

Preliminary study for the prevalence and causes of anemia in pregnant women attending an Antenatal Care Unit in different periods of gestation

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ABSTRACT

Background: One of common complications of pregnancy is an anemia which is effected by various causes. Anemia can develop throughout the pregnancy period and increase in severity upon the gestation times. WHO recommends all pregnant women should attend an antenatal care (ANC) unit in the first trimester of gestation for healthy promotion and complication prevention during pregnancy and after birth.

Objectives: The aim of this preliminary study is to find out the prevalence and causes of anemia in pregnant women who start attending an ANC program at different time points of gestation.

Materials and methods: Cross-sectional study was performed during May 2015 -February 2016. Hematological parameters were examined in all 190 pregnant women attended the ANC unit at Nayong Hospital. Participants were divided into three groups according to period of gestation at the first time of ANC admission. Serum ferritin, thalassemia screening, and hemoglobin typing were determined in anemia cases to analyze causes of anemia. Prevalence of anemia at each time point ANC attended groups were calculated. Mann-Whitney U test was used to compare the different of parameters between the groups.

Results: Prevalence of anemia in all attended pregnant women was 22.1%. According to the period of gestation at the first time of ANC admission, the prevalence of anemia was 17.2% (15 of 87) at the first trimester group, 22.5% (20 of 89) at the second trimester, and 50.0% (7 of 14) at the third trimester group. Levels of hemoglobin and hematocrit of the second and the third groups were significantly different from the first trimester group with $p < 0.05$. MCHC of the third trimester group showed significantly different from both the first and second trimester groups, $p < 0.05$. Causes of anemia were thalassemia/abnormal hemoglobin carriers in 11 cases (5.8%), Iron deficiency anemia (IDA) in 10 cases (5.3%), IDA with thalassemia/abnormal hemoglobin carriers in 6 cases (3.2%), and anemia with other causes in 15 cases (7.9%). For thalassemia cases, HbE trait without α -thalassemia had the highest prevalence (44.4%). There were two cases of severe anemia, which were Hb H-CS disease and IDA.

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Conclusion: Prevalence of anemia in pregnant women in this presentation was still high and increased throughout the period of gestation. Causes of anemia, such as IDA, can be prevented by early attention to an ANC unit. The promotion

of an ANC program for married couples and adolescent women should be considered to improve maternal and fetal health quality during pregnancy and after-birth.

Introduction

Anemia is a common complication during pregnancy. In 2011, World Health Organization (WHO) reported the prevalence of anemia in pregnant women to be about 41.8% worldwide, which is a higher rate than non-pregnant women.¹ In Thai population, the prevalence of anemia in pregnant women was still high.¹⁻³ Consistent studies had been reported in many areas.^{4, 5} Physiology changed during pregnancy and the increasing requirement of nutrients for red blood cell (RBC) production, both for mother and fetus, leads to anemia in insufficient nutrients taken for the mother.⁸⁻¹² Iron is the main component of RBC and a lack of iron can cause iron deficiency anemia (IDA). IDA is the most common cause of nutrient deficiency anemia in all ages. In pregnant women, at least half of anemia is caused by IDA. During pregnancy, the average amount of iron requirement is about 1200 mg or 4.4 mg/day, of which 450 mg can be used for the mother, about 350 mg for fetus development and 250 mg is lost via the digestion tract.⁹ As the requirement is increased upon the period of gestation, the prevalence of anemia is elevated in the last trimester of gestation. Thalassemia is another cause of anemia in pregnant women.¹¹ About 60% of the Thai population are thalassemia/abnormal hemoglobin carriers.¹⁰ Mothers carrying thalassemic/abnormal hemoglobin genes may have anemia during pregnancy. In high risk couples, meaning parents both carrying the same thalassemic/abnormal genes, the baby will have thalassemic and hemoglobinopathic diseases. There are three types of severe thalassemia diseases in Thailand: homozygous α -thalassemia-1, homozygous β -thalassemia and β -thalassemia/hemoglobin E disease, which are controlled for reducing incidences. These severe types can cause complications for the mother during pregnancy and also affect the fetus development.^{11, 13}

WHO recommends all pregnant women should attend an antenatal care (ANC) unit, which provides a program for the prevention and treatment of health problems throughout the pregnancy. Because of the severity of complications being high risk in the later period of pregnancy, all pregnant women should be screened and prevented for possible complications early on. The full course of ANC consists of attending four times with the first time during 8-12 weeks or the first trimester of gestation.¹⁴ The supplement of necessary nutrients, such as folic acid and iron, will be given to support the increase in demand during pregnancy and reduce the risk of low birth weight, maternal anemia and iron deficiency. Thalassemia risked couples should attend a genetic counseling process and prenatal diagnosis for information acknowledgement about the disease. Thus, an ANC is useful for complications prevention and to improve the quality of the pregnancy throughout the gestation and after delivery. However, anemia is still a common problem in pregnancy and lots of pregnant women are

not concerned about the suitable time for ANC attention. This preliminary study aims to find out the prevalence and causes of anemia in pregnant women who attended an ANC program at different time points of gestation. The data will be informatively used for all pregnant women about anemia and the importance of ANC programs.

Materials and methods

1. Participants and data collection

This study is a cross-sectional study. The subjects were 190 pregnant women, who attended Nayong Hospital in Trang Province, Thailand from May 2015 - February 2016. Period of gestation at the first time of ANC unit submitted and general data was recorded by Laboratory Division of the hospital. This study was approved by the Board of Committee on Ethics, Walailak University, Thailand (No. 15/041). Pregnant women were divided into three groups based on period of gestation at the first time of hospital submission. Group I was 1-12 weeks of gestation, first trimester. Group II was 13-27 weeks of gestation, second trimester, and Group III was 28-40 weeks of gestation, third trimester. Participants with incomplete data were excluded.

2. Hematological parameters and serum ferritin

Blood samples at the first time of hospital submission were collected for hematological parameters testing using a Mindray BC5300 hematology analyzer (Shenzhen, China). Hematological parameters included RBC count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), and red cell distribution width (RDW) results from the hospital were analyzed for anemia evaluation. Serum ferritin (SF) was also tested in anemic cases for iron deficiency determination using the immunologic method, VITROS ECI/ECiQ Immunodiagnostic Systems (Ortho-Clinical Diagnostics, Inc, New York, United States). Hb less than 11 g/dL for the first and third trimester, less than 10.5 g/dL for the second trimester, was defined as anemia.⁷ 15 SF<12 μ g/L with anemia was defined as IDA.¹³ The severity of anemia was categorized as following: mild, Hb 10.0-10.9 g/dl for the first and third trimester and 10.0-10.5 g/dL for the second trimester, moderate, Hb 7.0-9.9 g/dL and severe, Hb<7.0 g/dL.^{6, 13}

3. Thalassemia screening and hemoglobin typing

Thalassemia/abnormal hemoglobin were further studied in pregnant women who had anemia. MCV and dichlorophenol indophenol precipitation (DCIP) were used as the screening tests for Thalassemia/abnormal hemoglobin and hemoglobin E, respectively. Hemoglobin typing was performed by the HPLC technique VARIANT II (Biorad, California, USA) in subjects who had MCV<80 fL and/or DCIP positive. The types and % of hemoglobin were used for

thalassemia classification as described previously.¹⁶ The α -thalassemia was determined by PCR method.

4. Statistical analysis

Data was determined for normality of the distribution using the Kolmogorov-Smirnov test. The difference in parameters between groups was analyzed by the Mann-Whitney U Test. The p value of less than 0.05 was considered significant.

Results

General data

The study included 190 pregnant women who attended

the ANC unit of the hospital. Participants were divided into 3 groups based on period of gestation at the first ANC submission. Number and time of gestation of each group are shown in Table 1. Group I, II and III had 87, 89 and 14 cases, respectively. The average ages of groups I, II, and III were 29.7 ± 9.0 , 25.3 ± 7.1 and 25.2 ± 7.8 years old, respectively. Seventy-six cases (40%) were in the second time of gestation. Another 31.1%, 17.9% and 11.1% of all pregnant women were in the first, third and over 3 times of gestation, respectively.

Table 1 Summarized of 190 cases in total; period of gestation at the first time of ANC registration and times of current gestation.

Period of gestation	Age* (years)	Times of gestation (n)			
		1	2	3	>3
1 st trimester (n=87)	29.7 ± 9.0	27	39	14	7
2 nd trimester (n=89)	25.3 ± 7.1	28	32	18	11
3 th trimester (n=14)	25.2 ± 7.8	4	5	2	3
Total	190	59	76	34	21

* mean $\pm$ SD.

Hematological parameters

At the first time of ANC submission, complete blood count was analyzed for anemia diagnosis. Hb levels of the pregnant women in the first, second, and third trimesters were 12.1 (6.3-15.7), 11.3 (6.7-14.2), and 10.8 (9.2-12.6) g/dL, respectively. Hematocrit levels were 36.0% (22.0-46.1%),

33.3% (24.2-42.0%), and 33.8% (28.8-36.8%) in first, second, and third trimester groups, respectively. The results showed that RBC, Hb, Hct and MCHC between of group I and III were significantly different with $p < 0.05$. Only Hb and Hct showed significantly different between group I and II, $p < 0.05$ (Table 2).

Table 2 Hematological parameters of pregnancy attended the first ANC in different period of gestation.

Period of gestation	RBC ($\times 10^6/\mu\text{L}$)	Hb (g/dL)	Hct (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)
1 st trimester (n=87)	4.23 (2.99-5.35)	12.1 (6.3-15.7)	36.0 (22.0-46.1)	85 (58-93)	28.9 (17.7-32.9)	33.9 (28.7-36.0)	12.6 (11.1-26.0)
2 nd trimester (n=89)	4.12 (3.21-5.54)	11.3 ^a (6.7-14.2)	33.3 ^a (24.2-42.0)	85 (53-97)	28.4 (15.5-33.9)	33.7 (27.7-35.6)	12.9 (11.3-25.2)
3 th trimester (n=14)	3.90 ^a (3.53-4.78)	10.8 ^a (9.2-12.6)	33.8 ^a (28.8-36.8)	86 (71-96)	27.8 (22.0-32.8)	32.6 ^{a, b} (30.9-34.5)	12.8 (12.0-18.3)

Data were shown in median (minimum – maximum).

^{a, b} Significantly difference from the 1st and 2nd trimester groups, respectively (Mann-Whitney U test, $p < 0.05$)

Anemia and causes

Participants with anemia accounted for 42 cases in total with a prevalence of 22.1%, which consisted of 11 thalassemia/abnormal haemoglobin carrier cases (5.8%), 10 IDA cases (5.3%), 6 IDA with thalassemia/abnormal haemoglobin carrier cases (3.2%), and 15 anemia with other causes cases (7.9%), as shown in Table 3. The prevalence of anemia was 17.2% (15 of 87 cases) in the first trimester group, 22.5% (20 of 89) in the second trimester, and 50.0% (7 of 14 cases) in the third trimester group. In all anemia subjects, serum ferritin was examined for IDA diagnosis.

MCV and DCIP were used for thalassemia and abnormal haemoglobin screening and confirmed by haemoglobin typing. The results showed an increasing of IDA was upon the period of gestation (Table 3). There were 10 cases of IDA in total, consisting of 3 of 87 cases (3.4%), 5 of 89 cases (5.6%) and 2 of 14 cases (14.3%) in groups I, II and III, respectively. IDA with thalassemia/abnormal haemoglobin carrier was found in 6 cases. Anemia with other causes had 15 cases (7.9%), consisting of 6 cases (6.9%), 8 cases (9.0%) and 1 case (7.1%) in groups I, II and III, respectively. The severity of anemia is categorized by the level of Hb,

as defined in Table 3. There were 35 cases of thalassemia/ abnormal haemoglobin but only 18 cases (51.4%) were in anemia. HbE traits without α -thalassemia had the highest prevalence with 44.4% (Table 4). Only two cases of anemia

were severe, of which one case was in the first trimester and another in the second trimester, which were Hb H-CS disease and IDA, respectively.

Table 3 Prevalence of anemia, causes and severity in the pregnancy attended the first ANC in different period of gestation.

				Period of gestation		
			N (%) Total = 190	1 st trimester (n=87)	2 nd trimester (n=89)	3 th trimester (n=14)
Anemia cases			42 (22.1)	15 (17.2)	20 (22.5)	7 (50.0)
Causes of anemia	Anemia with thalassemia carrier/ abnormal hemoglobin		11 (5.8)	5 (5.7)	4 (4.5)	2 (14.3)
	IDA		10 (5.3)	3 (3.4)	5 (5.6)	2 (14.3)
	IDA with thalassemia carrier/ abnormal hemoglobin		6 (3.2)	1 (1.1)	3 (3.4)	2 (14.3)
	Anemia with other causes		15 (7.9)	6 (6.9)	8 (9.0)	1 (7.1)
Anemia severity			Anemia (cases)	1 st trimester	2 nd trimester	3 th trimester
Categories	Mild		28	12	11	5
	Moderate		12	2	8	2
	Severe		2	1	1	-

Table 4 Types of thalassemia/abnormal hemoglobin and number of cases.

Types of thalassemia/abnormal hemoglobin	Case (n)	Cases with anemia (%)
HbH-CS disease	1	1 (5.6)
α -thalassemia-1 trait	3	3 (1.7)
β -thalassemia trait without α -thalassemia	5	3 (1.7)
HbE trait without α -thalassemia	23	8 (44.4)
HbE trait with α -thalassemia	1	1 (5.6)
Homozygous HbE	1	1 (5.6)
Suspected abnormal Hb	1	0 (0)
Total	35	18 (51.4)

Discussion

Anemia is a condition in which the concentration of hemoglobin is less than normal range. Cut-off value for adult males and females is 13.0 g/dL and 12.0 g/dL, respectively.¹⁷ Hemoglobin is an important component in RBC that plays a role in oxygen being carried throughout the body. The reduction in RBC production or increase in RBC destruction by any causes, either genetic defects or acquired diseases, leads to anemia. Thus, anemia can occur in all ages and worldwide. Pregnant women are the highest risk group of anemia due to the physiology changes during pregnancy.^{7, 9, 10} The cut-off value of Hb level for the second trimester is lower than the first and third trimesters, which are 10.5 g/dL and 11 g/dL for the second trimester and the first/third trimester, respectively.^{7, 15} Following this criteria, the prevalence of anemia among pregnant women in the present study was 17.2%, 22.5 and 50.0% in pregnant

women who attended the ANC program at the first, second and third trimester of gestation, respectively. Causes of increasing in prevalence upon the period of gestation are the iron demand for RBC production and fetus development. In addition, plasma volume which significantly increasing in the second trimester and remain during pregnancy causes hemodilution and induces RBC production.^{7, 9, 10}

An oral iron supplement is one part of the nutrient supplements provided in all pregnant women who attend programs to reduce the risk of IDA. WHO recommends pregnant women should attend an ANC program early, within 8-12 weeks of gestation, for the comprehensive prevention of possible complications, including anemia.¹⁴ Pregnant women who admit to the ANC in the later period of gestation may have a greater chance of anemia developing due to insufficient iron intake. This result supports the ANC guideline that the prevalence of IDA is highest in the

third trimester ANC admitted group. In addition, this study detect only the SF which is recommended parameter for IDA diagnosis because of its stable, unaffected by recent iron intake, reflects iron stores accurately.^{8, 10} However, SF may elevated in inflammatory, so it might be the limitation of this report. Furthermore, Hct levels detected at 32-34 weeks of gestation in the IDA pregnant women who attended the ANC at the first and second trimester were increased (data not show). This improvement may result from the sufficient replacement of iron supplementation. The less number of pregnant women in the third trimester ANC admitted group in this study may result from the limit in period of data collection. In addition, it may indicate the awareness of maternal in early ANC attention.

Thalassemia is high in prevalence in Thailand.^{18, 19} Thalassemia gene carriers can cause anemia during pregnancy and low birth weight.²⁰ Twenty-six percentage of anemia cases in this report are accounted by thalassemia/abnormal hemoglobin carriers and 14.3% are thalassemia/abnormal hemoglobin carriers with IDA. The most frequent type is hemoglobin E trait, which is consistent with the other parts of Thailand.²¹⁻²³ The genetic counseling and screening program for thalassemia risk couples is an important step for safe pregnancy planning and reducing the incidence of thalassemia.^{11, 24} Thalassemic carrier pregnant women should be advised about complications prevention during pregnancy. In addition, anemia in pregnancy may be caused by folate and vitamin B12 deficiency, glucose-6-phosphate deficiency, Southeast Asian ovalocytosis (SAO) or anemia of chronic diseases.⁸ Nevertheless, this study determined only IDA and thalassemia.

Moreover, severity of anemia during pregnancy affects both maternal and fetal health. In mild cases, anemia may not effect but the insufficient amount of iron in the late period of gestation should be of concern. Weakness or fatigue may occur in moderate cases. For severe cases, the mother may have palpitations, tachycardia, and breathlessness and this may lead to preterm labor.^{8, 15} Although, most anemic pregnant cases in this presentation were mild anemia, the treatment of certain causes or prevention for severity improvement is necessary and should be done early.

Conclusion

This present study indicates that the prevalence of anemia in pregnant women is still high and increases in prevalence upon the period of gestation which may affect the maternal health and fetal development. The promotion of an ANC program for married couples and in adolescent women is necessary to improve the health quality during pregnancy and after-birth both for maternal and fetal health.

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Conflict of interests:

The authors claimed no conflicts of interests.

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