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Prevalence, Associated Factors and Pregnancy Outcomes of Anemia during Intrapartum Period in HIV-Infected Pregnant Women

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ABSTRACT

Objective: To determine prevalence, associated factors and pregnancy outcomes of anemia during intrapartum period in HIV-infected pregnant women.

Materials and Methods: A prospective and descriptive study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand from September 2011 to July 2013. One hundred and five HIV-Infected pregnant women during intrapartum period were included into the present study.

Results: The prevalence of anemia at intrapartum period was 41.0% (95% confidence interval = 32.0 - 50.5). Compared with normal group, anemia group had a higher rate of no antenatal care (ANC), anemia at first ANC, viral load ≥ 400 copies/ml and positive urine amphetamine. In addition, a lower mean age and a lower rate of known case of HIV infection before current pregnancy were found in anemia group. By multiple logistic regression analysis, anemia at first ANC and viral load ≥ 400 copies/ml were only two parameters that associated with anemia at delivery (p = 0.003, OR = 1.64, 95% CI = 1.16 - 2.23 and p = 0.000, OR = 4.5, 95% CI = 1.28 - 5.89, respectively). Regarding to pregnancy outcomes, the patients in anemia group had a higher rate of preterm birth, low birth weight and blood transfusion than the other group.

Conclusions: With two associated factors, anemia at first ANC and viral load ≥ 400 copies/ml, a high prevalence of anemia at delivery in HIV-infected pregnant women was found in the present study. Compared with normal group, the pregnancy outcomes in anemia group seem to be poorer. However, these conclusions should be interpreted in light of limitation of the number of patients in this study.

Keywords: anemia, HIV-infected pregnant women, pregnancy outcome

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Introduction

Anemia in pregnancy is a major global health problem. It is an important factor associated with an increased risk of maternal and neonatal morbidities such as reduced productivity at work, a higher risk of requiring a blood transfusion during delivery, intrauterine growth retardation, low birth weight, stillbirth and neonatal death[1-6]. The prevalence of anemia in pregnant women in undeveloped or developing and developed countries is 52% and 20%, respectively[1, 2, 5, 7]. Regarding to the prevalence of anemia in Thai pregnant women, only about 20% of prevalence had ever been reported[8, 9]. The causes of anemia in pregnancy are physiology and pathology. However, iron deficiency, malarial parasite, deficiencies in folic acid and other micronutrients, sepsis, malignancy and human immunodeficiency virus (HIV) infection are the common pathologic cause[2-4, 10]. In addition to the causes of anemia in pregnant women as mentioned, a consequence of inflammation, bone marrow suppression, hemolysis, parvovirus B19 co-infection, and antiretroviral therapy for prevention of mother-to-child transmission or PMTCT were the other causes of anemia in HIV-infected pregnant women[2, 5, 11, 12].

Regarding to HIV infected pregnant women, the prevalence of anemia from previous studies was varied from 38.7% to 96.8%[1,3,10,11,13]. However, the prevalence of anemia in HIV-infected pregnant women in Thailand had never been reported. The present study was designed to provide information on the prevalence, associated factors and pregnancy outcomes of anemia during intrapartum period in HIV-infected Thai pregnant women.

Materials and Methods

A prospective observational study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand which serves as a referral center, from September 2011 to July 2013. The study was conducted in accordance with the ethical principles stated in the most recent version of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Siriraj Hospital.

The patients enrolled in this study were all HIV infected pregnant women who were admitted and gave birth at the septic labor ward. The patients were verbally notified prior to participation. A sample of blood was routinely obtained and analyzed for complete blood count (CBC). Other blood tests such as serology for HBsAg, Anti-HCV, syphilis, hemoglobin typing were performed if the patients had never been tested. The eligible patients were classified to be either anemia, or no anemia group (normal group) following World Health Organization (WHO) criteria. A hemoglobin level of less than 11 g/dL, or hematocrit less than 33%, at any point during pregnancy was defined as anemia[13]. To diagnose iron deficiency, the rest of the blood samples in anemia group who tested for serum ferritin. Iron deficiency was diagnosed on the basis of low serum ferritin levels (<12 ng/ml)[14, 15]. The HIV-infected pregnant women who were <18 years old, multifetal pregnancy, major thalassemia disease or had poor communication skills in Thai language were excluded from the present study.

Data were collected and analyzed using SPSS Statistics version 18 (PASW Statistics) and were expressed as mean ± standard deviation (SD), median or number (%). Student's t-test was used to compare continuous data. Pearson chi-square test or Fisher's exact test were used to compare categorical data. Multiple logistic regression analysis was used to adjust for potential confounding factors by estimated odds ratio (OR) and 95% confidence interval (CI). Statistically significant differences were defined as $p < 0.05$.

Results

One hundred and five out of 109 HIV-infected pregnant women were included in the present study. Four patients were excluded because of twin pregnancy (n=2) and major thalassemia disease (n=2). With the mean age of 27.6 ± 5.8 years, the majority of patients in this study were of low socioeconomic status. The prevalence of anemia was 41% (95% confidence interval = 32.0-50.5). Sixty-one percent of HIV-infected pregnant women were first detected as such in the

current pregnancy. The rate of participants who attended at antenatal care (ANC) clinic was 81%. Eighty-seven percent of them were received AZT-based HAART regimen during ANC. Regarding to immunological AIDS defining illness, 11 out of 96 participants (11.5%) had CD4 count less than 200 cells/μL and 11 out of 55 participants (20%) had viral load ≥ 400 copies/ml. Fifteen of 27 (55.5%) had positive result for the urine amphetamine test, as shown in Table 1.

Table 1. Demographic data of HIV-infected pregnant women during intrapartum period

Demographic data	N	n (%) or Mean ± SD
Age (years)	105	27.6 ± 5.8
Body weight (kg)	105	59.1 ± 12.8
Body mass index (kg/m^2)	105	23.7 ± 4.7
Income (Baht/month)	105	
< 15,000		70 (66.7)
15,000 – 25,000		24 (22.8)
> 25,000		11 (10.5)
Occupation	105	
Unemployed/ Housewife		38 (36.2)
Employee/ Government officer		50 (47.6)
Business woman		14 (13.3)
Sex worker		3 (2.9)
Education	105	
Unlettered - Secondary level		85 (81.0)
Occupational certificate/ diploma		13 (12.3)
Bachelor's degree		7 (6.7)
Nulliparous	105	43 (41.0)
No antenatal care	105	20 (19.0)
Serology and Blood tests		
Thalassemia carrier	97	46 (47.4)
Anemia at delivery	105	43 (41.0)
Iron deficiency anemia at delivery	38	7 (18.4)
Reactive VDRL and TPHA	105	4 (3.8)
Positive HBsAg	105	9 (8.6)
Positive anti HCV	99	1 (1.0)
CD4 cell count (cells/μL)	96	
≥ 500		35 (36.5)
200-499		50 (52.1)
< 200		11 (11.5)
Viral load ≥ 400 copies/ml	55	11 (20.0)
Known case of HIV infection before current pregnancy	105	41 (39.0)
AZT-based HAART regimens during antenatal care	85	74 (87.0)
Positive urine amphetamine	27	15 (55.5)
Disclosure to husband	103	65 (63.1)
Serodiscordant husband	53	27 (50.9)

Abbreviations: HIV, Human Immunodeficiency Virus; AZT, Zidovudine; HAART, highly active antiretroviral therapy

Compared with normal group, anemia group had a significantly higher rate of no ANC, anemia at first ANC, viral load ≥ 400 copies/ml and positive urine amphetamine. In addition, a lower mean age and a lower rate of known case of HIV infection before current pregnancy were found in anemia group (Table 2). By multiple logistic regression analysis, only anemia at first ANC and viral load greater than 400 copies/ml were the two parameters that associated with anemia (p = 0.003, OR = 1.64, 95% CI = 1.16 - 2.23 and p = 0.000, OR = 4.5, 95% CI = 1.28 – 15.89, respectively).

Table 2. Comparison of characteristics of HIV-infected pregnant women during intrapartum period between anemia and normal group

Associated Factors	n (%) or mean ± SD		Mean difference	P
	anemia group	normal group	or OR (95% CI)	
Age (years)	25.6 ± 5.8	29.1 ± 5.5	-3.5 (-5.7, -1.3)	0.002
Body mass index (kg/m^2)	23.3 ± 4.6	24.0 ± 4.8	-0.7 (-1.1, 2.5)	0.447
Income (Baht/month)				
< 15,000	33 (76.7)	37 (59.7)		0.188
15,000 – 25,000	7 (16.3)	17 (27.4)		
> 25,000	3 (7.0)	8 (12.9)		
Occupation				
Unemployed/ Housewife	17 (39.5)	21 (33.9)		0.583
Employee/ Government officer	20 (46.5)	30 (48.4)		
Businesswoman	4 (9.3)	10 (16.1)		
Sex worker	2 (4.7)	1 (1.6)		
Education				
Unlettered - Secondary level	38 (88.4)	47 (75.8)		0.068
Occupational certificate/ diploma	5 (11.6)	8 (12.9)		
Bachelor's degree	0	7 (11.3)		
Nulliparous	13 (30.2)	30 (48.4)	0.63 (0.37, 1.05)	0.063
No antenatal care	13 (30.2)	7 (11.3)	1.84 (1.19, 2.84)	0.015
Thalassemia carrier	16 (39.0)	30 (53.6)	0.78 (0.55, 1.10)	0.156
Anemia at first antenatal care	21 (72.4)	20 (38.5)	1.64 (1.16, 2.33)	0.003
CD4 cell count (cells/μL)				
≥ 500	13 (34.2)	22 (37.9)		0.883
200-499	20 (52.6)	30 (51.7)		
< 200	5 (13.2)	6 (10.3)		
Viral load ≥ 400 copies/ml	9 (52.9)	2 (5.3)	4.50 (1.28, 15.89)	0.000
Known case of HIV infection before current pregnancy	11 (25.6)	30 (48.4)	0.68 (0.50, 0.93)	0.018
AZT-based HAART regimens during antenatal care	27 (90.0)	47 (85.5)	1.15 (0.77, 1.71)	0.551
Positive of urine amphetamine test	12 (70.6)	3 (30.0)	2.92 (0.95, 8.93)	0.040
Disclosure to husband	23 (56.1)	42 (67.7)	0.82 (0.57, 1.16)	0.231
Serodiscordant husband	9 (45.0)	17 (51.5)	0.85 (0.42, 1.71)	0.646

Abbreviations: HIV, Human Immunodeficiency Virus; AZT, Zidovudine; HAART, highly active antiretroviral therapy

With regard to pregnancy outcomes, the patients in anemia group had a significantly higher rate of preterm birth, low birth weight, blood transfusion, APGAR score < 7 at first minute than normal group. In addition, both a lower mean of gestational age at delivery and a lower mean of birth weight were found in anemia group. There were 5 patients having severe pregnancy outcome: all were in anemia group and there was no ANC. One had dead fetus in utero at 33 weeks of gestation, 3 newborns were admitted to Newborn Intensive Care Unit due to very low birth weight (900, 980, 1430 gm) and 1 newborn was sepsis. (Table 3.)

Table 3. Comparison of pregnancy outcomes of HIV-infected pregnant women during intrapartum period between anemia and normal group

Pregnancy outcomes	n (%) or mean ± SD		Mean difference or OR (95% CI)	P
	Anemia group (N=43)	Normal group (N=62)		
Gestational age of delivery (weeks)	36.3 ± 3.2	37.8 ± 1.7	1.5 (0.4, 2.6)	0.008
Preterm birth (< 37 weeks)	18 (41.9)	11 (17.7)	1.42 (1.07, 1.87)	0.007
Delivery < 34 weeks	7 (16.3)	1 (1.6)	1.18 (1.03, 1.35)	0.005
Cesarean delivery	26 (60.5)	31 (50.0)	1.23 (0.81, 1.98)	0.290
Postpartum hemorrhage	3 (7.0)	1 (1.6)	1.06 (0.97, 1.16)	0.303
Blood transfusion	6 (14)	0	1.16 (1.03, 1.31)	0.004
Birth weight (grams)	2650.9 ± 604.2	2864.5 ± 388.1	213.6 (4.9, 422.2)	0.045
Low birth weight (< 2,500 grams)	16 (37.2)	10 (16.1)	1.34 (1.04, 1.72)	0.014
Apgar score at first min < 7	7 (16.3)	0	1.19 (1.05, 1.36)	0.001
Apgar score at fifth min < 7	3 (7.0)	0		
Admitted in NICU	3 (7.0)	0		
Neonatal sepsis	1 (2.3)	0		
Death fetus in utero	1 (2.3)	0		

Abbreviations: NICU, Newborn Intensive Care Unit

Discussion

A high prevalence of anemia in HIV-infected present women was found from many studies especially in Africa such as Tanzania, Uganda and Nigeria[1, 3, 4, 10, 16]. With a high prevalence (41%), this is the first study determining the prevalence of anemia among HIV-infected pregnant women in Thailand which is comparable to the prevalence in India (38.7%)[5]. Several associated factors of anemia in this population had been reported, such as thalassemia carriers or having the disease, no ANC, no iron supplementation, low dosage of iron supplementation, consequences of inflammation, bone marrow suppression, hemolysis and AZT-based HAART regimens during ANC for viral suppression[9, 12].

The present study found that no ANC, anemia at first ANC, viral load ≥ 400 copies/ml, a lower mean age and positive urine amphetamine were associated factors of anemia at delivery in this group of patients. However, by multiple logistic regression analysis, only anemia at first ANC and viral load ≥ 400 copies/ml were associated with anemia in this group of patients (p = 0.003, OR = 1.64, 95% CI = 1.16 - 2.23 and p = 0.000, OR = 4.5, 95% CI = 1.28 - 15.89, respectively). Nevertheless, positive urine amphetamine was not included into our multiple logistic regression analysis due to small sample size. In contrast to the previous studies[9, 12], the no ANC and no iron supplement groups were the same group in the present study and they were not associated with factors of anemia at delivery by

multiple logistic regression analysis. It might be the difference in population between the present and previous studies. Although the no ANC group had a significantly higher rate of iron deficiency anemia (low ferritin level) than the ANC group (21.1% vs. 3.8%), the population in the present study had a very high prevalence (47.4%) of thalassemia carriers (Table 1) and the proportion of thalassemia carriers was significantly higher in ANC group, compared with the no ANC group (53.8 vs. 17.6%, p = 0.007), data not shown. Moreover, 13/29 (44.8%) of anemia in ANC group were thalassemia carriers without iron deficiency (high ferritin level). Only 3 patients in ANC group had iron deficiency anemia. All of them had very late and/or poor ANC. From aforementioned led to no association between no ANC and anemia at delivery in the present study.

Similar to a previous study[12], it is noticed that the known case of HIV infection before current pregnancy and viral load < 400 copies/ml were found as a protective factor of anemia in the present study. Almost all the known cases of HIV infection before current pregnancy in the present study had viral load < 400 copies/ml after highly active antiretroviral therapy (HAART) and patients intended to have pregnancy. Any direct cause of anemia from HIV infection in this group of patients, such as a consequence of inflammation, was eliminated. Regarding to the association between AZT-based HAART regimens during ANC for viral suppression and anemia, neither the present study nor the previous studies[12] found this association.

Regarding pregnancy outcomes, the rate of preterm delivery, low birth weight, blood transfusion and APGAR score < 7 at first minute in anemia group were significantly higher than those in normal group. In addition, a significant lower mean of gestational age at delivery and birth weight were found in anemia group. Although a small number of severe neonatal morbidities, admitted to Newborn Intensive Care Unit (NICU), neonatal sepsis and death of fetus in utero, were found in the present study, all of them were in the no ANC group. These findings were comparable to the previous studies[2-6, 11].

Conclusion

With regard to two associated factors, anemia at first ANC and viral load ≥ 400 copies/ml, a high prevalence of anemia at delivery in HIV-infected pregnant women was found in the present study. However, these conclusions should be interpreted in light of limitation of the number of patients in this study. Compared with normal group, the pregnancy outcomes in anemia group seem to be poorer. The authors believe that early ANC with adequate iron supplementation could reduce iron deficiency anemia and improve pregnancy outcomes.

Conflict of interest

The authors have no conflicts of interest.

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ความชุก ปัจจัยที่สัมพันธ์ และผลต่อการตั้งครรภ์ กับภาวะโลหิตจางขณะคลอดบุตร ในสตรีตั้งครรภ์ที่ติดเชื้อเอชไอวี

เพียงบุหลัน ยาปาน, อัมพัน เฉลิมโชคเจริญกิจ

วัตถุประสงค์ *: ศึกษาเกี่ยวกับ ความชุก ปัจจัยที่สัมพันธ์ และผลต่อการตั้งครรภ์ กับภาวะโลหิตจางในสตรีตั้งครรภ์ที่ติดเชื้อเอชไอวี โดยเก็บข้อมูลในระยะคลอดบุตรที่ห้องคลอดติดเชื้อของโรงพยาบาลศิริราช*

วัสดุและวิธีการ *: เป็นการวิจัยเชิงพรรณา ในสตรีตั้งครรภ์ที่ติดเชื้อเอชไอวี และเข้ารับการคลอดบุตรที่ห้องคลอดติดเชื้อในโรงพยาบาลศิริราช รวม 105 คน ระหว่างเดือนกันยายน พ.ศ.2554 ถึงกรกฎาคม พ.ศ.2556 หลังจากได้รับการรับรองจากคณะกรรมการจริยธรรมการวิจัยในคนของคณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล*

ผลการศึกษา *: ความชุกของภาวะโลหิตจางในสตรีตั้งครรภ์ที่ติดเชื้อเอชไอวีและเข้ารับการคลอดบุตรที่ห้องคลอดติดเชื้อ คือ ร้อยละ 41 (95% confidence interval = 32.0-50.5) ในกลุ่มที่มีภาวะโลหิตจาง จะมีอัตราของการไม่ฝากครรภ์, ภาวะโลหิตจางในครั้งแรกที่มาฝากครรภ์, ระดับไวรัสเอชไอวีในเลือด ≥ 400 copies/ml และตรวจพบสารแอมเฟตามีนในปัสสาวะ ที่สูงกว่ากลุ่มที่ไม่มีภาวะโลหิตจาง นอกจากนี้ ในกลุ่มที่มีภาวะโลหิตจาง ยังพบค่าเฉลี่ยของอายุและอัตราของจำนวนผู้ป่วยที่ทราบว่าติดเชื้อเอชไอวีก่อนการตั้งครรภ์ ที่น้อยกว่ากลุ่มที่ไม่มีภาวะโลหิตจางอีกด้วย เมื่อทำการวิเคราะห์แบบหลายปัจจัยแล้ว จะพบว่า เหลือเพียงสองปัจจัยที่สัมพันธ์กับภาวะโลหิตจาง คือ ภาวะโลหิตจางในครั้งแรกที่มาฝากครรภ์ และระดับไวรัสเอชไอวีในเลือด ≥ 400 copies/ml (p = 0.003, OR = 1.64, 95% CI = 1.16 - 2.23 และ p = 0.000, OR = 4.5, 95% CI = 1.28 - 15.89, ตามลำดับ) ส่วนผลต่อการตั้งครรภ์ พบว่า กลุ่มที่มีภาวะโลหิตจาง จะมีอัตราของการคลอดก่อนกำหนด ทารกแรกเกิดมีน้ำหนักตัวน้อย และการได้รับเลือด มากกว่ากลุ่มที่ไม่มีภาวะโลหิตจาง*

สรุป *: สตรีตั้งครรภ์ที่ติดเชื้อเอชไอวี ซึ่งเข้ารับการคลอดบุตร และตรวจพบว่ามีภาวะโลหิตจาง จะสัมพันธ์กับภาวะโลหิตจางในครั้งแรกที่มาฝากครรภ์และระดับไวรัสเอชไอวีในเลือด ≥ 400 copies/ml นอกจากนี้ ยังมีภาวะทุพพลภาพของมารดาและทารก มากกว่ากลุ่มที่ไม่มีภาวะโลหิตจาง อย่างมีนัยสำคัญทางสถิติ*