The Prevalence of Iron Deficiency Anemia in Pregnant Women in Nakhonsawan, Thailand

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Objective: *To determine the prevalence of iron deficiency anemia in pregnant women and the prevalence of thalassemia in both the anemic and non-anemic group.*

Material and Method: *At the first antenatal visit, blood was obtained for complete blood count. If hemoglobin < 11 g/dl or hematocrit < 33%, serum ferritin was performed. The authors used definition of anemia from CDC and WHO to determine the prevalence of anemia in pregnant women. Iron deficiency anemia was defined by anemia from CDC or WHO criteria in accordance with serum ferritin less than 30 mg/L. Cases of abnormal thalassemia screening were followed by hemoglobin electrophoresis and polymerase chain reaction (PCR) for diagnosis of alpha thalassemia 1 (SEA and Thai-deletion type). The data was analyzed by descriptive fashion and presented as mean, percentage, and standard deviation.*

Results: *Five hundred nineteen pregnant women were recruited. The prevalence of anemia from WHO (Hemoglobin < 11 g/dl), WHO (Hematocrit < 33%), and CDC criteria were 14.1, 9.8, and 10.6% respectively. The prevalence of iron deficiency anemia was 6.0, 4.6, and 4.8% in the same order. The prevalence of thalassemia was 39.7% in the anemic group and 24.4% in the non-anemic group.*

Conclusion: *The WHO criteria (Hemoglobin < 11 g/dl) gave the highest prevalence of anemia and iron deficiency anemia during pregnancy (14.1% and 6.0%). The prevalence of thalassemia in the anemic group (39.7%) was higher than non-anemic group (24.4%).*

Keywords: *Iron deficiency anemia, Pregnancy, Prevalence, Thalassemia*

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Iron deficiency is the most common nutritional disorder in the world[1]. Pregnant women are particularly at high risk for iron deficiency and iron-deficiency anemia (IDA) because of increased iron needed during pregnancy. The prevalence of iron-deficiency anemia in pregnant women is estimated to be between 35 and 75% (average 56%) in developing countries, whereas, in industrialized countries the average prevalence is 18%[2,3]. The health effects of anemia to both mothers and their fetuses, such as increased risk of maternal and child mortality due to severe anemia, preterm labor and small for gestational age have been well documented[5-10].

Hemoglobin concentration is the most reliable indicator of anemia at the population level[2-4]. Measuring hemoglobin and hematocrit level is relatively easy and inexpensive. The most commonly used definition of anemia was from the Centers for Disease Control and Prevention (CDC)[4] and the World Health Organization (WHO)[2].

Although iron deficiency is the major cause of anemia during pregnancy, anemia can be caused by factors other than iron deficiency, such as abnormal hemoglobin, folate and vitamin B12 deficiencies, kidney disease and parasitic infestation. In Thailand, the prevalence of thalassemia is high[11-13] so the mean level of hemoglobin and hematocrit concentration may be lowered. The gold standard for evaluating iron stores is bone marrow biopsy. However, this test is too invasive to be used routinely in clinical practice. Therefore, among many currently available tests, serum ferritin testing (SF) is currently considered as the best available measurement for iron stores[14-19].

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In most parts of Thailand, data about IDA in pregnancy is not well defined due to difficulty of iron assessment. SF is available only in secondary or tertiary center hospitals. Pregnant women with anemia often receive therapeutic trial of iron therapy and follow with rising of hemoglobin or hematocrit level[20,21]. The aims of the present study were to determine the prevalence of IDA which was defined by SF in pregnant women and to compare the prevalence of thalassemia in both anemic and non-anemic group.

Material and Method

The pregnant women who first attended the antenatal clinic at Health Promotion Hospital 8 region, Nakhonsawan, between October 1, 2008 and March 31, 2009 were recruited in the present study. The exclusion criteria were multiple pregnancies, pregnant women who had previously attended the antenatal clinic of another healthcare services and whose blood specimen was not collected. At the first antenatal visit, blood was collected and obtained for complete blood count (CBC), which was performed with SYSMEX XS-800i machine. Hemoglobin was determined by SLS-colorimetric method and hematocrit was deter-mined by electrical impedance including hydrodynamic focusing method. Thalassemia was screened by osmotic fragility test and dichlorophenolindophenol precipitation test. Cases of abnormal thalassemia screening were followed by hemoglobin electrophoresis with VARIANT II TURBO Hemoglobin system with fully automated HPLC precision. If the pregnant women were potential couple at risk for Hemoglobin Bart hydrops fetalis (homozygous alpha-1 thalassemia), their blood samples were sent to Regional Medical Sciences Center Nakhonsawan to perform polymerase chain reaction (PCR) for diagnosis of alpha thalassemia 1 (SEA and Thai-deletion type). In all cases of anemia, defined by any diagnostic criteria, serum ferritin were performed with IMMULITE/Ferritin *in vitro* diagnostic Kit, which serum ferritin was analyzed by chemiluminescent immunometric assay.

The authors used the definition of anemia from the Centers for Disease Control and Prevention (CDC)[4] and the World Health Organization (WHO)[2] (Table 1). Iron deficiency anemia was defined by anemia from any diagnostic criteria according to SF less than 30 μg/L[19]. The data was analyzed by descriptive statistic and presented as mean, standard deviation and percentage.

The present study was reviewed and approved by the Ethics Committee for Researches Involving Human Subjects, Regional Health Promotion Center 8, Nakhonsawan.

Results

Between October 1, 2008 and March 31, 2009, 519 pregnant women who attended the antenatal clinic at Health Promotion Hospital were recruited to the present study. The number of pregnant women who first attended the antenatal clinic during the first, second and third trimester were 376 (72.4%), 131 (25.2%) and 12 (2.3%) cases, respectively. The mean age was 26.8 $\pm$ 6.5 years (range 12-43 years). There were 300 (57.8%) nulliparous and 219 cases (42.2%) had one child or more. Baseline characteristics are shown in Table 2.

The mean hemoglobin level was 12.0 $\pm$ 1.1 g/dl (range 8.2-15.7 g/dl). The mean hematocrit level was 36.2 $\pm$ 3.1% (range 26-48%). The overall prevalence of anemia in pregnant women from WHO (hemoglobin < 11g/dl), WHO (hematocrit < 33%) and CDC criteria were 14.1, 9.8 and 10.6% respectively. SF was performed in the 75 potential cases of anemia. The prevalence of IDA defined by anemia according to SF less than 30 μg/L was found to be 6.0, 4.6 and 4.8%, respectively. Categorized by trimester, the prevalence of anemia by WHO (hemoglobin < 11 g/dl) criteria are 5.9, 33.6 and 50.0% in first, second, and third trimester respectively. The prevalence by WHO (hematocrit < 33%) and CDC criteria were shown in Table 3. In the same manner, the prevalence of IDA categorized by trimester are shown in Table 4.

Table 1. Diagnostic criteria for anemia in pregnancy

	WHO hemoglobin (g/dl)	WHO hematocrit (%)	CDC hemoglobin (g/dl)
First trimester	<11	<33	<11
Second trimester	<11	<33	<10.5
Third trimester	<11	<33	<11

Thalassemia screening was performed in all 519 cases and 209 cases had positive screening tests. Hemoglobin electrophoresis was performed in all 209 cases. There were 31 cases of potential couple at risk for Hemoglobin Bart hydrops fetalis and their blood samples were sent to Regional Medical Sciences Center Nakhonsawan to perform PCR for alpha thalassemia 1 gene (SEA and Thai-deletion type). Thalassemia carriers were found in 138 of 519 cases (26.6%). The prevalence of thalassemia carriers in anemic and non-anemic pregnant women was found to be 39.7 and 24.4%. By WHO criteria (hemoglobin < 11g/dl), IDA was coexisted with thalassemia in 11 from 31 cases (35.5%). The majority of abnormal hemoglobin in both the anemic and non-anemic group was heterozygous Hemoglobin E (27.4 and 22.2%) and homozygous Hemoglobin E (8.2 and 0.9%). All prevalence of thalassemia carriers is shown in Table 5.

Table 2. Baseline characteristics of 519 pregnant women

Characteristics	Number of cases	%
Profession		
Housewife	103	19.8
Student	38	7.3
Labor	141	27.2
Agriculture	93	17.9
Office employee	35	6.7
Government employee	44	8.5
Business owner	65	12.5
Income(bath/month)		
0	28	5.4
1-5,000	72	13.9
5,001-10,000	215	41.4
10,001-15,000	72	13.9
15,001-20,000	81	15.6
>20,000	51	9.8
Education		
Illiterate	1	0.2
Primary school	79	15.2
Secondary school	237	42.6
College school	97	18.7
Bachelor at least	121	23.3

Discussion

The prevalence of anemia during pregnancy in the present study was lower than previous studies[11-13]. This may be due to the different population background such as income and education. Health Promotion Hospital is not covered by Health Insurance of the government. However, most patients were in the middle class with income among 5,000-20,000 baht/month, extreme poverty cases rarely go to Health Promotion Hospital. From Table 2, all cases of no income were students who live with their families.

Table 3. Prevalence of anemia in pregnancy by different diagnostic criteria

	WHO (Hb < 11 g/dl)		WHO (Hct < 33%)		CDC	
	Cases	%	Cases	%	Cases	%
First trimester 376 cases	22	5.9	15	4.0	22	5.9
Second trimester 131 cases	44	33.6	30	22.9	27	20.6
Third trimester 12 cases	6	50.0	6	50.0	6	50.0
Total 519 cases	73	14.1	51	9.8	55	10.6

Table 4. Prevalence of iron deficiency anemia in pregnancy by different diagnostic criteria

	WHO (Hb < 11 g/dl)		WHO (Hct < 33%)		CDC	
	Cases	%	Cases	%	Cases	%
First trimester 376 cases	5	1.3	3	0.8	5	1.3
Second trimester 131 cases	21	15.3	16	12.2	15	11.5
Third trimester 12 cases	5	41.7	5	41.7	5	41.7
Total 519 cases	31	6.0	24	4.6	25	4.8

Table 5. Prevalence of thalassemia in anemic and non-anemic group

	Pregnancy without anemia		Pregnancy with anemia (Hb < 11 g/dl)		Total		Pregnancy with IDA (Hb < 11g/dl + SF < 30 μg/L)	
	Cases	%	Cases	%	Cases	%	Cases	%
Negative screening	277	62.1	33	45.2	310	59.7	15	48.4
Positive screening	169	37.9	40	54.8	209	40.3	16	51.6
Normal Hb typing	60	13.5	11	15.1	71	13.7	5	16.1
Alpha thal-1 trait	3	0.7	2	2.7	5	1.0	0	0
Hb E trait	99	22.2	20	27.4	119	22.9	9	29.0
Homozygous Hb E	4	0.9	6	8.2	10	1.9	1	3.2
Beta trait	3	0.7	1	1.4	4	0.8	1	3.2
Total thalassemia carriers	109	24.4	29	39.7	138	26.6	11	35.5
Total cases	446	100	73	100	519	100	31	100

The prevalence of IDA from the present study, only 4.6-6.0% according to diagnostic criteria, was obviously lower than the results from previous studies too[12,13]. This may be due to different diagnostic criteria. The previous studies did not perform SF in all anemic cases and IDA was determined by SF or significant rising of hemoglobin or hematocrit after therapeutic trial of iron supplementation. The cutoff value of SF is still in debate. Level less than 12-15 μg/L confirm IDA but has low sensitivity[14-17]. In pregnancy, Van den Broek et al found that a cutoff point of 30 μg/L has an 85% positive and a 90% negative predictive value[19]. In the present study, the authors used the cutoff value of 30 μg/L according to the result from van den Broek study and recommendation from Thai Society of Hematology[21].

By trimester, the prevalence of IDA obviously increased from first to third trimester. This finding was the same as many previous studies[11-13] that found women at late antenatal visit were at risk for anemia during pregnancy. This finding may reflect the importance of iron supplementation in early pregnancy.

WHO (hemoglobin < 11g/dl) should be the most suitable criteria for population screening. Theoretically, hemoglobin is more sensitive than hematocrit for IDA screening. Hematocrit from most automated machine is calculated from mean corpuscular volume (MCV) x number of red blood cells. Hematocrit does not change until the late stage of IDA because MCV is changed only in late stage of IDA. The result that prevalence of IDA from WHO (hemoglobin < 11g/dl) criteria (6.0%) was higher than WHO (hematocrit < 33%) criteria (4.6%) confirmed this theory. WHO (hemoglobin < 11g/dl) also are more convenient than CDC criteria because CDC criteria needs accurate gestational age that still a problem in most antenatal clinics in Thailand. The authors cannot directly calculate the sensitivity and specificity of these tests because SF is not a true gold standard for iron assessment.

The prevalence of thalassemia carriers in the present study was 26.6% (138 from 519 cases). The true prevalence of alpha thalassemia1 trait should be higher than the results from the present study because PCR for alpha-thalassemia 1 was done in only couple at risk for Hb Bart hydrops fetalis. The prevalence of thalassemia carriers in anemic pregnant women was higher than non-anemic group (39.7 and 24.4%) (Table 5). That was not a causal relationship because not all thalassemia carriers were anemia. The mean hemoglobin level in heterozygous hemoglobin E carriers was 11.6 $\pm$ 0.8 g/dl, which was slightly lower than mean hemoglobin level in all samples (12.0 $\pm$ 1.1 g/dl). In the present study, iron deficiency anemia coexisted with thalassemia carriers in 11 from 31 cases (35.5%). Therefore, the authors couldn't exclude the condition of iron deficiency anemia while the pregnant women were thalassemia carriers.

Despite WHO and US Preventive Services Task Force recommended routine screening for anemia in all pregnant women, recommendation for routine iron supplementation was not clear[2,18]. There were many emerging evidences concerning the potential harmful effect of iron supplementation in pregnancy[22-24]. The future target should be how to screen and treat "iron

deficiency" anemic pregnant women, not only anemic pregnant women.

The result from the present study confirmed that hemoglobin < 11 g/dl was the most suitable screening criteria for anemia. Presently, automated CBC is available in nearly all hospitals in Thailand. Capillary hematocrit should be replaced by CBC for anemia screening even if CBC is slightly more expensive as CBC has higher sensitivity and lower technical errors for hemoglobin level than capillary hematocrit. Furthermore, CBC has additional benefits from other blood parameters such as MCV and MCHC for thalassemia screening. However, how to assess iron status and diagnostic test for IDA is still a challenge. SF is costly and not widely available. Future prospective study about accuracy, potential risks, and cost effectiveness of therapeutic trial of iron supplementation[20,21] as well as therapeutic and diagnostic test in low-resource hospital should be done.

References

1. World Health Organization. The World Health Report 2002: Reducing risks, promoting healthy life. France: WHO Press; 2002.
2. World Health Organization. Iron deficiency anaemia: assessment, prevention, and control: A guide for programme managers. Geneva: WHO Press; 2001.
3. World Health Organization. Worldwide prevalence of anaemia 1993-2005: WHO Global database on anaemia. Geneva: WHO Press; 2008.
4. Centers for Disease Control (CDC). CDC criteria for anemia in children and childbearing-aged women. MMWR Morb Mortal Wkly Rep 1989; 38: 400-4.
5. Klebanoff MA, Shiono PH, Selby JV, Trachtenberg AI, Graubard BI. Anemia and spontaneous preterm birth. Am J Obstet Gynecol 1991; 164: 59-63.
6. Scholl TO, Hediger ML, Fischer RL, Shearer JW. Anemia vs iron deficiency: increased risk of preterm delivery in a prospective study. Am J Clin Nutr 1992; 55: 985-8.
7. Lieberman E, Ryan KJ, Monson RR, Schoenbaum SC. Association of maternal hematocrit with premature labor. Am J Obstet Gynecol 1988; 159: 107-14.
8. Scanlon KS, Yip R, Schieve LA, Cogswell ME. High and low hemoglobin levels during pregnancy: differential risks for preterm birth and small for gestational age. Obstet Gynecol 2000; 96: 741-8.
9. Levy A, Fraser D, Katz M, Mazor M, Sheiner E. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery. Eur J Obstet Gynecol Reprod Biol 2005; 122: 182-6.
10. Tomashek KM, Ananth CV, Cogswell ME. Risk of stillbirth in relation to maternal haemoglobin concentration during pregnancy. Matern Child Nutr 2006; 2: 19-28.
11. Wanapirak C, Muninthorn W, Sanguansermsri T, Dhananjayanonda P, Tongsong T. Prevalence of thalassemia in pregnant women at Maharaj Nakorn Chiang Mai Hospital. J Med Assoc Thai 2004; 87: 1415-8.
12. Chotnopparatpattara P, Limpongsanurak S, Charnngam P. The prevalence and risk factors of anemia in pregnant women. J Med Assoc Thai 2003; 86: 1001-7.
13. Sukrat B, Sirichotiyakul S. The prevalence and causes of anemia during pregnancy in Maharaj Nakorn Chiang Mai Hospital. J Med Assoc Thai 2006; 89(Suppl 4): S142-6.
14. Fairbanks VF. Laboratory testing for iron status. Hosp Pract (Off Ed) 1991; 26(Suppl 3): 17-24.
15. Zanella A, Gridelli L, Berzuini A, Colotti MT, Mozzi F, Milani S, et al. Sensitivity and predictive value of serum ferritin and free erythrocyte protoporphyrin for iron deficiency. J Lab Clin Med 1989; 113: 73-8.
16. Guyatt GH, Oxman AD, Ali M, Willan A, McIlroy W, Patterson C. Laboratory diagnosis of iron-deficiency anemia: an overview. J Gen Intern Med 1992; 7: 145-53.
17. Cook JD. Diagnosis and management of iron-deficiency anaemia. Best Pract Res Clin Haematol 2005; 18: 319-32.
18. U.S. Preventive Services Task Force. Screening for iron deficiency anemia-including iron prophylaxis. In: Guide to clinical preventive services. 2nd ed. Baltimore: Williams & Wilkins; 1996:231-46.
19. van den Broek NR, Letsky EA, White SA, Shenkin A. Iron status in pregnant women: which measurements are valid? Br J Haematol 1998; 103: 817-24.
20. Nuchprayoon I, Sukthawee B, Nuchprayoon T. Red cell indices and therapeutic trial of iron in diagnostic work-up for anemic Thai females. J Med Assoc Thai 2003; 86(Suppl 2): S160-9.
21. Jetsrisuparb A, Sriphaisal T, Hathirat P, Futrakul P, Seksarn P, Lekakul A. Iron deficiency anemia: Evidence-based guideline for treating hematologic

disease in Thailand. Bangkok: Beyond Enterprise; 2000.
22. Ziaei S, Norrozi M, Faghihzadeh S, Jafarbegloo E. A randomised placebo-controlled trial to determine the effect of iron supplementation on pregnancy outcome in pregnant women with haemoglobin > or = 13.2 g/dl. BJOG 2007; 114: 684-8.
23. Chan KK, Chan BC, Lam KF, Tam S, Lao TT. Iron supplement in pregnancy and development of gestational diabetes - a randomised placebo-controlled trial. BJOG 2009; 116: 789-97.
24. Lachili B, Hininger I, Faure H, Arnaud J, Richard MJ, Favier A, et al. Increased lipid peroxidation in pregnant women after iron and vitamin C supplementation. Biol Trace Elem Res 2001; 83: 103-10.

ความชุกของภาวะโลหิตจางจากการขาดธาตุเหล็กในหญิงตั้งครรภ์

บุญฤทธิ์ สุขรัตน์, ปราณี สุวัฒนพิเศษ, ศุภฤกษ์ ศิริทวี, ธัญญาภรณ์ พวงทอง, กรวิกา ภู่พงศ์พันธ์กุล

วัตถุประสงค์: *เพื่อศึกษาถึงความชุกของภาวะโลหิตจางจากการขาดธาตุเหล็กในหญิงตั้งครรภ์ และเปรียบเทียบความชุกของธาลัสซีเมียในหญิงตั้งครรภ์กลุ่มที่มี และไม่มีภาวะโลหิตจาง*

วัสดุและวิธีการ: *หญิงตั้งครรภ์ที่มาฝากครรภ์เป็นครั้งแรกจะได้รับการเก็บเลือดเพื่อตรวจ complete blood count ในหญิงตั้งครรภ์ที่มีระดับฮีโมโกลบิน < 11 g/dl หรือมีระดับฮีมาโทคริต < 33%, จะได้รับการตรวจหาระดับ serum ferritin การหาความชุกของภาวะโลหิตจางในหญิงตั้งครรภ์ใช้เกณฑ์ของ Centers for Disease Control and Prevention และองค์การอนามัยโลก ภาวะโลหิตจางจากการขาดธาตุเหล็กหมายถึงหญิงตั้งครรภ์ที่มีภาวะโลหิตจางตามเกณฑ์ที่กำหนดร่วมกับมีระดับ serum ferritin ต่ำกว่า 30 μg/L ในรายที่การตรวจคัดกรองธาลัสซีเมียผิดปกติจะได้รับการตรวจ hemoglobin electrophoresis และ polymerase chain reaction (PCR) for diagnosis of alpha thalassemia 1 (SEA and Thai-deletion type) ข้อมูลจะถูกวิเคราะห์ด้วยสถิติเชิงพรรณนาและนำเสนอในรูปแบบของค่าเฉลี่ย, ร้อยละและส่วนเบี่ยงเบนมาตรฐาน*

ผลการศึกษา: *มีหญิงตั้งครรภ์ทั้งหมด 519 คน เข้าร่วมในการศึกษาความชุกของภาวะโลหิตจางตามเกณฑ์ของ WHO (ฮีโมโกลบิน < 11 g/dl), WHO (ฮีมาโทคริต < 33%) และ CDC เท่ากับร้อยละ 14.1, 9.8 และ 10.6 ตามลำดับ ความชุกของภาวะโลหิตจางจากการขาดธาตุเหล็กเท่ากับร้อยละ 6.0, 4.6 และ 4.8 ตามลำดับเดิม ความชุกของธาลัสซีเมียเท่ากับร้อยละ 39.7 ในกลุ่มที่มีภาวะโลหิตจาง และเท่ากับร้อยละ 24.4 ในกลุ่มที่ไม่มีภาวะโลหิตจาง*

สรุป: *ความชุกของภาวะโลหิตจาง และภาวะโลหิตจางจากการขาดธาตุเหล็กจะมีค่าสูงที่สุดเมื่อใช้เกณฑ์การวินิจฉัยขององค์การอนามัยโลก (ฮีโมโกลบิน < 11 g/dl) โดยเท่ากับร้อยละ 14.1 และร้อยละ 6.0 ตามลำดับ ความชุกของธาลัสซีเมียในกลุ่มที่มีภาวะโลหิตจาง (ร้อยละ 39.7) สูงกว่าในกลุ่มที่ไม่มีภาวะโลหิตจาง (ร้อยละ 24.4)*