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Анемии и тромбоцитопении у ВИЧ-инфицированных беременных

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Обоснование. При беременности и в родах у ВИЧ-инфицированных женщин анемия и тромбоцитопения встречаются в 2 раза чаще, чем в общей популяции. Степень влияния ВИЧ-инфекции на развитие данных цитопений определена в недостаточной степени, необходимо дальнейшее изучение зависимости частоты их развития от количества РНК ВИЧ и CD4-лимфоцитов в крови у ВИЧ-инфицированных беременных, а также роли антиретровирусной терапии.

Цель — изучить влияние количества РНК ВИЧ и CD4-лимфоцитов на частоту развития анемий и тромбоцитопений у ВИЧ-инфицированных беременных.

Материалы и методы. Проанализированы социально-демографические характеристики, эпидемиологический анамнез, частота осложнений беременности и родов, сроки начала антиретровирусной терапии у 303 ВИЧ-инфицированных беременных, а также данные обследования на ВИЧ-инфекцию рожденных ими детей. В исследование были включены 27 пар мать – ребенок с перинатальной передачей ВИЧ и 276 пар мать – ребенок без перинатального заражения ВИЧ. Все беременные были разделены на группы в зависимости от количества CD4-лимфоцитов и РНК ВИЧ. В группах проведен сравнительный анализ по частоте выявления анемий и тромбоцитопений.

Результаты. Установлена прямая корреляционная зависимость между частотой развития анемий и тромбоцитопений у ВИЧ-инфицированных беременных с маркерами прогрессирования ВИЧ-инфекции: тяжелым иммунодефицитом (CD4 ⩽ 200 кл/мкл, $p < 0,01$), высоким уровнем РНК ВИЧ (более 100 000 копий/мл, $p < 0,01$) в периферической крови.

Заключение. Подтверждена высокая встречаемость цитопений при ВИЧ-инфекции у беременных, превышающая общепопуляционный уровень, а также эффективность назначения антиретровирусной терапии женщинам репродуктивного возраста, планирующим или не исключающим наступления беременности (не применяющим эффективную контрацепцию), в качестве профилактики развития анемий и тромбоцитопений во время беременности.

Ключевые слова: ВИЧ-инфицированные беременные; иммуносупрессия; анемия беременных; тромбоцитопения беременных; осложнения беременности и родов; антиретровирусная терапия у беременных.

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Anemia and thrombocytopenia in HIV-positive pregnant women

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BACKGROUND: During pregnancy and childbirth, anemia and thrombocytopenia are twice as common among HIV-positive women as in the general population. It has not been yet clear to what extent HIV affects the incidence of cytopenias, therefore, the correlation between the incidence and the HIV RNA level and CD4 count in HIV-positive pregnant women, as well as the role of antiretroviral therapy, requires further study.

AIM: The aim of this study was to assess the effect of the HIV RNA level and CD4 count on the frequency of anemia and thrombocytopenia in HIV-positive pregnant women.

MATERIALS AND METHODS: In this study, we analyzed social and demographic features, epidemiological personal history data, the frequency of pregnancy and delivery complications, and the timing of the initiation of antiretroviral therapy in 303 HIV-positive pregnant women, as well as the data of screening for HIV infection of their children. The study included 27 mother-child pairs with perinatal HIV transmission and 276 mother-child pairs without mother-to-child transmission of HIV. All pregnant women were divided into groups depending on the CD4 count and HIV RNA level. A comparative analysis of anemia and thrombocytopenia frequencies was carried out in the study groups.

RESULTS: A direct correlation was revealed between the frequency of anemia and thrombocytopenia in HIV-positive pregnant women and markers of HIV infection: severe immunodeficiency (CD4 ⩽ 200 cells/μl, $p < 0.01$) and high HIV RNA levels (more than 100,000 copies / ml, $p < 0.01$) in peripheral blood.

CONCLUSIONS: We confirmed the high frequency of cytopenias in HIV-positive pregnant women, which exceeds the general population level. In addition, we demonstrated the effectiveness of prescribing antiretroviral therapy among women of reproductive age who planned to become pregnant or did not exclude the possibility of pregnancy (who did not use the effective methods of contraception), as a means of anemia and thrombocytopenia prevention during pregnancy.

Keywords: HIV-positive pregnant women; immunosuppression; anemia in pregnancy; thrombocytopenia in pregnancy; pregnancy and delivery complications; antiretroviral therapy during pregnancy.

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BACKGROUND

The course of pregnancy in women infected with the human immunodeficiency virus (HIV) is characterized by a high incidence of obstetric complications with repercussions on peripheral blood parameters. The incidence of anemia in nonHIV-infected pregnant women is 15%–50%, and in Russia, it is 32% [1]. However, this incidence increases by a factor of 1.5 in HIV-positive pregnant women [2]. The same situation is noted in relation to thrombocytopenia which is detected in 6.6%–11.6% of nonHIV pregnant women, and in 10%–15% of HIV-positive pregnant women [3, 4].

The etiologies of anemia in HIV-positive pregnant women include direct viral damage to the bone marrow, chronic systemic inflammation, and intake of some antiretroviral drugs (zidovudine and phosphazide) [5, 6].

The latter mechanism is of utmost importance as International and National Clinical Guidelines on the prevention of perinatal transmission of HIV have included zidovudine (a drug that has a toxic effect on the bone marrow) in the preferred treatment regimen for pregnant women [7–10]. This drug drastically drops the viral load in the maternal circulation, and causes anemia especially in pregnant women with low or borderline initial hemoglobin levels. Thus, zidovudine is often replaced with drugs that do not have a toxic effect on the bone marrow in obstetrical cases. This change in the antiretroviral therapy (ART) usually occurs at the end of the trimester II or within trimester III when the decrease in hemoglobin level is exacerbated by an increase in the volume of blood in the maternal circulation [11].

During pregnancy, HIV-positive patients are predisposed to malabsorption that leads to a deficiency of nutrients, trace elements, and vitamins such as B_{12} and folic acid [12].

The pathogenesis of anemia in patients with HIV is associated with chronic systemic inflammation that adversely affects hematopoiesis in the bone marrow. This mechanism is based on the action of pro-inflammatory cytokines (TNF-alpha, and IL-1-beta) that causes the level of hepcidin to spike thereby blocking the absorption of iron from the gastrointestinal tract [5]. This leads to the formation of iron-deficient hypoproliferative hematopoiesis, as well as a decrease in the lifespan of erythrocytes [13]. The presence of opportunistic diseases in an HIV-positive pregnant woman enhances chronic inflammation that accelerates the development and severity of anemia [5].

Other risk factors also influence the development of iron deficiency anemia. In most cases (up to 90%), pregnant women are diagnosed with anemia associated with an iron deficit or iron metabolism disorder [14]. The course of anemia can be complicated by alimentary factors such as a decrease in the iron intake from food due to unbalanced nutrition, impaired iron absorption processes due to chronic diseases of the gastrointestinal tract, vomiting of pregnant women in trimester I, and bleeding during placenta previa [1]. Hypervolemic hemodilution (an increase in circulating blood volume by 30%–33% toward the end of pregnancy) can complicate the course of anemia [12].

Thrombocytopenia due to HIV infection can be primary (due to direct damage of megakaryocytes and their microenvironment by the HIV) or secondary, and serve as a marker of the disease progression. Due to the damage caused by the virus on the bone marrow, the differentiation of the stem cells is also impaired thereby accelerating their death. Cytopenias are based on complex multi-stage cyclic immune responses involving B-lymphocytes, T-lymphocytes, NK cells, macrophages, and cytokines that lead to the formation of various classes of antiplatelet antibodies. The binding of antibodies to platelets causes Fcγ receptor (FcγR)-mediated destruction of platelets by phagocytes, and antiplatelet antibodies themselves accelerate the clearance of platelet from the circulation [15]. Thrombocytopenia is an indicator of advanced liver disease (chronic viral hepatitis) often associated with HIV infection. Increased destruction of platelets in this case, in addition to the autoimmune mechanism, is associated with hypersplenism and portal hypertension, resulting in the destruction of formed elements in the hypertrophied spleen [16]. It is also known that some antiretroviral drugs directly lower the level of platelets. Thus, in the first weeks of treatment with non-nucleoside reverse transcriptase inhibitors (with known toxic effect on the bone marrow and liver), fibrinolysis is activated, and the production of antiplasmin decreases [17].

Anemia and thrombocytopenia in HIV-positive women are associated with an increase in the incidence of chronic placental insufficiency, preterm labor, poor uterine contraction, increased incidence of bleeding during childbirth and postpartum, as well as maternal and infant mortality [4, 18]. These complications by themselves also increase the incidence of perinatal HIV transmission [19]. Thus, a reduction in the incidence of anemia and thrombocytopenia in HIV-positive pregnant women indirectly reduces the incidence of perinatal transmission of HIV.

We therefore aimed at analyzing the effect of the levels of HIV-RNA and CD4-lymphocytes on the incidence of anemia and thrombocytopenia in pregnant women with HIV.

MATERIALS AND METHODS

We included 303 HIV-positive pregnant women whose ended in childbirth at St. Petersburg within 2014–2018. In the study group, 276 (91.1%) women gave birth to children without HIV infection, and in 27 (8.9%) cases, perinatal

transmission of HIV to a child was registered. All HIV-positive pregnant women were sectioned into four groups depending on the CD4 lymphocyte counts (group 1 with ⩽200 cells/μL, group 2 within 201–350 cells/μL, group 3 within 351–500 cells/μL, and group 4 with >500 cells/μL). According to the level of HIV-RNA, they were distributed into five groups (group A with <40 copies/mL, group B with 41–1000 copies/mL, group C with 1001–10,000 copies/mL, group D with 10,000–100,000 copies/mL, and group E with >100,000 copies/mL).

We analyzed the social, epidemiological, and clinical characteristics pregnant women with HIV as well as the history (the duration of HIV infection), regimens and timing of initiation of ART. All HIV-positive pregnant women underwent conventional explorations such as the quantitative measure of HIV-RNA and CD4-lymphocytes in peripheral blood, a qualitative blood test for the presence of hepatitis B and C viruses, and a detailed general clinical blood test. All newborns from HIV-positive mothers included in the study were equally examined for the presence of HIV DNA or RNA using polymerase chain reaction (PCR).

The stages of the PCR study included plasma sampling, HIV-RNA isolation, PCR reverse transcription, and detection of PCR products using the enzyme hybridization method and real time PCR. HIV-RNA was quantified using an automated Abbott m2000 Real Time System through reverse transcriptase PCR (RT-PCR) *in vitro* to determine the level of HIV-1 RNA in the range of 20–10 million copies/mL. The study was performed using Abbott Real Time HIV-1 test systems. This immunological study included the determination of quantitative indicators of cellular immunity, namely T-helpers/inducers (CD4) obtained from the sera of patients. Berhing monoclonal antibodies were used in the lymphocytotoxic test (NIH, USA). A clinical blood test was performed for all HIV-positive pregnant women, as well as a full blood count, and erythrocyte sedimentation rate. The study was performed using automated analyzers Cell DXN 3700 and SYSMEX 400T. Markers of viral hepatitis B and C (HBsAg, HBcAg, HBcorAB, HBcAB, HBsAB, and HCVAB) were determined in all patients using chemiluminescence immuno assay on an automatic analyzer Architect I2000.

Overall statistical analysis of data obtained during the study was done using the STATISTICA for Windows system (version 10) at a significance level corresponding to a p-value of less than 0.05.

RESULTS

On dividing the 303 HIV-positive pregnant women into groups based on the CD4 lymphocyte count, we observed that less than half of the group 4 patients (140 cases, 46.2%) had a normal count by the time of pregnancy. Group 1 included 31 HIV-positive pregnant women with severe immunodeficiency (the count of CD4 lymphocytes ⩽200 cells/μL); group 2 consisted of 52 HIV-positive pregnant women with pronounced immunodeficiency (CD4-lymphocyte count between 201 and 350 cells/μL); group 3 included 80 pregnant women with moderate immunodeficiency (CD4-lymphocyte count was between 351 and 500 cells/μL). A similar relationship was noted when the study population was divided into groups based on the level of HIV-RNA. Group A (<40 copies/mL) involved 110 patients, group B (41–1000 copies/mL) involved 48 patients, group C (1001–10,000 copies/mL) involved 44 patients, group D (10,000–100,000 copies/mL) involved 45 patients, and group E (>100,000 copies/mL) involved 36 patients.

Groups with different HIV-RNA levels and CD4-lymphocyte counts were comparable in age; the average age of HIV-positive pregnant women was 32.4 ± 5.0 years. The proportion of wanted pregnancies was higher in the group without immunodeficiency (97.1%, n = 136); and as the severity of immunodeficiency increased, the number of wanted pregnancies decreased (80.6%, n = 25) (p < 0.01). Groups of HIV-positive pregnant women with varying degrees of immunodeficiency were characterized by a high proportion of the parenteral route of contamination (48.4%, n = 18 in the group with severe immunodeficiency) (p < 0.001) compared to those without immunodeficiency (25%, n = 35). Patients with severe immunodeficiency adhered to ART less often than HIV-positive pregnant women without immunodeficiency (p < 0.05). Moreover, 135 HIV-positive pregnant women without immunodeficiency (96.4%) and 26 HIV-positive pregnant women with severe immunodeficiency (83.9%) presented at the antenatal clinic. Furthermore, 134 HIV-positive pregnant women without immunodeficiency (95.1%) and 22 patients with severe immunodeficiency (71%) were registered in the AIDS Center. In the group with severe immunodeficiency, 3 patients presented with co-infection of chronic hepatitis B (9.7%), and chronic hepatitis C co-infection in 17 (54.8%) cases; while in the group of women without immunodeficiency, chronic hepatitis B co-infection was registered in 7 patients (5%), and chronic hepatitis C co-infection in 51 cases (36.4%), p < 0.001. There were more injectable drug users in the group of HIV-positive pregnant women with severe immunodeficiency than in the normal immunogram group (32.3% and 6.5%, respectively, p < 0.001) (Table 1).

We observed that as time went on, there was an increase in the number of women who became pregnant with undetectable levels of HIV-RNA while on ART (p < 0.001). In the undetectable HIV-RNA level group, all women desired pregnancy. The largest proportion of unwanted pregnancies was in the group of women with HIV-RNA

Table 1. Socio-epidemiological characteristics of groups of human immunodeficiency virus (HIV)-positive women based on the CD4-lymphocyte count, *n* = 303

Parameter		Groups with different counts of CD4-lymphocytes, cells/μl				*p*
		≤200	201–350	351–500	>500	
Proportion of wanted pregnancies, %		80.6	84.5	93.8	97.1	<0.01
Route of HIV infection, %	sexual	41.9	59.6	68.8	73.6	<0.001
	parenteral	48.4	36.5	28.7	25	<0.001
	no data	9.4	3.9	2.5	1.4	
Proportion of HIV-positive women with antenatal monitoring at the AIDS Center, %		71	73.1	87.5	95.1	<0.05
Proportion of HIV-positive women with antenatal monitoring in antenatal clinics, %		83.9	78.9	91.3	96.4	
Frequency of co-infection with CHC, %		54.8	50	37.5	36.4	<0.001
Frequency of co-infection with CHB, %		10.3	5.6	6.3	5	<0.001
Proportion of active drug users during pregnancy, %		32.3	17.3	11.3	6.5	<0.001
Timing of ART start, %	before pregnancy	0.8	33.3	46.8	84.3	<0.001
	during pregnancy	83.3	47.1	49.4	13.7	<0.001
	without ART during pregnancy	15.9	19.6	3.8	2	<0.001

Note. HIV, human immunodeficiency virus; CHC, chronic hepatitis C; CHB, chronic hepatitis B; ART, antiretroviral therapy.

Table 2. Socio-epidemiological characteristics of groups of HIV-positive women depending on the level of HIV-RNA, *n* = 303

Parameter		Groups with different levels of HIV-RNA, copies/mL					*p*
		≤40	41–1000	1001–10,000	10,001–100,000	>100.000	
Proportion of wanted pregnancies, %		100	96.8	86.4	91.5	90.2	<0.001
Route of HIV infection, %	sexual	63.4	61.8	54.5	53.9	48.2	<0.001
	parenteral	26.1	29.8	33.3	34.1	39.8	<0.001
	no data	10.5	8.4	12.2	12	12	
Proportion of HIV-positive women with antenatal monitoring at the AIDS Center, %		100	97.9	79.6	64.6	83.3	<0.001
Proportion of HIV-positive women with antenatal monitoring in antenatal clinics, %		100	97.9	86.4	70.8	94.4	
Frequency of co-infection with CHC, %		35.6	43.5	38.6	46.2	52.8	<0.001
Frequency of co-infection with CHB, %		5.1	4.3	4.5	7.7	8.3	
Proportion of active drug users during pregnancy, %		3	5.3	10.9	23.1	27.8	<0.001
Timing of ART start, %	before pregnancy	99.3	53.8	4.5	0	0	<0.001
	during pregnancy	0.7	46.2	79.5	86.9	83.3	<0.001
	without ART during pregnancy	0	0	16	13.1	16.7	<0.001

Note. CHC, chronic hepatitis C; CHB, chronic hepatitis B; ART, antiretroviral therapy.

Table 3. Incidence of anemia and thrombocytopenia in groups of pregnant women with different counts of CD4-lymphocytes and levels of HIV-RNA, *n* = 303

Group	Group (CD4-lymphocyte and HIV-RNA counts in groups), *n*	Anemia, *n* (%)	Thrombocytopenia, *n* (%)
HIV-positive pregnant women with different baseline CD4 counts, *n* = 303	1 (CD4 ⩽ 200 cells/μL), *n* = 31	20 (64.5)*	13 (41.9)*
	2 (CD4 = 201–350 cells/μL), *n* = 52	26 (50)	11 (21.2)
	3 (CD4 = 351–500 cells/μL), *n* = 80	42 (52.5)	21 (26.3)
	4 (CD4 > 500 cells/μL), *n* = 140	61 (43.6)	39 (27.9)
HIV-positive pregnant women with different baseline levels of HIV-RNA, *n* = 303	A (HIV-RNA ⩽ 40 copies/mL), *n* = 110	38 (34.6)**	38 (34.6)**
	B (HIV-RNA = 40–1000 copies/mL), *n* = 48	27 (56.3)	9 (18.8)
	C (HIV-RNA = 1001–10,000 copies/mL), *n* = 44	28 (63.4)	13 (29.6)
	D (HIV-RNA = 10 001–100,000 copies/mL), *n* = 45	33 (50.8)	15 (23.1)
	E (HIV-RNA > 100 000 copies/mL), *n* = 36	23 (63.9)	9 (25)

Note. HIV, human immunodeficiency virus; CHC, chronic hepatitis C; CHB, chronic hepatitis B; ART, antiretroviral therapy.
* $p < 0.01$ between group 1 and groups 2, 3, 4; ** $p < 0.01$ between group A and groups B, C, D, E.

levels of 10,001–100,000 copies/mL (14.6%; *n* = 16) that was significantly higher than in any other group ($p < 0.001$). In the group with undetectable levels of HIV-RNA, women with sexually transmitted infection prevailed (63.4%, *n* = 101), while HIV-positive women with parenteral routes had high levels of HIV-RNA more often ($p < 0.001$). Thus, 39.8% of HIV-positive pregnant women from the group with HIV-RNA levels higher than 100,000 copies/mL were infected parenterally (*n* = 14). Thus, the frequency of refusals from management during pregnancy increased with an increase in the level of HIV-RNA ($p < 0.001$).

All (*n* = 110) pregnant women with undetectable HIV-RNA levels, and 83.3% of patients (*n* = 30) in the group with HIV-RNA levels higher than 100,000 copies/mL were registered at the AIDS Center. The incidence of chronic hepatitis C co-infection was higher in the high HIV-RNA group (52.8%, *n* = 19) than in the undetectable HIV-RNA group (35.6%, *n* = 48) ($p < 0.001$). Active injectable drug users amounted to 3% in the group with undetectable HIV-RNA levels (*n* = 9), and 27.8% (*n* = 10) in the group with HIV-RNA over 100,000 copies/mL ($p < 0.001$). Impaired adherence to ART during pregnancy was more common (12.8%) in the group with high HIV-RNA levels (2.8% in the group with undetectable levels, $p < 0.001$) (Table 2).

Anemia was most often diagnosed in pregnant women of group 1 (64.5%, *n* = 20) and in group E (63.9%, *n* = 23); in patients with severe immunodeficiency and HIV-RNA levels higher than 100,000 copies/mL. A lower incidence of anemia was noted in pregnant women without immunodeficiency and in those with undetectable levels of HIV-RNA; in group 4 and group A (43.6%, *n* = 61 and 34.6%, *n* = 38, respectively) ($p < 0.01$) compared to that in group 1 and group E.

Thrombocytopenia was more common in the group with severe immunodeficiency (41.9%; *n* = 13) ($p < 0.01$ compared with groups 2, 3, 4) and in HIV-positive pregnant women with undetectable HIV-RNA levels (34.6%; *n* = 38) ($p < 0.01$ compared with groups B, C, D, E). Table 3 shows the incidence of hematological disorders among the groups of HIV-positive pregnant women with different levels of HIV-RNA and CD4-lymphocyte counts.

DISCUSSION

Our findings revealed that the incidence of anemia in HIV-positive pregnant women with normal CD4-lymphocyte counts (43.6%) and undetectable HIV-RNA levels (34.6%) were comparable to the incidence of anemia in pregnant women in St. Petersburg (47%–51%) and RF (32%) [1, 20]. However, our findings are not consistent with that of some studies that indicate a significantly higher incidence of anemia in HIV-positive pregnant women compared to that in HIV-seronegative women [11, 21, 22]. These studies were conducted in Africa, where, unlike the Russian Federation, the main proportion of people had a different HIV genotype, a low standard of living, and reduced access to medical care, even during pregnancy.

A direct correlation was established between the level of HIV-RNA in the blood of pregnant women and the incidence of anemia. In other words, anemia was diagnosed in every third pregnant woman with an undetectable viral load (34.6%, $n = 38$), and was detected twice more often in women with HIV-RNA levels more than 100,000 copies/mL (63.9%, $n = 23$, $p < 0.01$). An inverse correlation was revealed between the incidence of anemia and the CD4-lymphocyte count of these pregnant women (from 64.5% in patients with CD4-lymphocyte count ⩽200 cells/μL to 43.6% in patients with CD4-lymphocyte count >500 cells/μL, $p < 0.01$). Our findings demonstrate the relationship of anemia in pregnant women with the progression of HIV infection. A number of researchers had similar findings when studying the course of pregnancy in HIV-positive women, and noted that a high level of HIV-RNA and severe immunodeficiency (CD4-lymphocyte count < 200 cells/μL) are risk factors for anemia during pregnancy [11, 23].

In our study, thrombocytopenia was significantly more frequent in the group of pregnant women with severe immunodeficiency than in those without immunodeficiency ($p < 0.01$). Thus, thrombocytopenia in HIV-positive patients serves as a marker of disease progression in the absence of ART, as approximately half of patients with thrombocytopenia (48%) who required specific treatment started it only during pregnancy.

Moreover, every second female with thrombocytopenia, included in the study, was co-infected with hepatitis C virus (51.1%), as well as a significant decrease in platelet levels was noted in them. Thrombocytopenia is due to hypersplenism which developes in presence of portal hypertension due to a long-term pathogenesis in the hepatobiliary system [16]. Secondary thrombocytopenia that occurs during ART is due to reduced production of platelets and their accelerated destruction. Moreover, nucleoside reverse transcriptase inhibitors (zidovudine, lamivudine, phosphazide) have a suppressive effect on the red bone marrow (particularly the megakaryocytic and erythropoietic lineage) thereby leading to reduced platelet production and anemia [24, 25]. Our findings were consistent with the results of O.A. Adesina, who registered an increase in the incidence of thrombocytopenia in HIV-positive pregnant women with severe immunodeficiency. The authors attribute this to the deregulatory effect of HIV on the function of hematopoietic precursor cells [26]. The incidence of thrombocytopenia in HIV-positive patients can be reduced by timely prescription of ART with minimal toxic effect on the bone marrow, as well as timely treatment of chronic hepatitis C in pregnancy [7–10, 26].

CONCLUSION

HIV-positive pregnant women with co-infection with chronic viral hepatitis, with low adherence to management, not undergoing ART, and who use injectable drugs, are at risk of anemia and thrombocytopenia during pregnancy. We established a direct correlation between the incidence of anemia and thrombocytopenia in HIV-positive pregnant women and markers of HIV infection progression: severe immunodeficiency ($p < 0.01$) and viral load (>100,000 copies/mL) in peripheral blood ($p < 0.01$). The use of ART by women of reproductive age who desire pregnancy (those who do not use effective contraception) prevents anemia and thrombocytopenia in HIV-positive pregnant women. When choosing antiretroviral drugs included in the ART regimen, preference should be given to drugs with minimal toxic effects on the bone marrow. Declining the incidence of anemia in HIV-positive pregnant women will indirectly reduce the incidence of associated obstetric complications (threatened preterm delivery and preterm childbirth), as well as perinatal transmission of HIV.

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