A Comparison of Maternal Anemia between HIV Infected Pregnant Women Receiving Zidovudine-Based and Zidovudine-Free Highly Active Antiretroviral Therapy (HAART)

Pattaramas Lertcheewakarn MD*,
Fuanglada Tongprasert MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*

Objective: *To compare the prevalence of maternal anemia associated with usage of Zidovudine-free and Zidovudine-based HAART during pregnancy.*

Material and Method: *A retrospective cohort study was conducted in HIV-infected pregnant women receiving HAART between January 2006 and December 2012 in Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand. Changes in hemoglobin levels were compared between zidovudine-free and zidovudine-based HAART groups.*

Results: *Sixty-six pregnant women who received HAART, pre-exposure hemoglobin levels showed no significant difference between the zidovudine-free (14 cases) and the zidovudine-based (52 cases) groups. In non-anemic pregnant women before HAART initiation, the prevalence of post-exposure anemia was 40.5%, and similar in both groups. Post-exposure, decreased hemoglobin levels were greater in the zidovudine-based group (-1.46±0.64 g/dL) than the zidovudine-free group (-1.29±1.26 g/dL), but the difference was not significant (p = 0.766). Duration of the lowest post-exposure hemoglobin levels was shorter in the zidovudine-based group than the zidovudine-free group, but the difference was not significant (71.5 days and 105.6 days, p = 0.123).*

Conclusion: *In almost half of the cases, both zidovudine-based and zidovudine-free HAART exposure was associated with substantial risk of maternal anemia during pregnancy. Pregnant women receiving HAART regimens may be at significant risk of anemia two to three months after exposure and should be adequately monitored for this complication.*

Keywords: *HIV, Zidovudine, HAART, Maternal anemia, Antiretroviral drug*

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The optimal management of pregnancies complicated with HIV infection had been studied to maximize maternal health and prevent HIV transmission to the newborn. Nowadays, in a setting of universal prenatal HIV testing and counseling, highly active antiretroviral therapy (HAART), elective cesarean delivery and breastfeeding avoidance, the rate of HIV mother-to-child transmission (MTCT) is between 0.1 to 1%[1]. Antiretroviral drug combinations of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) have been shown to effectively reduce the risk of vertical transmission by adequate viral suppression in pregnant women. A highly recommended NRTI is zidovudine (ZDV), which should be a component of HAART regimens in all HIV-infected pregnant women who are antiretroviral naive.

However, pregnant women treated with ZDV have a significant risk of hematological toxicities. ZDV is known to suppress hemoglobin synthesis and globin gene expression. Acute toxic effects on hematopoiesis cause varying degrees of maternal anemia, resulting in drug intolerance[2,3]. Prenatal exposure to ZDV is also associated with hematological abnormalities in neonates via transplacental drug transfer, which negatively affects fetal erythropoiesis[4-7].

ZDV-free HAART regimens are an option for pregnant women who cannot tolerate ZDV due to severe maternal anemia. Because of toxicity concerns, continuing administration of these ZDV-free drugs is also recommended in HIV-infected women on antiretroviral therapy who become pregnant. However, there is a paucity of data on the effect of these combination drugs on maternal outcomes, including

Correspondence to:
Tongprasert F, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.
Phone: 053-945-552, Fax: 053-946-112
E-mail: fpunyath@med.cmu.ac.th

hematological toxicity. From previous research, ZDV-free regimens seem to be associated with a significant risk of maternal anemia at the end of pregnancy, similar to ZDV-based regimens[8]. Among their participants, anemia was not common at the beginning of pregnancy, differing from our populations in the area of high incidence of anemia such in Thailand or Southeast Asia. Moreover, comparisons of the hematological changes during pregnancy between ZDV-based and ZDV-free regimens have not been studied. The present study aimed to compare the prevalence of maternal anemia associated with use of ZDV-based and ZDV-free HAART regimens during pregnancy in Thai women.

Material and Method

A retrospective cohort study was conducted at Maharaj Nakorn Chiang Mai Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, with approval of the Research Ethics Committee, using a database of HIV-infected pregnant women who received antenatal care at the hospital between January 2006 and December 2012. Eligibility criteria included 1) HIV-infected pregnant women who received HAART during pregnancy, 2) at least one laboratory result of hemoglobin level in the first trimester or before HAART exposure, and 3) at least one laboratory result of hemoglobin level obtained at follow-up visit (4, 8, 12, 16, 20, or 24 weeks after HAART exposure) or before delivery. Exclusion criteria were 1) multiple pregnancies, 2) antepartum hemorrhage, and 3) failure of HAART drug compliance. The sample size was calculated based on maternal anemia prevalence of 42.4% among pregnant women receiving ZDV-based HAART regimen in previous study[8]. Twenty-five pregnant women were needed in each treatment group for a 0.05 two-sided type 1 error with 0.9 powers.

The definition of anemia in pregnancy was a hemoglobin level of less than 11.0 g/dL in the first or third trimester or less than 10.5 g/dL in the second trimester[9]. The hemoglobin level was analyzed with an automated complete blood count (CBC) machine (Coulter STKS analyzer; Beckman, Brea, CA, USA). HAART was defined by at least three antiretroviral drug combinations of two NRTIs (e.g. zidovudine, lamivudine, stavudine, tenofovir, and emtricitabine) plus either one NNRTI (e.g. nevirapine, efavirenz) or one PI (e.g. lopinavir/ritonavir, atazanavir, indinavir, and darunavir). ZDV-based HAART regimen was defined as a regimen that included of zidovudine and ZDV-free HAART regimen was defined as a regimen that did not include zidovudine.

The patient demographic data, CD4 cell counts before and after HAART exposure, HIV RNA viral load before delivery, gestational age at the beginning of HAART, gestational age at the switch of HAART regimen (if any), hemoglobin levels and other hematologic profiles, any treatment of anemia such as iron supplementation or blood transfusion and pregnancy outcomes were obtained from database and medical records.

Statistical analysis

All statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL). The demographic characteristics were described and compared between the ZDV-based and ZDV-free groups by the independent samples t-test, Mann-Whitney U test and Chi-square test. The categorical data were presented as frequencies (%) and the continuous data were presented as mean and standard deviation (SD). Hemoglobin levels were compared between both groups using the Chi-square test and the Fisher's exact test for categorical variables and the independent samples t-test for continuous variables. The $p<0.05$ was considered statistically significant.

Results

During the seven-year study period, 67 HIV-infected pregnant women received HAART during pregnancy. The laboratory result of hemoglobin level during follow-up visits was missing in one patient. Of the remaining 66 cases, 52 cases (78.8%) received ZDV-based regimens and 14 cases (21.2%) received ZDV-free regimens. The ZDV-based group, antiretroviral drugs combination were zidovudine plus lamivudine plus lopinavir/ritonavir (45 cases), zidovudine plus lamivudine plus nevirapine (6 cases), and zidovudine plus lamivudine plus efavirenz (1 case). The ZDV-free group, antiretroviral drugs combination were lamivudine plus stavudine plus lopinavir/ritonavir (3 cases), lamivudine plus tenofovir plus lopinavir/ritonavir (3 cases), lamivudine plus stavudine plus nevirapine (2 cases) and the other drugs combination e.g. lamivudine plus stavudine plus atazanavir or indinavir, emtricitabine plus tenofovir plus atazanavir or efavirenz, etc. (6 cases).

Among all participants, 55 pregnant women (83.3%) were antiretroviral naive and 37 pregnant women (56.1%) were first diagnosed with HIV infection during pregnancy. Most participants were

Table 1. Baseline characteristics of HIV- infected pregnant women receiving ZDV-free or ZDV-based HAART regimens

Baseline characteristics	Total (66 cases)	ZDV-based group (52 cases)	ZDV-free group (14 cases)	*p*-value
Maternal age (yrs, mean ± SD)	29.91±6.25	29.26±6.16	32.36±6.18	0.982
$CD4^+$ cell count pre-HAART exposure ($cells/mm^3$, mean ± SD)	395.45±202.32	413.64±211.70	326.57±148.61	0.738
$CD4^+$ cell count before delivery ($cells/mm^3$, mean ± SD)	470.80±167.78	490.00±175.95	391.63±102.18	1.000
HIV RNA before delivery (copies/mL, median and 25^{th}, 75^{th} percentile)	51.00 (40.00, 400.00)	51.00 (40.00, 400.00)	51.50 (40.00, 15,158.50)	0.313*
GA at the beginning of HAART (wks, median and 25^{th}, 75^{th} percentile)	16.00 (5.00, 21.00)	17.00 (11.25, 20.25)	5.00 (0.75, 21.25)	0.030*
GA at delivery (wks, mean ± SD)	37.55±2.46	37.66±2.14	37.14±3.50	0.500
Birth weight (g, mean ± SD)	2,773.98±537.52	2,830.25±471.13	2,565.00±717.04	0.781
Route of delivery (%)				
ND	67.2	64.3	67.9	0.826
Elective CS	10.4	7.1	11.3	
Emergency CS	19.4	28.6	17.0	
VE, FE, BA	3.0	0	3.8	

ZDV = zidovudin; HAART = highly active antiretroviral therapy; yrs = years; $cells/mm^3$ = cells per cubic millimeter; copies/mL = copies per milliliter; GA = gestational age; wks = weeks; g = gram; ND = normal delivery; CS = cesarean section; VE = vacuum extraction; FE = forceps extraction; BA = breech assisting delivery; SD = standard deviation
* Mann-Whitney U-test

multipara (74.6%) and history of previous abortion was identified in 41.8% of participants. Before HAART initiation, the average $CD4^+$ cell count was 395.45 (range 10-927 $cells/mm^3$). At 36 weeks of gestation, the average $CD4^+$ cell count was 470.80 (range 174-859 $cells/mm^3$) and HIV RNA viral load was 51.0 (range 20.0-69, 500.0 copies/mL). The baseline characteristics of the study population were not significantly different between the ZDV-based and ZDV-free group, as presented in Table 1.

Table 2 compares the prevalence of anemia and changes in hemoglobin and hematocrit levels during pregnancy between the ZDV-free and ZDV-based groups. Among all participants, the prevalence of anemia at the beginning of pregnancy was 44.8% (39.6% in the ZDV-free group and 64.3% in the ZDV-based group). The prevalence of thalassemia carriers in all study populations was 24.4%. Subgroup analyses of non-anemic and anemic HIV-pregnant women at baseline are shown in Table 3 and Table 4, respectively.

Discussion

HAART is currently recommended for all HIV-infected pregnant women, since it dramatically reduces the maternal-to-child transmission rate regardless of the $CD4^+$ cell count or HIV RNA level. However, pregnant women should be counseled regarding the benefits and risks of antiretroviral agents and drug toxicities should be monitored. Current recommendations are also to add zidovudine (ZDV) to all regimens based on efficacy studies and extensive experience in MTCT prevention[10]. In a previous study, the most common adverse effect of ZDV-based regimens used in pregnancy was maternal anemia (42%)[11]. As a result, a regimen not containing ZDV, or ZDV-free HAART, is a reasonable option for pregnant women with anemia. However, hematologic side effects from the combination of multiple drugs in ZDV-free regimens are still a concern, especially in pregnant women with preexisting anemia before HAART exposure. Maternal anemia at 36 weeks of gestation was reported more frequently among women on ZDV-free regimens (51.2%) than ZDV-based regimens (42.4%), although the difference was not significant[8]. However, that report studied a population with a low prevalence of anemia at the beginning of pregnancy (6.7%), unlike Thai population with a prevalence of preexisting anemia of 20.1%[12].

In the present study, the prevalence of preexisting anemia was 44.8% (39.6% in the ZDV-based group and 64.3% in the ZDV-free group) before HAART exposure. At the beginning of pregnancy, the

Table 2. Comparisons of changes in hematological profiles during pregnancy of HIV-pregnant women receiving ZDV-free or ZDV-based HAART regimens

Variables	Total (66 cases)	ZDV-based group (52 cases)	ZDV-free group (14 cases)	*p*-value
Pre-HAART exposure hematological profiles				
Hb (g/dL, mean ± SD)	10.95±1.28	11.12±1.11	10.34±1.63	0.041
Hct (%, mean ± SD)	33.07±3.44	33.53±3.11	31.32±4.18	0.032
Anemia rate (%)	44.8	39.6	64.3	0.099
The lowest point hematological profiles				
Hb (g/dL, mean ± SD)	10.10±1.33	10.21±1.34	9.71±1.23	0.209
Hct (%, mean ± SD)	30.42±3.92	30.54±4.08	29.98±3.33	0.635
Anemia rate (%)	62.1	59.6	71.4	0.541*
Before delivery hematological profiles				
Hb (g/dL, mean ± SD)	11.12±1.10	11.24±1.15	10.71±0.78	0.110
Hct (%, mean ± SD)	33.38±3.14	33.61±3.35	32.50±2.04	0.240
Anemia rate (%)	31.8	28.8	42.9	0.318
The maximum changes in hematological profiles[a]				
Hb (g/dL, mean ± SD)	-0.95±1.22	-1.05±1.23	-0.63±1.16	0.262
Hct (%, mean ± SD)	-2.68±4.04	-3.04±4.09	-1.34±3.65	0.165
Changes in hematological profiles from pre-HAART exposure until delivery[b]				
Hb (g/dL, mean ± SD)	0.09±1.14	0.002±1.11	0.37±1.25	0.292
Hct (%, mean ± SD)	0.28±3.65	0.04±3.63	1.18±3.73	0.302
Time at the lowest point of Hb level (days post-HAART exposure, mean ± SD)	70.48±43.16	65.42±38.00	89.92±56.69	0.068
Treatment of anemia				
Medical treatment (%)	57.4	54.2	69.2	0.324*
Blood transfusion (%)	4.5	3.8	7.1	0.618*

Hb = hemoglobin; Hct = hematocrit; g/dL = gram per deciliter

[a] The maximum changes in hematological profiles calculated by the lowest point Hb/Hct minus pre-HAART exposure Hb/Hct

[b] Changes in hematological profiles from pre-HAART exposure until delivery calculated by Hb/Hct before delivery minus pre-HAART exposure Hb/Hct

* Fisher's exact test

lower hemoglobin and hematocrit levels in the ZDV-free group might be a result of avoiding zidovudine use in pregnant women with preexisting anemia to prevent hematologic toxicity. Undoubtedly, the higher occurrence of anemia at the lowest point (71.4%) and before delivery (42.9%) could be explained by the higher prevalence of preexisting anemia in the ZDV-free group. This proportion was comparable with the rate of maternal anemia at 36 weeks of gestation in pregnant women receiving ZDV-free regimens in a previous study (51.2% among the low incidence of anemia in their populations)[8]. Based on real practice in the present study, the rate of maternal anemia at the end of pregnancy was almost one-third of HIV-infected pregnant women, regardless of HAART regimens, despite medical treatment (57.4%) and blood transfusions (4.5%).

In the subgroup of non-anemic pregnant women at baseline, the rates of maternal anemia at nadir and before delivery were approximately 40% and 15%, respectively, and similar in both the ZDV-free and ZDV-based groups. Moreover, changes in hemoglobin and hematocrit levels during pregnancy were no different between both groups. Generally, a 3% drop in hematocrit levels is predicted, whether zidovudine is used or not. Although these findings may partly result from the dilution effect of hypervolemia in pregnancy, frequent monitoring of hematologic profiles is suggested, even in non-anemic pregnant women receiving ZDV-free HAART regimens. On average, the lowest hemoglobin levels were observed 71 days and 105 days after first exposure to ZDV-based and ZDV-free regimens, respectively. To explain this finding, it might be hypothesized that the anemic event

Table 3. Comparison of changes in hematological profiles during pregnancy of non-anemic HIV-pregnant women receiving ZDV-free or ZDV-based HAART regimens

Variables	Total (36 cases)	ZDV-based group (31 cases)	ZDV-free group (5 cases)	*p*-value
Pre-HAART exposure hematological profiles				
Hb (g/dL, mean ± SD)	11.90±0.65	11.86±0.67	12.16±0.52	0.345
Hct (%, mean ± SD)	35.39±1.99	35.35±1.90	35.64±2.75	0.764
The lowest point hematological profiles				
Hb (g/dL, mean ± SD)	10.70±1.12	10.70±10.18	10.70±0.72	0.995
Hct (%, mean ± SD)	32.01±3.46	31.97±3.66	32.28±2.07	0.855
Anemia rate (%)	40.5	40.6	40.0	1.00*
Before delivery hematological profiles				
Hb (g/dL, mean ± SD)	11.59±1.03	11.64±1.08	11.32±0.66	0.531
Hct (%, mean ± SD)	34.42±2.96	34.54±3.05	33.68±2.34	0.551
Anemia rate (%)	16.2	15.6	20.0	1.00*
The maximum changes in hematological profiles[a]				
Hb (g/dL, mean ± SD)	-1.31±1.18	-1.29±1.26	-1.46±0.64	0.766
Hct (%, mean ± SD)	-3.38±4.21	-3.38±4.47	-3.36±2.14	0.993
Changes in hematological profiles from pre-HAART exposure until delivery[b]				
Hb (g/dL, mean ± SD)	-0.35±1.06	-0.26±1.08	-0.84±0.82	0.262
Hct (%, mean ± SD)	-0.96±3.26	-0.80±3.36	-1.96±2.65	0.469
Time at the lowest point of Hb level (days post-HAART exposure, mean ± SD)	76.11±45.79	71.50±43.13	105.60±56.51	0.123

Hb = hemoglobin; Hct = hematocrit; g/dL = gram per deciliter

[a] The maximum changes in hematological profiles calculated by the lowest point Hb/Hct minus pre-HAART exposure Hb/Hct

[b] Changes in hematological profiles from pre-HAART exposure until delivery calculated by Hb/Hct before delivery minus pre-HAART exposure Hb/Hct

* Fisher's exact test

in pregnant women receiving ZDV-free regimens did not represent direct hematological toxicity of these drugs, but may relate to the relatively higher fetal iron consumption, especially during the second and third trimesters[8]. In contrast to ZDV-based regimens, the inhibitory effect on erythropoiesis was already established at the initiation of zidovudine[2]. The late onset of anemia among HIV-infected pregnant women receiving ZDV-free regimens highlights the necessity of adequately monitoring hemoglobin concentration, especially two to three months after HAART exposure.

In the subgroup of anemic pregnant women at baseline, pre-exposure hemoglobin levels were significantly lower in the ZDV-free group than ZDV-based group. This finding reflects the decision to avoid adding zidovudine to antiretroviral drug combinations in HAART regimens for already anemic patients. Nevertheless, mildly anemic, asymptomatic pregnant women can opt for ZDV-based regimens under close surveillance for the early detection of adverse effects. In anemic pregnant women receiving ZDV-free regimens, almost 3% of hematocrit level is expected to increase before delivery. In spite of any HAART regimens, the rate of maternal anemia at the end of pregnancy remained approximately 50%, indicating that medical treatment (elemental iron and folic acid) and blood transfusion in pregnancies complicated with severe anemia (hemoglobin of less than 8.0 g/dL or hematocrit of less than 24%) had corrected approximately half of the cases.

An important limitation of the present study was the small number of cases in the ZDV-free group. This may have limited the power to detect significant differences in some variables. Larger studies or multicenter collaborative analyses are needed to confirm our results. However, our findings that anemia occurred similarly in pregnant women receiving ZDV-free regimens as well as ZDV-based regimens, consistent with a previous larger study, indicated that maternal hemoglobin level monitoring should be considered during pregnancy. Another limitation is that we were not able to specify the causes of preexisting

Table 4. Comparison of changes in hematological profiles during pregnancy of anemic HIV-pregnant women receiving ZDV-free or ZDV-based HAART regimens

Variables	Total (30 cases)	ZDV-based group (21 cases)	ZDV-free group (9 cases)	*p*-value
Pre-HAART exposure hematological profiles				
Hb (g/dL, mean ± SD)	9.89±0.91	10.14±0.77	9.32±0.98	0.021
Hct (%, mean ± SD)	30.21±2.56	30.76±2.47	28.92±2.54	0.075
The lowest point hematological profiles				
Hb (g/dL, mean ± SD)	9.34±1.18	9.43±1.23	9.16±1.12	0.580
Hct (%, mean ± SD)	28.40±3.55	28.27±3.74	28.70±3.28	0.766
Anemia rate (%)	89.7	90.0	88.9	1.000*
Before delivery hematological profiles				
Hb (g/dL, mean ± SD)	10.52±0.88	10.60±0.97	10.37±0.63	0.526
Hct (%, mean ± SD)	32.04±2.89	32.14±3.34	31.84±1.63	0.807
Anemia rate (%)	51.7	50.0	55.6	1.000*
The maximum changes in hematological profiles[a]				
Hb (g/dL, mean ± SD)	-0.54±1.14	-0.71±1.12	-0.17±1.15	0.246
Hct (%, mean ± SD)	-1.79±3.69	-2.49±3.45	-0.22±3.93	0.128
Changes in hematological profiles from pre-HAART exposure until delivery[b]				
Hb (g/dL, mean ± SD)	0.59±1.04	0.37±1.06	1.04±0.87	0.109
Hct (%, mean ± SD)	1.86±3.55	1.38±3.71	2.92±3.08	0.287
Time at the lowest point of Hb level (days post-HAART exposure, mean ± SD)	56.48±40.62	49.65±27.39	71.67±60.15	0.182

Hb = hemoglobin; Hct = hematocrit; g/dL = gram per deciliter

[a] The maximum changes in hematological profiles calculated by the lowest point Hb/Hct minus pre-HAART exposure Hb/Hct

[b] Changes in hematological profiles from pre-HAART exposure until delivery calculated by Hb/Hct before delivery minus pre-HAART exposure Hb/Hct

* Fisher's exact test

anemia in pregnant women due to incomplete medical records. However, a previous study from our hospital reported that the main causes of maternal anemia were thalassemia carriers and diseases (54.9%) and iron deficiency anemia (43.1%)[12].

Conclusion

Generally, exposure to both zidovudine-based and zidovudine-free HAART regimens were associated with substantial risk of maternal anemia during pregnancy in nearly half of all cases. Pregnant women receiving HAART regimens may be at significant risk of anemia two to three months after exposure and should be adequately monitored for this complication. Pregnant women should be counseled regarding the benefits and risks of antiretroviral agents in order to be able to make an informed decision on her HAART regimen.

What is already known on this topic?

Zidovudine (ZDV) has a significant risk of hematological toxicities. ZDV-free HAART regimens seem to be an option for pregnant women who cannot tolerate to zidovudine due to maternal severe anemia.

What this study adds?

Almost half of pregnant women who were exposed to ZDV-free HAART regimens had anemia at the end of pregnancy, similar to ZDV-based HAART regimens exposure. Duration from HAART initiation led to anemia was longer in ZDV-free group comparing with ZDV-based group (105 days and 71 days, respectively). Therefore, pregnant women receiving any HAART regimens should be adequately monitored for this complication.

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Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบการเกิดภาวะเลือดจางในสตรีตั้งครรภ์ติดเชื้อเอชไอวีที่ได้รับยาต้านไวรัสที่มี zidovudine และไม่มี zidovudine เป็นส่วนประกอบ

ภัทรามาส เลิศชีวกานต์, เฟื่องลดา ทองประเสริฐ

วัตถุประสงค์: *เพื่อเปรียบเทียบอัตราการเกิดภาวะเลือดจางจากการใช้ยาต้านไวรัสในสตรีตั้งครรภ์ติดเชื้อเอชไอวี ในกรณีที่ได้รับยาต้านไวรัสชนิดรวมกันหลายตัวที่มี zidovudine และไม่มี zidovudine เป็นส่วนประกอบ*

วัสดุและวิธีการ: *การศึกษาเชิงวิเคราะห์ชนิดโคฮอร์ตแบบย้อนหลังในสตรีตั้งครรภ์ติดเชื้อเอชไอวี ที่มารับการฝากครรภ์ที่โรงพยาบาลมหาราชนครเชียงใหม่ ตั้งแต่เดือนมกราคม พ.ศ. 2549 ถึง เดือนธันวาคม พ.ศ. 2555 โดยเก็บข้อมูลลักษณะพื้นฐานของสตรีตั้งครรภ์ ชนิดของยาต้านไวรัส ผลการตรวจทางโลหิตวิทยา และผลลัพธ์ของการตั้งครรภ์ จากเวชระเบียนทำการศึกษาเปรียบเทียบระหว่างกลุ่มที่ได้รับยาต้านไวรัสชนิดรวมกันหลายตัวที่มี zidovudine และไม่มี zidovudine เป็นส่วนประกอบ*

ผลการศึกษา: *จากสตรีตั้งครรภ์จำนวนทั้งหมด 66 ราย แบ่งเป็นกลุ่มที่ได้รับยาต้านไวรัสที่มี zidovudine เป็นส่วนประกอบ 52 ราย และไม่มี zidovudine เป็นส่วนประกอบ 14 ราย ขณะเริ่มตั้งครรภ์ระดับฮีโมโกลบินของทั้งสองกลุ่มไม่ต่างกันหลังจากที่เริ่มรับประทานยาต้านไวรัสในสตรีตั้งครรภ์ที่ไม่มีภาวะเลือดจางมาก่อน พบภาวะเลือดจาง ร้อยละ 40.5 (กลุ่มที่ได้รับยาต้านไวรัสที่ไม่มี zidovudine เป็นส่วนประกอบ พบภาวะเลือดจาง ร้อยละ 40.6 เทียบกับกลุ่มที่มี zidovudine เป็นพบภาวะเลือดจาง ร้อยละ 40.0, ค่า p = 1.00) โดยในกลุ่มที่ได้รับยาต้านไวรัสที่ไม่มี zidovudine เป็นส่วนประกอบ จะมีค่าเฉลี่ยของระดับฮีโมโกลบินที่ลดลงมากกว่าแต่ไม่มีความแตกต่างอย่างมีนัยสำคัญ (กลุ่มที่ได้รับยาต้านไวรัสที่ไม่มี zidovudine เป็นส่วนประกอบ ลดลง 1.46±0.64 เทียบกับกลุ่มที่มี zidovudine ลดลง 1.29±1.26, ค่า p = 0.766) ทั้งนี้ระยะเวลาตั้งแต่ได้รับยาต้านไวรัสจนกระทั่งมีระดับฮีโมโกลบินต่ำที่สุดมีแนวโน้มที่นานกว่าในกลุ่มที่ไม่มี zidovudine เป็นส่วนประกอบ (กลุ่มที่ได้รับยาต้านไวรัสที่ไม่มี zidovudine เป็นส่วนประกอบใช้เวลานาน 105.6 วัน เทียบกับกลุ่มที่มี zidovudine ใช้เวลานาน 71.5 วัน, ค่า p = 0.123)*

สรุป: *ประมาณร้อยละ 40 ของสตรีตั้งครรภ์ติดเชื้อเอชไอวี ที่ได้รับยาต้านไวรัสชนิดรวมกันหลายตัวที่ไม่มี zidovudine เป็นส่วนประกอบ มีความเสี่ยงที่จะเกิดภาวะเลือดจางได้ไม่ต่างจากกลุ่มที่ได้รับยาต้านไวรัสที่มี zidovudine โดยระยะเวลาตั้งแต่ได้รับยาต้านไวรัสจนกระทั่งมีระดับฮีโมโกลบินต่ำที่สุดใช้เวลาประมาณ 2-3 เดือน ดังนั้นควรตรวจติดตามระดับฮีโมโกลบินเพื่อเฝ้าระวังภาวะเลือดจางที่อาจเกิดขึ้นได้ทั้งสองกลุ่ม*