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Literature Review

MANAGEMENT OF HIV/AIDS INFECTION IN PREGNANCY

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ABSTRACT

Twenty years since identified for the first time, the disease of HIV/AIDS spread and cause greater damage than the previous prediction. According to the Director General of P2M and Environmental Sanitation Department of Health by the end of 1999, there were 1066 people in Indonesia who are infected with HIV even though this must be realized that the rate is still far lower than the actual numbers, because there are many cases of HIV infection reported in addition to energy awareness health of the possibility of HIV infection has not been evenly distributed. Management of HIV infection/AIDS in pregnancy is done in time of antepartum, intrapartum and post partum, for mother and the baby, in general and specific. The important matters include the use of ART, nutrition and psychological support. Prevention and management of opportunistic infections to PWHA are not different with that of non pregnant woman. However, it is not routinely advised because of drug toxicity.

Key words: *HIV, AIDS, pregnancy, anti retroviral, PLWHAt*

ABSTRAK

Dua puluh tahun sejak pertama kali diidentifikasi, penyakit HIV dan AIDS menyebar dan menyebabkan kerusakan yang lebih besar dari prediksi sebelumnya. Menurut Direktur Jenderal Pemberantasan Penyakit Menular (P2M) dan Sanitasi Lingkungan Departemen Kesehatan pada akhir tahun 1999, terdapat 1066 orang di seluruh Indonesia yang terinfeksi HIV meski harus disaadari bahwa angka ini masih jauh lebih rendah daripada jumlah sesungguhnya, karena ada banyak kasus infeksi HIV yang dilaporkan disamping kesadaran tenaga kesehatan dari kemungkinan infeksi HIV yang belum merata. Manajemen infeksi HIV dan AIDS pada kehamilan dilakukan pada saat antepartum, intrapartum dan post partum, untuk ibu dan bayi, secara umum dan khusus. Hal yang penting adalah penggunaan terapi anti retroviral, dukungan gizi dan psikologi. Pencegahan dan pengendalian infeksi oportunistik dari ODHA untuk tidak berbeda dengan yang non wanita hamil. Akan tetapi, hal ini tidak dianjurkan secara rutin karena narkoba.

Kata kunci: *HIV, AIDS, kehamilan, anti retroviral, OHDHA*

INTRODUCTION

Twenty years since identified for the first time, the disease of HIV/AIDS spread and cause greater damage than the previous prediction. This disease can affect men, women and children around the world. In 1999 it was noted that HIV/AIDS is the fourth leading cause of death in the world, while in Africa is a cause of death terbanyak. Dalam 2000, about 3 million people, including 500,000 children died of AIDS, and 5.3 million people, including 600,000 children received new HIV infections, most due to mother-to- child transmission.[1]

The disease caused a crisis on various sectors including health. The majority of patients, ie 95 % are in developing countries, so far-reaching impact in the increase and population growth is even said to the population of a Contracting State may decline not because of the family planning program but rather due to AIDS deaths[1]

According to the Director General of Infectious Disease Eradication and Environmental Sanitation Department of Health by the end of 1999, there were 1066 people in Indonesia who are infected with HIV even though this must be realized that the rate is still far lower than the actual numbers, because there are many cases of HIV

infection reported in addition to energy awareness health of the possibility of HIV infection has not been evenly distributed.[2]

Although various attempts have been made to control the increasing number of incidence and mortality due to HIV/AIDS but the transmission still continues until now. HIV transmission occurs through three main lines, namely: horizontal transmission is contact with blood (transfusions contaminated, use needles interchangeably in drug addicts, injury, etc.), vertical transmission (from mother to fetus during pregnancy, childbirth and breastfeeding), sexual transmission (homosexual or heterosexual) [3]

Management of infectious diseases of HIV/AIDS in pregnancy need to consider two important things, namely the impact of HIV/AIDS infection in pregnancy and the impact of pregnancy on the progression of infection than HIV/AIDS. Various important things that need to be considered in the management of HIV/AIDS infection in pregnancy, namely the provision of anti- retroviral therapy, nutrition, psychological support.

Here are discussed the management of HIV/AIDS infection in pregnancy with the hope to increase knowledge of the health workers, reducing the incidence of HIV infection, reduced mortality due to AIDS, and reduces transmission of HIV infection.

PREGNANCY AND HIV INFECTION

Effect of pregnancy on HIV Disease Journey

In normal pregnancy there is a decrease in the number of CD4 + fetus early in pregnancy to maintain. In women who do not have HIV +, CD4 + percentage will rise again started the third trimester to 12 months after birth; whereas in HIV decline persist during pregnancy and after childbirth.[4]

Pregnancy is only slightly increase levels of virus (viral load) HIV. Kehamilan also does not accelerate disease progression to AIDS. (DN Burns, 1998; Crombleholme WR MD, 2002).[4,5]

Effect of HIV Infection in Pregnancy

Research in developed countries before the era of antiretroviral showed that HIV does not cause an increase in prematurity, low birth weight, or intrauterine growth retardation. While in developing countries, HIV infection increases the incidence of abortion, prematurity, intrauterine growth retardation, especially at an advanced stage. This is because the mother ‘s physical condition is worse and the possibility of a higher perinatal transmission.[1]

Vertical Transmission of HIV

Without intervention, the risk of HIV transmission from mother to fetus are reported to range between 15–40%. [6,7] The risk of vertical transmission varies in different countries, depending on anti- retrovirals that can be given. The risk of transmission is higher in developing countries than in developed countries. Transmission can occur during pregnancy, intrapartum and post partum. Most of the intrapartum transmission occurs.[8]

Transmission mechanism in pregnancy is unclear, presumably through the placenta. Pathological examination finding in the placenta in HIV-infected women HIV. Sel lymphocytes or monocytes infected mother or HIV virus itself can be reached directly through the fetal syncytiotrophoblast layer, or indirectly through the trophoblast cells and infect placental macrophages (Hofbauer cells) that have CD4 + receptor. According to the Pediatric Virology Committee of the AIDS Clinical Trials Gruoup (PACTG), said in utero transmission/infection if the initial positive virological test within 48 hours after birth and the next test is also positive.[9]

In the intrapartum transmission, infection was diagnosed if a negative virological examination in the first 48 hours after birth, and the first test next week to be positive and the baby is not breastfeeding.[9] As long delivery, the baby may be infected blood or servikovaginal fluid containing HIV through exposure to tracheobronchial or ingested in the birth canal.[9]

Infections associated with post partum lactation. Virus particles can be found in the cell components and nonmilk cells ibu.Konsentrasi highest virus in colustrum. Kadar highest HIV in breast milk occurred from the first week to three months after delivery. HIV in low concentrations can still be detected in breast milk to 9 months after delivery.[6,9]

MANAGEMENT OF HIV/AIDS INFECTION IN PREGNANCY

Management of HIV/AIDS infection in pregnancy during antepartum, intra -partum and post partum for mother and baby, both generally and specifically.[10]

A. General Treatment:
   - Take a rest
   - Adequate Nutrition Support
   - Psychosocial Therapy

B. Special Treatment
   - Provision of antiretroviral therapy (ART) combination, by Highly Anti Retroviral Therapy (HAART)
   - Management of obstetric
   - Treatment of Opportunistic Infections
   - Treatment of malignant

Provision of Antiretrovirus (ART)

ART is recommended for all people with HIV who are pregnant to reduce the risk of perinatal transmission. The purpose of the provision of antiretroviral therapy in pregnancy is to maximize maternal health and reduce the risk of HIV transmission as low as possible. The advantage must be weighed against the potential toxicity, teratogenesis, and long -term side effects. Side effects are expected to increase in the provision of a combination ART.

Namun, recent research by Toumala, et al showed that, compared with monotherapy, combination antiretroviral therapy does not increase the risk of prematurity, low birth weight, or intrauterine fetal death.[11]

Currently in Indonesia, some of HAART has been available in generic form at a lower price, such as zidovudine, lamivudine, nevirapine and stavudin. Antiretroviral drugs are first examined to reduce perinatal transmission is zidovudine (ZDV). In PACTG protocol 076, ZDV given orally start week 14 of pregnancy, followed by the time iv ZDV intrapartum to the mother, followed by ZDV syrup given to infants from the age of 6-12 hours to 6 weeks. In this study, infants are not breastfed. This method was effective at lowering the perinatal transmission of 25.5 % in the control group to 8.3 %.[12]

The longer the use of antiretroviral therapy, the more likely a reduced risk of transmission HIV. Joao, et al revealed in infants who are not infected with HIV, the average duration of use of ART in mothers compared with 16.63 weeks old maternal ART use 6.28 weeks in the group of infants infected with HIV.[13]

Explanation

Category B: There is no risk to the fetus in animal studies, but there has been no studies in pregnant women; or animal studies showed side effects according to controlled studies in pregnant women first trimester (and no proven risk in subsequent trimesters).

Category C: In animal studies found adverse effects on the fetus (teratogenic or embriosidal, or other), and there has been no controlled studies in pregnant women, there has been no research or drug side effects in animals or pregnant women. Drugs in this category is given only if the benefits exceed the potential risk to the fetus.

Category D: There is positive evidence of fetal risk of side effects in humans, but the gain in pregnant women may be acceptable than the risks, especially for life-saving.

Perinatal HIV Guidelines Working Group in the United States put forward the recommendations of antiretroviral with some scenarios.[14] (Table 2)

Tabel 1. Categories Food and Drug Administration (FDA) antiretroviral for use in pregnancy (Watts DH, 2002)[10]

Division	Drug	Categories FDA
Nucleoside Reverse Transcritase Inhibitor (NRTI)	Zidovudin/ZDV/ AZT	C
	Zalsitabin/ddC	C
	Didanosin/ddI	B
	Stavudin/d4T	C
	Lamivudin/3TC	C
	Abacavir/ABC	C
	Tenofovir DF	B
Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)	Nevirapin	C
	Delavirdin	C
	Efavirenz	C
Protease Inhibitor (PI)	Indinavir	C
	Ritonavir	B
	Saquinavir	B
	Nelvinavir	B
	Amprenavir	C
	Lopinavir	C
Others	Hidroksiurea	D

Nutritional Support in HIV/AIDS

Nutritional management is important to prevent and cope with HIV infection. Provision of antiretroviral therapy is still needed, but without adequate nutrition therapy intervention difficult to stem the negative effects of reactive oxygen species (ROS), which induces cell death as well as disease progression. Management of nutrition in pregnant women with HIV/AIDS, people live with HIV/ AIDS (PLWHA) can increase resistance to opportunistic infections and to improve the tolerance to the side effects of drugs, protection of cell viability, ensure continuity of organ function, improve the function of the immune system to prevent other microorganisms including viruses, bacteria, tumor cells and fungi.

In pregnancies with HIV/AIDS infection is often accompanied by a deficiency of antioxidant vitamins and minerals, increased levels of ROS which promotes apoptosis in immune cells and increased morbidity. ROS can trigger the onset of the crisis scavenger enzyme-deficit micronutrient components such as Fe, Zn, selenium, vitamin C, vitamin B6, vitamin E, or an imbalance of some nutrients, such as essential amino acids can cause damage to components of the immune system. Decreased antioxidant PLWHA very dangerous, because the more encouraging apoptosis in various cells and promotes the progression of HIV infection to AIDS.[15,16]

One complication that almost always accompanies HIV/AIDS patients is weight loss. When weight loss exceeds 10 % with chronic diarrhea over 1 month, and general weakness with fever or prolonged over 1 month called HIV/AIDS wasting syndrome.[16] The cause of wasting in PLWHA is a decrease in the intake, malabsorption and increased metabolism. Potential for more severe wasting in PLWHA. This is due to the higher nutritional needs with respect to pregnancy and emerging opportunistic infections, nutritional intake while on the other hand decreases with time and complexity of infections.

Immunocompromised immune system which can be inhibited by preventing through medical nutrition therapy (MNT).With MNT expected to reduce morbidity, improve quality of life, lower costs, shorten the hospital stay,

Tabel 2. Recomendation of antriretroviral (ART) to reduce perinatal transmission (Perinatal HIV Guidelines Working Group, 2002)[13]

Pregnancy Condition	Recomendation
HIV-positive pregnancy who had never used antiretroviral earlier	Pregnant HIV-positive who undergoing clinical examination, standard immunological and virology. Consideration of ART initiation and selection are the same as non-pregnant HIV-positive people with consideration of the effect of the three-part ZDV pregnancy. Regimen recommended after the first trimester regardless of the levels of HIV of mother. Regimen combination is recommended in HIV clinical status, immunological and its virology heavy or HIV levels > 1000 copies /mL. If people with HIV come in the first trimester of pregnancy, provision of ART can be delayed until 10-12 weeks gestation.
HIV-positive pregnancy who are getting pregnant and pregnant ART	If the pregnancy is known after the first trimester, prior antiretroviral therapy forwarded, preferably by including ZDV. If in the first trimester of pregnancy is known, people with HIV are given counseling about the benefits and risks of antiretroviral therapy in first HIV-positive. If trimester pick off treatment during the first trimester, all drugs should be stopped and then given simultaneously after the first trimester to prevent drug resistance. Without considering the previous regimen, ZDV is recommended to be administered during the intrapartum and infants.
HIV-positive pregnancy in childbirth and had never get ART before	There are several regimens are recommended : • single dose nevirapine during labor and a single dose to the infant at age 48 hours • oral ZDV and 3TC during labor, followed by ZDV / 3TC in infants during the week • intrapartum ZDV, ZDV in infants followed for 6 weeks • two-dose of nevirapine combined with ZDV during labor followed iv ZDV in infants for 6 weeks Immediately after delivery, such as people with HIV undergoing CD4 + and HIV levels to determine whether the treatment will be continued.
If infants of HIV-positive mothers came after childbirth, while the mother has not received antiretroviral therapy during pregnancy or intrapartum	ZDV syrup is given to infants for 6 weeks, starting as soon as possible within 6-12 hours after birth. Some doctors may choose a combination of ZDV with other antiretroviral drugs, especially if the mother is known to be resistant to ZDV. However, the efficacy of this regimen is not yet known and the dose for children not yet fully known. Immediately after delivery, HIV-positive undergo examination such as CD4 + and HIV levels to determine whether the treatment will continue. Infant undergo early diagnostic tests that antiretroviral therapy can be given as soon as possible if it were HIV positive.

improve the quality of life of patients with HIV/AIDS. Ideal in the handling of involving doctors and nutritionists. MNT can increase the intake of energy, protein and micronutrient that can improve nutritional parameters. To obtain optimal effect of MNT, the nutritional therapy should be programmed so the diagnosis of HIV infection is established.[17] According to The Canadian Dietetic Association and the ADA developed an HIV/AIDS Medical Nutrition Therapy protocol on medical therapy interventions are promptly determine satus PLWHA nutrition, maintain and prevent the loss of body mass and nutritional deficiencies, support and improve the quality of life PLWHA. The protocol was evaluated two times a year in people living with HIV asymptomatic, and six times a year in patients who are symptomatic or AIDS.

Macronutrients

1. Total calories, 35–40 kcal/kg weight/hr enough to fulfill the needs if patients in general
2. Glucose, 30–70% of the total heat supplied in the form of glucose.
3. Fat, 20–30% of the total calories. Omega-6 polyunsaturated fatty acid (PUFA) triglycerides should be given in doses sufficient to prevent fatty acid deficiency.
4. Protein, 15–20% of total calories given as a protein or amino acids.

Micronutrients

Purposes of vitamins, minerals and trace elements need to be taken into account in the preparation of nutrient PLWHA every day. Potassium, magnesium, Fe, Zn, phosphate is maintained in order to stay within normal levels in the blood.

Nutritional status assessment done based on anthropometric, clinical performance, and BMI laboratory parameters should be monitored every week. Every PLWHA need to be briefed about the weakness of the

immune system that allows the transmission of disease through food. Knowledge of the type, form, delivery and quality procedures is important to address these risks.

Counseling in People with Pregnancy

Implemented since antepartum care. HIV-positive people are given information about the effects of pregnancy on HIV infection, the effect of HIV on pregnancy including perinatal transmission, the role of viral load monitoring, the use of drugs in pregnancy, use of zidovudine benefit in pregnancy and possible protection to Sectio Caesaria intrapartum.[10,19]

Factors affecting HIV-positive woman's decision to continue or terminate a pregnancy, including stage of HIV infection, the use of antiretroviral and other drugs, pregnancy planning, the desire to have children, religion and belief, economic status, social support for children.[18]

Obstetric Management

Perinatal HIV Guidelines Working Group in the United States submit obstetric management recommendations to reduce vertical HIV transmission in some conditions.

Prevention and Management of Opportunistic Infections during Pregnancy

Prophylaxis therapy and therapy against infection with Mycobacterium tuberculosis, Pneumocystis carinii, M avium complex, Toxoplasma gondii, and herpes simplex virus in pregnant HIV-positive people are no different from non-pregnant. However, primary prophylaxis against cytomegalovirus, candida and invasive fungal infections is not recommended routinely given drug toxicity. Fluconazole for example, is known to cause skeletal and craniofacial deformities in long -term use during pregnancy.[10]

Tabel 3. Recomendation of childbirth method to reduce HIV transmission from mother to child[14]

Childbirth Method	Recomendation
HIV-positive pregnancy who come in pregnancies over 36 weeks, has not received antiretroviral therapy, and awaiting the results of the HIV and CD4 + levels are thought to exist before childbirth	HIV-positive people should receive antiretroviral therapy regimens PATCG (pediatric AIDS clinical trials group) 076. Performed as like counseling about caesarean section for reducing the risk of transmis and the risk of post operative complications, the risk of anesthesia and surgery was decided others. If SC, SC planned at week 38 pregnancy. Over SC, people living with HIV received ZDV intravenous who started three hours earlier, and infants received ZDV syrup for 6 weeks. Decission will continue therapy after delivery or not depends on the results of virus levels and CD4 +
HIV-positive pregnancy who came in early pregnancy, is being awarded a combination antiretroviral therapy, and HIV levels remained above 1000 copies/ml at week 36 of pregnancy	Anti retroviral therapy (ART) regimens used are continued. People living with HIV should be counseled that HIV levels may not go down to less than 1000 copies/mL before delivery, so it is recommended to the SC. Likewise, the increased risk of complications such as infection SC, anesthesia operation if disconnected SC, SC planned in the 38th week of pregnancy. During the SC, people living with HIV receive intravenous ZDV initiated at least 3 hours in advance. Another therapy be continued before and after childbirth. Infants received ZDV syrup for 6 weeks
HIV-positive pregnancy who are on combination antiretroviral therapy, and HIV RNA levels at week 36 of pregnancy	People living with HIV were counseled that the likelihood of transmission if HIV RNA levels may be less than 2% even in labor pervagina. Selection of mode of delivery should weigh the benefits and risks of complications SC
HIV-positive pregnancy who had planned elective SC, However came at the onset of labor or after rupture of membranes.	Intravenous zidovudine (ZDV) given immediately. If the rapid progress of labor, people with HIV are offered to undergo a vaginal delivery. If cervical dilatation is minimal and supposedly will last long labor, can be chosen between intravenous ZDV and do SC or provide pitosin to speed up delivery. If people with HIV decided to undergo a vaginal delivery, avoid the head electrode, invasive monitors and other tools. Infants should receive ZDV syrup for 6 weeks

Tabel 4. Management of Opportumistic Inffections in Pregnancy in Women with HIV Infection[10]

Causing	Explanation
Mycobacterium avium complex	Azithromycin is the first choice for primary prophylaxis during pregnancy; clarithromycin teratgenik in animals; for maintenance therapy of azithromycin plus ethambutol
Mycobacterium tuberculosis	Isoniazid is preferred for prophylaxis during pregnancy; for TB that are resistant to combination therapy, consult to the experts
Herpes simplex virus	Prophylaxis and therapy as in non- pregnant
Pneumocystis carinii	Prophylaxis and therapy as in non- pregnancy; attention to neonate in women who received therapy Sulfa
Cryptococcus neoformans	Primary prophylaxis is not recommended; abnormalities after long -term exposure; consider switching to amphotericin B in the first trimester for long-term suppression
Coccidioides immitis	Primary prophylaxis is not recommended; anomalies as mentioned above after long-term exposure to fluconazole; consider switching to Amphotericin B in the first trimester when the long-term suppression continues
Histoplasma capsulatum	Primary prophylaxis is not recommended, for causing anomalies due to exposure to Fluconazole and security is not yet clear from chronic Itraconazole during pregnancy, consider switching to Amphotericin B in the first trimester when the long -term suppression continues
Cytomegalovirus	Primary prophylaxis is not recommended; the management of long-term suppression should be consulted with the experts
Candida species	Prophylaxis is not indicated during pregnancy; craniofacial and skeletal abnormalities were reported in four infants after long-term exposure to fluconazole in utero
Toxoplasma gondii	Treatment and secondary prophylaxis (maintenance therapy) as in patients who are not pregnant; only primary prophylaxis with trimethoprim-sulfamethoxazole.

Vaccination against hepatitis B, influenza and pneumococcal remains can be given during pregnancy. The vaccination should be given after the levels dropped to undetectable HIV to prevent HIV-RNA levels after vaccination.[10]

SUMMARY

Management of HIV infection/AIDS in pregnancy is was performed in time of antepartum, intrapartum and post partum, for mother and the baby, in general and specific. The important matters including the use of ART, nutrition and psychological support. Prevention and management of opportunistic infections to people live with HIV/AIDS (PLWHA) are not different with that of non pregnant woman. However, the administration of ART is not routinely advised because of drug toxicity.

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