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Triple Elimination Program for Pregnant Women at A Tertiary Hospital in Surabaya, Indonesia

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Abstract: **Background:** Triple elimination is a World Health Organization's strategy to eliminate transmission of Human Immunodeficiency Virus (HIV), syphilis, and hepatitis B from mother to child. This study aimed to evaluate the management of triple elimination and infants outcome at dr. Soetomo Hospital Surabaya, Indonesia in 2019. **Methods:** This research is a descriptive retrospective study using medical records at dr. Soetomo Hospital in 2019. It has been approved by the Ethics Commitee of dr. Soetomo Hospital. **Results:** There were 1,150 patients in our obstetric outpatient clinic in 2019. Among them, 50 (4.3%) patients were infected by HIV, five (0.4%) were infected by syphilis, 16 (1.4%) were infected by hepatitis B, and two (0.2%) were infected by HIV and hepatitis B. Early detection was carried out for all patients. Forty eight among 73 infected patients were hospitalized until delivery. There were 17.1% HIV patients that had no antiretroviral (ARV) during pregnancy due to lack of ante natal care. All infants received prophylaxis ARVs and none of them, who routinely visited pediatric outpatient clinic, were positive for HIV (72.4%). In syphilis cases, all patients had benzathine penicillin during pregnancy. Unfortunately, one (33%) had congenital syphilis. In hepatitis B cases, all patients didn't tested for hepatitis B virus deoxyribonucleic acid (HBV DNA) which wasn't covered by national insurance. All infants were injected with imunoglobulin of hepatitis B (HBIg) and hepatitis vaccine, but one of the baby was positive at follow up.

Keywords: pregnancy, HIV, syphillis, hepatitis B

INTRODUCTION

More than a million people are infected with sexually transmitted diseases every day [1], including HIV, syphilis and hepatitis B. The prevalence of Human Immunodeficiency Virus (HIV), syphilis, and hepatitis B in Indonesia are 0.33%, 1.6%, and 7.1%, respectively [2].

In 2016, a coordinated strategy to eliminate transmission of HIV, syphilis, and hepatitis B from mother to child was launched by World Health Organization (WHO), called Triple Elimination. The goal is at the year 2027, 90% of pregnant women know their HIV, syphilis, and hepatitis B status.

Dr. Soetomo General Hospital run this triple elimination program as an integrated program from screening to management of mother and child.

II. METHODS

This study was a retrospective descriptive study using medical records at dr. Soetomo General Hospital Surabaya in 2019. We used total sampling. The inclusion criterias were pregnant women with HIV and/ or syphilis, and/ or hepatitis B. The exclusion criteria was incomplete medical records data.

The prevalence of each disease was calculated. Characteristics, risk factors, mode of delivery and contraception were described for each disease. The triple elimination management for patients and their newborns were described and they were followed up at pediatric outpatient clinic for their transmission status.

The study was conducted in accordance with the guidelines determined by the ethics committee of Academic Soetomo General Hospital Surabaya and was approved by the institutional review board (Approval No. 0282/LOE/301.4.2/I/2021).

III. RESULTS

3.1 Data collection

There were 1,150 new patients based in our obstetric outpatient clinic register book, dr. Soetomo General Hospital in 2019. Patients positive for HIV were 50 patients, five syphilis patients, 19 hepatitis B patients and two patients with HIV and hepatitis B (table 1).

Table 1. The prevalence of HIV, syphilis, and hepatitis B patients at the obstetric outpatient clinic, dr. Soetomo General Hospital (Total patient in 2019: 1150)

Patients	Numbers n	Prevalence %	Hospitalized n
HIV	50	4,3	35
Syphilis	5	0,4	3
Hepatitis B	16	1,4	9
HIV and Hepatitis B	2	0,2	1

HIV Human Immunodeficiency Virus

3.2 Characteristic of patients

There were total 73 pregnant women infected by HIV, syphilis, and/ or hepatitis B who had their antenatal care at the clinic. Age ranged from 18 to 41 years old. Not all patients knew their status of HIV, syphilis, or hepatitis B but many of them (49,3%) had been diagnosed before getting pregnant in 2019 and had their medication. Among these 73 patients, only 48 patients were hospitalized in dr Soetomo hospital until delivery (table 2).

Table 2. Characteristic patients with HIV, syphilis, and hepatitis B in outpatient clinic

Characteristics	**HIV n(%)**	**Syphilis n(%)**	**Hepatitis B n (%)**	**HIV and hepatitis B n (%)**
Age				
<20 y.o	1(2)	0(0)	0(0)	0(0)
20-24 y.o	12(24)	0(0)	2(12.5)	0(0)
25-29 y.o	16(32)	1(20)	5(31.25)	1(50)
30-34 y.o	11(22)	2(40)	5(31.25)	1(50)
≥ 35 y.o	10(20)	2(40)	4(25)	0(0)
Parity				
Nulliparous	11(22)	1(20)	5(31.25)	0(0)
Parous	39(78)	4(80)	11(68.75)	2(100)
Time of screening				
Before pregnancy	24(48)	1(20)	7(43.75)	0(0)
During pregnancy In first health facility	22(44)	4(80)	5(31.25)	2(100)
In dr. Soetomo Hospital	4(8)	0(0)	4(25)	0(0)
Therapy	ARV	Benzathine Penicillin	Antiviral	ARV, antiviral
Before pregnancy	24(48)	1(20)	0(0)	0(0), 0(0)
During pregnancy	17(34)	4(80)	0(0)	1(50), 0(0)
No therapy	9(18)	0(0)	16(100)	1(50), 2(100)
Place of delivery				
dr. Soetomo General Hospital	35(70)	3(60)	9(56.25)	1(50)
Elesewhere	15(30)	2(40)	7(43.75)	1(50)
Total	50	5	16	2

3.3 Risk factors

The risk factors for HIV were multiple sex partners, injected drug user, contaminated blood transfusions, and tattoos. No medical records were recorded regarding the risk factors for syphilis. One pregnant woman with hepatitis B known to have multiple partners and one had a husband with multiple partners.

IV. DISCUSSION

4.1 Management of pregnant women with HIV

Pregnant women with no data of HIV in their previous ante natal care (ANC), were screened at the clinic. Even though it is a government policy, there were patients who had never been tested for HIV during pregnancy in primary health facilities. Early screening of HIV will decrease the vertical transmission itself because earlier initiation of antiretroviral (ARV) declined the transmission rate, but unfortunately only a few pregnant women check themselves at early trimester. Administration of antiretroviral for pregnant women with HIV is very important in order to eliminate the transmission from mother to child.

It is known that giving less than four weeks of ARVs to pregnant women with HIV has a 5.5 folds of transmission risk to their children than those who have received ARV for 13 weeks or more [3]. In the group of patients who had been diagnosed with HIV before pregnancy in 2019, all patients received ARVs in combined form (zidovudine, duviral). Whereas in the group with positive screening during pregnancy, only 19 out of 28 patients received ARVs during pregnancy starting at different gestational ages. There were five pregnant women who had just been diagnosed with HIV just before delivery and did not get the ARVs.

If there were no obstetric contra indications for vaginal delivery, then based on undetectable viral load (<1000 copies / mL) and / or the patient is on ARV therapy for at least six months, the patient can give birth vaginally. A study in United Kingdom and Ireland included 10,000 HIV positive pregnant women, mother-to-child transmission was found to be lower in women with a viral load less than 50 copies/mL at the time of delivery than in mothers who had a viral load of 50-399 copies/mL and viral load 400-999 copies/mL with the percentage of transmission respectively 0.09%, 1.0% and 2.6% [4].

Thirty five patients with HIV were hospitalized until delivery. One patient had curretage due to incomple abortion. One patient had laparotomy due to abdominal pregnancy and twenty five patiens had cesarean section. Viral load and CD4 were described in table 3. Patients who had viral load less than 1000 copies/mL were terminated by cesarean section due to obstetric indications. Three out of five patients who had antiretroviral more than six months but the viral load more than 1000 copies/mL also terminated by cesarean section.

Table 3. Examination of patients with HIV in pregnancy

Screening location	Gestational age at screening (weeks gestational age)	Patients with HIV positive	Patients were checked for CD4 and viral load			
			CD4	Viral load	CD 4 and viral load	None
		n	n (%)	n (%)	n (%)	n (%)
Public health care or others (n=24)*	< 13	7	0(0)	1(14.3)	3(42.9)	3(42.8)
	13-27	8	2(25)	1(12.5)	2(25)	3(37.5)
	≥ 28	9	0(0)	0(0)	0(0)	9(100)
Obstetric outpatient clinic dr. Soetomo General Hospital (n=4)	< 13	1	0(0)	1(100)	0(0)	0(0)
	13-27	1	0(0)	1(100)	0(0)	0(0)
	≥ 28	2	0(0)	0(0)	0(0)	2(100)
Total		28	2 (7.1%)	4 (14.3%)	5 (17.9%)	17 (60.7%)

* Two patients with HIV and hepatitis B. HIV Human Immunodeficiency Virus, ARV Anti Retro Viral

Table 4. MOD of HIV patients based on ARV treatment and viral loads

	Viral Load <1000	Viral Load >1000	No Data
C-Section (n=26)			
ARV < 6 months	1	2	4
ARV > 6 months	4	3	7
No ARV	0	0	5
Vaginal delivery (n=8)			
ARV < 6 months	0	0	0
ARV > 6 months	7	0	0
No ARV	0	0	1

MOD Mode of Delivery; ARV Anti Retro Viral

Starting from the third trimester of pregnancy, maternal antibodies, including antibodies to HIV, are passively received. It can be detected until 18 months of age. ARV therapy in newborns is divided into three categories, [5]: 1) ARV prophylaxis: administering one or more ARVs to newborns without evidence of HIV infection data to reduce the risk of exposure to the baby during the perinatal period. 2) Presumptive HIV therapy: administering three ARV regimens to newborns with high risk of HIV exposure during the perinatal period. Presumptive therapy is intended as an initial therapy for infants who later proven to be HIV positive, but also as prophylaxis for newborns exposed to HIV during the perinatal period.
3) HIV therapy: administration of three ARV regimens with therapeutic doses or antiretroviral therapy to newborns who were proved to be HIV positive.

Breast milk may contain the free HIV virus or HIV infected cells. The consequence of breastfeeding is the risk of HIV exposure. However, in this study we did not get any data regarding breastfeeding in newborns.
There were 33 live infants from 35 mothers with HIV who delivered in our hospital. Four infants had no complete data. There were 29 infants who received prophylaxis ARVs. Twenty one (63.6%) infants routinely went to pediatrics outpatient clinic and all were declared not affected of HIV based on 6 months laboratory data. We had no data regarding the other twelve infants (table 5).

The management of HIV patients in a triple elimination perspective is prioritizing early detection and HIV therapy in pregnant women with HIV. Management of HIV is carried out in co-treatment with the Internal Medicine Departement. Counseling for pregnant women and their partners to reduce the risk of HIV transmission was rare at the obstetric outpatient clinic because of limited time and space. Further treatment for postpartum mothers with HIV was continued at the internal medicine outpatient clinic.

4.2 Management of pregnant women with syphilis

Penicillin is the therapy of choice for syphilis. In principle, proper management of syphilis in pregnancy can effectively prevent mother-to-child transmission. Benzathine penicillin G 2.4 million IU injected intramuscularly as a single dose in the early phase, repeated two times with one week interval. Serologic follow-up were performed at one, two, six, and twelve months of the first month and every six months in the second year. In order to prevent further transmission, patients need to be given a clear and comprehensive explanation of their disease and the possible mother-to-child transmission.

Pregnant women who have adequate therapy allowed to deliver vaginally with standard precautions [5]. All pregnant women with syphilis in this study were not screened at our outpatient clinic. All patients had received benzathine penicillin therapy but none of them had serological data during pregnancy.

Three patients with syphilis were hospitalized and were delivered by cesarean section. The contraception for each patient was Intra Uterine Device (IUD), sterilization, and the last patient did not use family planning. Two infants were injected with procaine penicillin and were tested for rapid plasma reagen (RPR) and treponemal pallidum hemagglutination assay (TPHA) tests. One infant

was not injected by procaine penicillin and was not tested for RPR or TPHA. All test came back negative except TPHA result of one of the infants. He was diagnosed with congenital syphilis and was discharged after 20 days in a good condition (table 5).

Infants who delivered from mothers with syphilis should be injected with procaine penicillin 50,000 IU/kg intramuscular. They should also be examined for clinical evidence of congenital syphilis such as non-immune hydrops, jaundice, rhinitis, hepatosplenomegaly, skin spots, and pseudo paralysis of the extremities [6]. Staining of the placenta or umbilical cord or polymerase chain reaction (PCR) test for *Treponema pallidum* may be performed. Dark field microscopy or PCR examination of the lesion or body fluids (bullous lesions or nasal mucosa) may be performed. Radiological examination may also be performed to identify typical bony lesions in addition to the diagnosis of congenital syphilis.

Table 5. Infants born to woman with HIV, syhilis, and hepatitis B

HIV						
Infants (n=33)	**ARVs prophylaxis**			**Follow up**		
	Therapy	No Therapy	No Data	Affected	Not Affected	No Data
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total	29 (87.9)	0 (0)	4 (12.1)	0 (0)	21 (63.6)	12 (36.4)
Syphilis						
Infants (n=3)	**Procaine penicillin injection**			**Follow up**		
	Therapy	No Therapy	No Data	Affected	Not Affected	No Data
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total	2 (66.7)	0 (0)	1 (33.3)	1 (33.3)	1 (33.3)	1(33.3)
Hepatitis B						
Infants (n=6)	**HBIg + Vaccine**			**Follow up**		
	Therapy	No Therapy	No Data	Affected	Not Affected	No Data
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total	6 (100)	0 (0)	0 (0)	1 (16.7)	3 (50)	2 (33.3)

The management of syphilis patients at the oupatient clinic in the perspective of triple elimination is prioritizing early detection of every pregnant woman with an unknown syphilis status. Management of syphilis therapy is carried out in co-treatment with Dermatology and Venereology Department. Counseling for pregnant women and their partners to reduce the risk of syphilis transmission was rare at the obstetric outpatient clinic because of limited time and space. Further treatment for postpartum mothers with syphilis was continued at the dermatology and venereology outpatient clinic.

4.3 Management of pregnant women with hepatitis B

Nine patients with hepatitis B were hospitalized until delivery. During hospitalized, they didn't examined for hepatitis B virus deoxyribonucleic acid (HBV DNA) because it was not covered by national insurance. They also didn't get antiviral therapy.

Six out of nine infants were born alive. Five of them were delivered by cesarean section and the other were delivered spontaneously. All of them get injected by hepatitis B immunoglobulin before 12 hours post natal. They also got the hepatitis vaccine.

Mechanism of intrapartum transmission occurs due to exposure to vaginal secretions in the cervical canal [7]. Mode of delivery did not affect fetal transmission as long as the protocol for administration of imunoglobulin of hepatitis B (HBIg) and hepatitis B vaccine at 12 hours post natal was performed according to the procedure. With the administration of immunoprophylaxis, the incidence of perinatal transmission is greatly reduced [8]. There is another opinion that suggests if mother's HBV DNA levels was high, cesarean section is preferable [9].

In our study, one infant was turned out to be positive for hepatitis B at follow up and was given tenofovir (table 5). This infant was delivered spntaneously at 38 weeks of gestational age from mother who had no status for her HBV DNA and had no antiviral therapy as all other patients. Though this infant had HBIg and hepatitis B vaccine, however, we didn't have the mother's HBV DNA status. This HBV DNA test should be an uncharged laboratory test for pregnant women with hepatitis B.

In this study we did not get any data regarding breastfeeding in newborns. It was in line with a study that breastfeeding was neither associated with chronic HBV infection. [10] Counseling for pregnant women and their partners to reduce the risk of hepatitis B transmission was rare at the obstetric outpatient clinic because of limited time and space. Further treatment for postpartum mothers with hepatitis B was continued at the internal medicine outpatient clinic.

There was one patient with HIV and also hepatitis B who were hospitalized. She had no therapy for either ARVs or antiviral for hepatitis B. The infant was delivered by cesarean section due to unknown viral load at 39 weeks of gestational age. The infant had prophylaxis ARVs, but other than that we had no data for the follow up.

V. CONCLUSION

In conclusion, dr. Soetomo General Hospital, as a tertiary and referral hospital in east part of Indonesia, carried out the triple elimination programme. All pregnant women were screened if they did not screened before. In 2019, the prevalence of pregnant women was 4.3% for HIV, was 0.4% for syphilis, was 1.4% for hepatitis B, and was 0.2% for HIV and hepatitis B. Only 48 patients were hospitalized until delivery. Triple elimination in terms of early detection has been carried out well at our obstetric outpatient clinic, however in terms of management such as laboratory support services for both mothers and babies as well as providing comprehensive therapy had not been carried out well. Therefore this management needs to be improved in the following years.

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