

Prevalence of Anemia and Abnormal Hemoglobin Typing Results in Hill Tribe Women in Nan, Thailand

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Objective: To investigate the prevalence of anemia and hemoglobin types among hill tribe women of Nan Province, Thailand

Materials and Methods: A cross-sectional study was conducted in 658 women from Hmong, Khamu, Lua, Mien and Mlabri hill tribes who lived in Tha Wang Pha, Pua and Bo Kluea Districts of Nan Province. Complete blood counts and hemoglobin typing were performed

Results: The prevalence of anemia in the overall group was 12.5%. The highest and lowest prevalence rates of anemia were detected in Mlabri (42.9%) and Mien women (9.5%). In the overall group the prevalence of hemoglobin E traits was 9.1% and beta-thalassemia was 2.1%. Khamu women had the highest prevalence (8.3%) of beta-thalassemia trait whereas Lua and Mlabri women had a higher prevalence of hemoglobin E trait (14.4% and 14.3%, respectively) than other tribes.

Conclusion: The prevalence of anemia and abnormal hemoglobin typing among hill tribe women of Nan Province in northern Thailand varied among hill tribes. These data may be beneficial for the prevention and control of thalassemia in hill tribe population and in genetic counseling.

Keywords: Anemia, Hemoglobinopathy, Thalassemia, Hill tribes, Nan Province

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Thalassemia is a group of inherited red blood cell disorders caused by mutations of globin genes, resulting in imbalanced globin synthesis, ineffective erythropoiesis and varying degrees of chronic hemolytic anemia⁽¹⁾. Different thalassemia genotypes have greatly variable severity. The two major alpha thalassemic diseases are Hb Bart's hydrops fetalis or homozygous alpha thalassemia 1 (homozygous alpha⁺ thalassemia), and Hb H disease that occurs from interaction between alpha thalassemia 1 (alpha⁺ thalassemia) and alpha thalassemia 2 (alpha⁺ thalassemia) or between

alpha thalassemia 1 and Hb Constant Spring (Hb CS). In beta thalassemia/Hb E disease, although the patients have identical genotype, the degree of anemia varies greatly with hemoglobin levels. Thalassemia does not only affect individual health, but it also has a substantial impact on the family and psychosocial and economic life of patients. Thalassemia and abnormal hemoglobin are common in Southeast Asia. In Thailand, the prevalence rates of thalassemia in general population are as follows: the average frequencies are 20 to 30% for alpha-thalassemia, 3 to 9% for beta-thalassemia, and up to 50% for HbE⁽²⁾. HbCS gene frequencies vary between 1 and 8%⁽²⁾. HbE is commonly observed in Southeast Asia, with a frequency of 50 to 60% in the population in the region at the junction of Thailand, Laos and Cambodia⁽³⁾.

The hill tribe people of northern Thailand live in the country's mountainous border areas. In 2015, the population in Nan Province in northern Thailand was 479,518, and 19% of the population is hill tribes⁽⁴⁾. The hill tribes are classified into five main groups: Hmong, Khamu, Lua, Mien and Mlabri. Socioeconomic development in hill tribe villages is poor. When the patients in hill tribe regions have thalassemia disease, it will make them more suffer from a low quality of life⁽⁵⁾. This study aimed to investigate the prevalence of anemia and hemoglobin types among women of the five main hill tribes of Nan Province, Thailand. Because thalassemia is

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inherited disorders, these data will be beneficial for the prevention and control of thalassemia in hill tribe population and in genetic counseling.

Materials and Methods

Participants

The present study included 658 Thai hill tribe women aged 30 to 60 years who were living in Tha Wang Pha, Pua and Bo Kluea districts of Nan Province. The women were from the main hill tribes in the region: Lua, Hmong, Mien, Khamu and Mlabri. All blood specimens were collected between November 9 and November 13, 2015. Demographic data, complete blood count (CBC) and hemoglobin typing results were collected and analyzed. The study was approved by the Ethics Committee for Human Research of Chulabhorn Research Institute (EC No. 038/2560).

CBC and hemoglobin analysis

All blood specimens were submitted for CBC, with erythrocyte indices obtained using an automated blood cell counter. Anemia was defined as a hemoglobin concentration less than 12 g/dL. The type and level of hemoglobin fractions were analyzed by capillary electrophoresis hemoglobin analyzer (Capillarys 2 Flex Piercing, Sebia, Lisses, France) combined with mean corpuscular volume (MCV). However, polymerase chain reaction (PCR) testing for alpha-thalassemia was not possible in this study due to a lack of appropriate facilities; therefore, the diagnosis of thalassemia and abnormal hemoglobin was estimated⁽⁶⁾. In cases with hemoglobin typing is A2A and hemoglobin A2 (HbA2) levels is in the normal range (HbA2 less than 4%) and MCV ≥ 80 fL, normal or non-clinically significant thalassemia was diagnosed. Moreover, in cases with hemoglobin typing is A2A and HbA2 levels is in the normal range but MCV < 80 fL, normal hemoglobin with or without alpha-thalassemia was diagnosed. Furthermore, in cases with hemoglobin typing is A2A and HbA2 levels 4 to 8% and MCV < 80 fL, beta-thalassemia trait with or without alpha-thalassemia was indicated.

HbE trait was diagnosed in cases with hemoglobin typing is EA and HbE level of 25 to 35%. For hemoglobin typing is EA and HbE $< 25\%$, HbE trait with or without alpha-thalassemia was noted. With hemoglobin typing is EE and HbE $> 80\%$, homozygous HbE with or without alpha-thalassemia was indicated. When hemoglobin typing is A2AH or A2A Bart's H was diagnosed as hemoglobin H disease (HbH). HbH disease with HbCS was considered when hemoglobin typing is CSA2A Bart's H. Hemoglobin typing CS A2A was determined for those with suspected homozygous or heterozygous HbCS. Hemoglobin typing A2F was interpreted as homozygous beta⁰-thalassemia with or without alpha-thalassemia. Cases with hemoglobin typing EF were defined as beta⁰-thalassemia/HbE. Hemoglobin typing A2FA was diagnosed as suspected beta⁺-thalassemia/beta⁺-thalassemia or beta⁻-thalassemia/beta-thalassemia with or without alpha-thalassemia. Hemoglobin typing EFA indicated beta⁺-thalassemia/HbE with or without alpha-

thalassemia.

Statistical analysis

Demographic data and prevalence of anemia and hemoglobin typing results among hill tribe women were presented using descriptive statistics, frequency, percentage, mean, standard deviation (SD), median and range. All data analysis was performed using Stata/SE version 12.1 (StataCorp., College Station, TX, USA).

Results

The demographic characteristics of the participants are given in Table 1. Among the 658 participants, there were 313 (47.6%), 175 (26.6%), 127 (19.3%), 36 (5.5%), and 7 (1.1%) women from the Lua, Hmong, Mien, Khamu and Mlabri hill tribes, respectively. Among Lua, Hmong, Mien, and Khamu women, the mean age was 43.9 years; Mlabri women had an average age of 38.0 years. Women from most hill tribes had no schooling, but 55.6% of Khamu women had completed primary school. Nearly all participants (72.3%) had an income of less than 5,000 Baht per month.

The prevalence of anemia among the hill tribe women was 12.5%, with a high prevalence in Mlabri and Khamu women, at 42.9% and 19.4%, respectively. Women in the Mien population had the lowest prevalence of anemia (9.5%). Abnormal MCV was detected in 18.5% of all participants, with Mlabri and Hmong women having the highest (42.9%) and lowest prevalence (11.4%), respectively. Abnormal mean corpuscular hemoglobin (MCH) was found in 189/658 (28.7%) participants including Mlabri (57.1%), Lua (33.9%), and Khamu (33.3%) women. There was only one Lua participant with abnormal mean corpuscular hemoglobin concentration (MCHC) (Table 2).

Hemoglobin typing was performed for all study participants. The overall prevalence of beta-thalassemia trait was 2.1%; Khamu hill tribe women had the highest prevalence at 8.3%, followed by Hmong (3.4%), Mien (2.4%), Lua (0.6%) and Mlabri (0.0%) women. In terms of HbE trait, the overall prevalence was 9.1%, with the following prevalence rates in each tribe: Lua (14.4%), Mlabri (14.3%), Khamu (8.4%), Mien (4.7%) and Hmong (2.9%). The overall prevalence of homozygous HbE was 0.6%. There were four Lua women with homozygous HbE; no women from the remaining tribes had homozygous HbE (Table 3).

The overall prevalence of Hb H disease with HbCS was 0.1% and this was only found in one Lua woman. In terms of homozygous or heterozygous HbCS, the overall prevalence was 0.1%. There was only one Lua woman with suspected homozygous or heterozygous HbCS; no other women from the remaining tribes had Hb H disease with HbCS (Table 3).

Discussion

Thalassemia and hemoglobinopathy are the most common inherited disorders and represent a major public health problem in many areas of the world, including Southeast Asia⁽²⁾. Thalassemia and abnormal hemoglobin are causes of

Table 1. Demographic data, classified by hill tribe

Demographics	Total	Hill tribe, n (%)				
		Lua	Hmong	Mien	Khamu	Mlabri
Total samples	658	313	175	127	36	7
Residence						
Tha Wang Pha District	217 (33.0)	0 (0.0)	74 (42.3)	107 (84.3)	36 (100.0)	0 (0.0)
Pua District	220 (33.4)	99 (31.6)	101 (57.7)	20 (15.7)	0 (0.0)	0 (0.0)
Bo Kluea District	221 (33.6)	214 (68.4)	0 (0.0)	0 (0.0)	0 (0.0)	7 (100.0)
Age (years)						
Mean±SD	43.9±8.2	43.4±8.1	42.7±7.7	46.4±8.9	45.8±7.8	38.0±7.8
Median	43.1	42.8	41.3	47.5	45.7	33.9
Range	30.2 to 60.0	30.3 to 60.0	30.2 to 60.0	30.6 to 60.0	31.7 to 59.6	30.9 to 49.9
Education						
No schooling	358 (54.4)	159 (50.8)	94 (53.7)	92 (72.4)	9 (25.0)	4 (57.1)
Primary school	179 (27.2)	97 (31.0)	45 (25.7)	16 (12.6)	20 (55.6)	1 (14.3)
High school	91 (13.8)	40 (12.8)	26 (14.9)	16 (12.6)	7 (19.4)	2 (28.6)
Diploma	9 (1.4)	6 (1.9)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Bachelor's degree or more	20 (3.0)	11 (3.5)	7 (4.0)	2 (1.6)	0 (0.0)	0 (0.0)
Unknown	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Income (baht/month)						
<5,000	476 (72.3)	262 (83.7)	115 (65.7)	65 (51.2)	27 (75.0)	7 (100.0)
5,000 to 9,999	130 (19.8)	30 (9.6)	42 (24.0)	50 (39.4)	8 (22.2)	0 (0.0)
10,000 to 14,999	24 (3.6)	10 (3.2)	8 (4.6)	5 (3.9)	1 (2.8)	0 (0.0)
15,000 to 19,999	12 (1.8)	7 (2.2)	1 (0.6)	4 (3.1)	0 (0.0)	0 (0.0)
≥20,000	16 (2.4)	4 (1.3)	9 (5.1)	3 (2.4)	0 (0.0)	0 (0.0)

Table 2. Complete blood counts, classified by hill tribe

CBC	Total	Hill tribe, n (%)				
		Lua	Hmong	Mien	Khamu	Mlabri
Total samples	658	313	175	127	36	7
Hb, abnormal <12 g/dL	82 (12.5)	37 (11.8)	23 (13.1)	12 (9.5)	7 (19.4)	3 (42.9)
MCV, abnormal <80 fL	122 (18.5)	64 (20.5)	20 (11.4)	27 (21.3)	8 (22.2)	3 (42.9)
MCH, abnormal <27 pg	189 (28.7)	106 (33.9)	30 (17.1)	37 (29.1)	12 (33.3)	4 (57.1)
MCHC, abnormal <28 g/dL	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

CBC = complete blood count; Hb = hemoglobin; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration

the most common chronic hemolytic anemias in Thailand, particularly in northern and northeastern regions⁽²⁾. Thalassemia does not only affect individual health, but also has a significant impact on the family, psychosocial and economic life of patients. The disease severity has been quantified by factors such as age of anemia onset and age at first transfusion⁽⁷⁾.

The aim of screening for thalassemia and hemoglobinopathy disorders is to identify carrier couples and inform them of the risk and their options. Targets of prevention and control of severe thalassemia are homozygous α^0 -thalassamia (Hb Bart's hydrops fetalis syndrome), homozygous beta⁰-thalassemia and beta⁰-thalassemia/HbE.

In the present study, the authors found that the

Table 3. Hemoglobin typing results, classified by hill tribe

Interpretation	Total	Hill tribe, n (%)				
		Lua	Hmong	Mien	Khamu	Mlabri
Total samples	658	313	175	127	36	7
Beta-thalassemia trait with or without alpha thalassemia	14 (2.1)	2 (0.6)	6 (3.4)	3 (2.4)	3 (8.3)	0 (0.0)
HbE trait	54 (8.2)	41 (13.1)	5 (2.9)	5 (3.9)	2 (5.6)	1 (14.3)
HbE trait with or without alpha-thalassemia	6 (0.9)	4 (1.3)	0 (0.0)	1 (0.8)	1 (2.8)	0 (0.0)
Homozygous HbE with or without alpha-thalassemia	4 (0.6)	4 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hb H disease with Hb constant spring	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suspected homozygous or heterozygous Hb constant spring	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Normal Hb type with or without alpha-thalassemia	81 (12.3)	42 (13.4)	14 (8.0)	20 (15.7)	2 (5.6)	3 (42.9)
Normal or non-clinically significant thalassemia	497 (75.5)	218 (69.7)	150 (85.7)	98 (77.2)	28 (77.8)	3 (42.9)

overall prevalence of beta-thalassemia trait among the hill tribe women in Nan Province was lower (2.1%) than that of the general Thai population (3 to 9%)⁽⁸⁾. Among the five main hill tribes in the region, Khamu women had the highest prevalence (8.3%) of beta-thalassemia trait, followed by Hmong (3.4%) women. The prevalence in women from both tribes was within the normal range for the general Thai population. In contrast, the prevalence among Mien (2.4%), Lua (0.6%), and Mlabri (0.0%) women was lower than that of the general Thai population.

The overall prevalence of HbE trait (9.1%) among the hill tribe women of this province was lower than that of the general population living in northern Thailand (11.2%). The prevalence of HbE trait among Hmong, Mien and Khamu women was 2.9%, 4.7% and 8.4%, respectively. However, Lua and Mlabri women had a higher prevalence of HbE trait (14.4% and 14.3%, respectively) than the general population in northern Thailand.

The overall prevalence of homozygous HbE (0.6%) among the hill tribe women in this area was lower than that of the general northern Thai population (0.73%)⁽⁹⁾. There were only four Lua women with homozygous HbE; no other women from the remaining tribes had homozygous HbE.

According to a previous study of the Lahu hill tribe population in Chiang Rai Province, Thailand, the prevalence of beta-thalassemia trait was 3%, HbE trait was 13% and homozygous HbE was 3%⁽¹⁰⁾. A study by Porniammongkol et al reported an anemia prevalence of 31% among 181 hill tribe children of Chiang Mai Province; in this group, 8% of children had the thalassemia trait⁽¹¹⁾. Yanola et al also showed that 8% of 265 Karen hill-tribe children in Chiang Mai Province showed the beta-thalassemia trait, including one child with HbE trait⁽¹²⁾.

The limitations of this study included a relatively small sample size for the Khamu and Mlabri hill tribe populations. Furthermore, there was a lack of PCR testing for alpha-thalassemia; therefore, the diagnosis of thalassemia

and abnormal hemoglobin was estimated. In this study, the overall prevalence of HbH disease with Hb CS was 0.1%. Moreover, the overall prevalence of homozygous or heterozygous Hb CS (0.1%) among the hill tribe women in this area was lower than that of the general Thai population (1% to 8%)⁽²⁾.

For the general population in Thailand, the prevalence rates of thalassemia are as follows: the average frequencies are 20 to 30% for alpha-thalassemia, 3 to 9% for beta-thalassemia, and up to 50% for HbE⁽²⁾. However, no alpha-thalassemia-1 SEA was detected in the study of the Lahu hill tribe population in Chiang Rai Province, Thailand⁽¹⁰⁾. A study of 265 Karen hill tribe children in Chiang Mai Province also showed no alpha-thalassemia-1 SEA⁽¹²⁾.

According to a previous study of Tai and Mon-Khmer ethnic groups residing in northern Thailand, the prevalence of α -thalassemia carriers varied between the different ethnic groups, with the Yuan having the highest prevalence of α -thalassemia carriers (50%) while the Lawa had the lowest prevalence (0%). The Paluang had a high prevalence (42%) of a single deletion type ($-\alpha 3.7$)⁽¹³⁾.

Although there are no overt clinical symptoms associated with the inheritance of one or two aberrant α -globin genes, three aberrant α -globin genes result in hemoglobin H disease. The symptoms of this disease can be moderate, and blood transfusion or iron chelation therapy are only occasionally required. The most severe form of α -thalassemia is characterized by the deletion of all four α -globin genes, which results in Hemoglobin Bart's hydrops fetalis syndrome.

To date, there have been no studies of thalassemia among the five hill tribes-Lua, Hmong, Mien, Khamu and Mlabri-investigated in this study. The data obtained from this study will be useful for public health planning of necessary interventions for thalassemia among minority hill tribe populations living in remote areas with barriers to

accessing health services and education.

Conclusion

The prevalence of beta-thalassemia trait and HbE trait among hill tribe women of Nan Province in northern Thailand varied among hill tribes. The overall prevalence of beta-thalassemia trait was 2.1% and that of HbE trait was 9.1% in this population. These data may be beneficial for the prevention and control of thalassemia in hill tribe populations and in genetic counseling of families affected by the disease.

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What is already known on this topic?

There are no previous reports on anemia prevalence and abnormal hemoglobin among women of the five main hill tribes in Nan Province, Thailand, namely the Hmong, Khamu, Lua, Mien and Mlabri groups.

What this study adds?

This study added the prevalence of anemia and abnormal hemoglobin among women of the five main hill tribes in Nan Province, Thailand. The prevalence of anemia was 12.5%. The overall prevalence of beta-thalassemia trait was 2.1% and that of HbE trait was 9.1%. The degree of disease varies among hill tribes.

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Potential conflicts of interest

The authors declare no conflict of interest.

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