sampling, the use of instruments to assist delivery, and other procedures that might be traumatic to the infant should be avoided. Avoidance of episiotomy may decrease the exposure of the infant to maternal blood. Midazolam and ergot preparations should not be used in women receiving protease inhibitors, efavirenz, or delavirdine, because their metabolism may be delayed by such antiretroviral drugs.[69] The infant should be washed before any blood is drawn or any injections or other invasive procedures are performed.

Mode of delivery

Care during labour for HIV positive women should follow routine practice in most respects. As a general rule, any procedure which breaks the baby's skin or increases the baby's contact with the mother's blood - such as scalp electrodes or scalp blood sampling - should be avoided unless absolutely necessary. As for the role of elective C-sections, a stratified analysis of PACTG 367 data and a chart-abstraction study of pregnancy outcomes demonstrated that combination antiretroviral therapy decreased transmission rates significantly, regardless of viral load strata. The study analysis showed that there was no benefit of elective C-section in reducing HIV transmission if patients received multiagent antiretroviral therapy or had a plasma HIV RNA level at delivery of < 1000 copies/mL.[73]

Postpartum Care

Among women in whom antiretroviral therapy is continued after delivery, measures to enhance adherence to the regimen may be needed because of the demands of newborn care, the loss of the incentive of preventing transmission, and postpartum depression. Options for contraceptive methods should be discussed during pregnancy and the need for condom use should be emphasized. If a woman elects to use additional methods, interactions with other therapies must be considered. Estradiol levels from oral contraceptives are reduced by nevirapine, ritonavir, nelfinavir, rifampin, rifabutin, and possibly amprenavir, which may reduce the contraceptive efficacy.[69] Interactions between medroxyprogesterone acetate and antiretroviral drugs are under study, but this agent is a reasonable choice. Intrauterine contraceptive devices may be offered to HIV -infected women who have a low risk of sexually transmitted infections and do not have severe immune suppression.[74]

STRATEGIES IN DEVELOPING WORLD

In more developed countries, integration of prenatal HIV-counselling and testing programmes into an existing antenatal infrastructure, availability of effective antiretroviral prophylaxis and access to infant formula have resulted in new perinatal infections becoming rare. In resource-poor setting antenatal care is limited, testing programmes are almost non-existent, effective interventions remain unimplemented, and prevention of postnatal transmission through adequate infant nutrition is a major dilemma. First and foremost task is proper antenatal care. Time has come in India to recognize the importance of counselling and voluntary screening for HIV among pregnant women. Use of rapid test for diagnosis is a potential solution that may greatly influence the epidemic in developing countries. In a practical sense to consider use of combination ART or HAART would be impossible. Short course ZDV regimens may have significant repercussions in terms of practical feasibility of perinatal therapy. Above all, the recent demonstration of the significant efficacy of NVP in decreasing perinatal transmission in Uganda is expected to have far-reaching consequences.

Universal nevirapine (NVP) therapy (provision of the drug without HIV testing) has been suggested as potentially superior to *targeted* NVP therapy (provision of the drug to seropositive patients identified through voluntary HIV counseling and testing [VCT]) for perinatal HIV prevention in low-resource, high-prevalence settings. Status of Nevirapine from Hero to Villain is also being coined. Undoubtedly, the findings that nevirapine reduced mother-to-child transmission (MTCT) of HIV by 50% in resource-limited settings at the cost of 2 pills per patient was potentially one of the most hopeful discoveries of HIV research within the last decade. Subsequent implementation of nevirapine delivery programs in the developing world have helped avoid thousands of new infections, nevertheless the issue is far from being settled. Although viral resistance and toxicity profiles

are concerning issues, the legacy of nevirapine for reduction of MTCT cannot be disregarded. Several developing countries have reported the success of the nevirapine single-dose strategy and continue to work on the implementation of this practice which, although imperfect, is still life-saving in the absence of additional resources or lack of feasibility for more all-encompassing MTCT prevention measures.[75-78] As if the issue of nevirapine resistance were not enough to give the drug a controversial reputation, some recent studies have questioned the safety of nevirapine when used as part of HAART regimens during pregnancy.[79,80]

Appropriate nutritional status and avoidance of additional infections and other non-antiretroviral interventions should be in the priority list. It is extremely difficult to consider use of cesarean section as a method of decreasing the risk of perinatal HIV-1 transmission in developing countries. Needless to say, we need creative interventions for better management of HIV-infection during pregnancy.

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