

PREVALENCE OF CARRIERS OF THALASSEMIA AND HEMOGLOBINOPATHIES IN ETHNIC GROUPS' PREGNANT WOMEN AND SPOUSES AT THE ANTENATAL CLINIC MAE FAH LUANG HOSPITAL, CHIANG RAI (2552 – 2556 B.E.)

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ABSTRACT:

Background: Thalassemia is globally the most widespread genetic disease commonly found in Thailand causing chronic anemia in humans. It is caused by a genetic defect that leads to abnormal or no globin chain synthesis in the hemoglobin molecule. However, survey for prevalence of these disorders has never been conducted in ethnic groups at Mae Fah Luang District, Chiang Rai, Thailand.

Methods: A retrospective descriptive study aimed to determine the prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups' pregnant women and their spouses who attended in 1st antenatal clinic during 1st January 2552 to 31st December 2556 B.E. at Mae Fah Luang Hospital, Mae Fah Luang District, Chiang Rai Province, Thailand. There were 2,731 pregnant women and 370 spouses recruited into the study. Secondary data of sex, age, races, One-tube osmotic fragility test (OFT), Dichlorophenol indophenol precipitation (DCIP), Mean corpuscular volume (MCV) and Hemoglobin (Hb) typing were analyzed by descriptive statistics.

Results: The prevalence of carriers of thalassemia and hemoglobinopathies among ethnic pregnant women to be 37.5%, their spouses 28.7% and the overall prevalence was estimated to be 33.1%. Hemoglobin E trait was predominantly observed in both pregnant women (15%) and spouses (12.5%). However, considerable amount of samples were not identified in this study and they could be of other types of thalassemia/hemoglobinopathies. The Shan/Tai-Yai ethnic group had the highest prevalence of thalassemia and hemoglobinopathies (19.3%) whilst the lowest prevalence was among Haw/Chinese Yunnan (1.2%).

Conclusion: The prevalence of thalassemia and hemoglobinopathies in ethnic groups of Mae Fah Luang District was considerably high among ethnic groups. Therefore, it is important to establish the thalassemia screening program in pregnant women and spouses with the aim to prevent and control this disease in ethnic groups in Mae Fah Luang District.

Keywords: Thalassemia, Hemoglobinopathies, Ethnic groups, Pregnant women, Thailand

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INTRODUCTION

Thalassemia is globally the most widespread genetic disease causing chronic anemia in human. It is associated with abnormalities of 4 genes that lead to decreased or no globin chain synthesis in

hemoglobin molecule. Those who are affected by the disorder have varying clinical symptoms ranging from mild to severe anemia and in the most severe case, dead fetus *in utero*. Thalassemia is highly prevalent in Thailand [1, 2]. Thirty-Forty percent or about 24 millions of Thai people have a thalassemia gene. About 1% of the population or 670,000 people have thalassemia disease forms [3]. At least 12,000

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new thalassemia patients or about 12 per 1,000 are born each year [4]. Thalassemia is not only an important public health problem, but also a socio-economic problem of many countries including Thailand. Thai government has to provide large funding for medical care to maintain good quality of life of thalassemia patients [5]. Hemoglobinopathies are characterized by the synthesis of abnormal globin chains from defective globin genes. The defective globin genes may lead to the replacement of certain amino acids position in hemoglobin tetramers; this abnormal globin chains cause alterations of physico-chemical properties of the relevant hemoglobin molecules, which are then called hemoglobin variants. To date, there are more than 700 hemoglobin variants worldwide. However only three, Hemoglobin S (HbS), Hemoglobin C (HbC) and Hemoglobin E (HbE), are the most globally widespread. Hb E is very common in Southeast Asian ethnicities, while HbS and HbC are endemic in Africa and middle-east nations [6-8]. Thalassemia and hemoglobinopathies are commonly found in Southeast Asian countries attaining approximately 20-30% prevalence [9, 10]. For Thailand, the Ministry of Public Health of Thailand launched the first national policy of thalassemia prevention and control on 9th February 2005. A sum of not less than 5,000-6,000 million baht/year was pledged in the public health system in 2007 to support this policy which would be reviewed every five years [3]. Five strategies integrating antenatal clinic (ANC) guidelines were set up for hospitals and public health offices. The pre-pregnancy campaign has been applied while expect 50% reduction of new cases of severe thalassemia. There have been in-depth research projects about thalassemia situation in many regions of the world, while helped with the prevention and control of the disease and to guide treatment which improves the quality of life of the patients [5].

In this study “ethnic groups” is the term used to refer to people who are not original Thai descendants. Most of them migrated from the southern part of China through Myanmar and People Republic of Laos. The population of the ethnic groups in Thailand is over 1 million who mostly live in several provinces of the northern part of Thailand including Chiang Rai, Chiang Mai, Mae Hong Sorn and Tak. Mae Fah Luang District is located 70 km north-west of Chiang Rai Province, near Thailand/Myanmar border. Ethnic groups living in this area include Akha, Lahu, Karen, Hmong/Miao, Mien/Yao, Lisu, Shan/Tai-Yai and Chinese Yunnan/Haw [11]. These ethnic groups have their own languages and many have not acquired

sufficient communication skill in Thai language. This language barrier has prevented them from accessing various informations especially those concerning public health issues. They lack of the knowledge and awareness that thalassemia and hemoglobinopathies can affect newborn children and that prenatal screening may present the disease. In addition, the common practice of inter-group marriage makes the spread of thalassemia and hemoglobinopathies among these people highly probable. Although problem of thalassemia and hemoglobinopathies is evident in these ethnic groups of Mae Fah Luang district, surveys of their prevalence have never been substantially conducted.

For that reason, the purpose of this study was to determine the prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups’ pregnant women and their spouses. Additionally, this study has to provide useful information for the future management of thalassemia and hemoglobinopathies in the ethnic groups residing in Mae Fah Luang district or around Thailand.

MATERIAL AND METHODS

Research setting

The study was conducted at antenatal clinic Mae Fah Luang Hospital in the area of Mae Salong-Nai and Thoed Thai Sub-District, Mae Fah Luang District, Chiang Rai Province, Thailand. Around 99% of population are ethnic groups divided in to 8 races were living in this area. The ANC clinic provided thalassemia blood screening program for both pregnant women and their spouses, pre and post counseling, follow-up evaluations for pregnant women and spouses.

Participants

During the study period there were 3,356 pregnant women and 420 spouses who were of ethnic groups and attending ANC clinic for the first time at Mae Fah Luang Hospital. The sample was then selected by inclusion criteria. A total of 2,731 records of pregnant women and 370 records of spouses were used in the study. Inclusion criteria were: (1) the subjects must be of ethnic groups origin, being one of the following races: Akha, Lahu, Haw/Chinese Yunnan, Karen, Shan/Tai Yai, Hmong, Yao and Lisu; (2) the pregnant women must visit the ANC clinic at Mae Fah Luang Hospital for the first time during 1st January 2552 to 31st December 2556 B.E; (3) the each records must have complete data of thalassemia screening results which include: Mean corpuscular volume (MCV), One-tube osmotic fragility test (OFT) and

Table 1 General characteristic of 2,731 ethnic groups' pregnant women and 370 spouses

Characteristics	Pregnant women (2,731)	%	Spouse (370)	%
Age (years)				
11-20	865	31.67	56	15.13
21-30	1,259	46.10	179	48.37
31-40	521	19.07	102	27.56
≥ 41	86	3.16	33	8.94
	Min-Max (12-52)		Min-Max (14-64)	
Races				
Lahu	888	32.50	100	27.00
Akha	885	32.40	96	25.90
Shan/Tai Yai	350	12.80	83	22.40
Haw/Chinese Yunnan	329	12.00	40	10.80
Lisu	158	5.80	29	7.80
Hmong	117	4.30	22	5.90
Yao	4	0.10	0	0

Dichlorophenol indophenol precipitation (DCIP) as well as Hospital number (HN).

Material

The obtained secondary data which included sex, age, races, MCV, OFT, DCIP, Hb typing by weak-cation High performance liquid chromatography (HPLC) and Gap-Polymerase chain reaction (Gap-PCR) for α -thalassemia 1 Southeast Asia type (SEA type) from the thalassemia screening program for ANC clinic in the Medical Laboratory and Hospital Information System (LIS and HIS).

Data collection and analysis

Descriptive statistics of percentage, frequency, mean, standard deviation (SD) and prevalence were used to conclude the prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups' pregnant women and their spouses at ANC clinic, Mae Fah Luang Hospital.

Ethical considerations

All research procedure and ethical consideration were submitted on Mae Fah Luang University committee for approval (No. 5914(2)/1220).

RESULTS

Demographic information

The pregnant women with age averaged to be 25.02 ± 7.12 (mean $\pm$ SD) years old were classified by age into 4 groups. Forty six point one percentage with the age of 21-30 years old were the largest groups, while 31.67% had the age of 11-20 years old. The lowest age was 12 years old and the highest was 52 years old. Regarding to the races, the studied sample comprised Lahu (32.50%), Akha (32.40%), Shan or Tai Yai (12.80%), Haw or Chinese Yunnan (12.00%), Lisu (5.80%), Hmong (4.30%) and Yao

(0.10%). No Karen pregnant women were recruited in this study (Table 1).

Three hundred and seventy spouses were recruited to the study and all of them were identified to be ethnic groups. These spouses were classified by ages into 4 groups. Most spouses had the age of 21-30 years old, being the largest groups (48.37%), followed by a group having the age of 31-40 years old (27.56%). The mean age was 28.74 years old (SD=8.48), the lowest age was 14 years and the highest was 64 years. Concerning races, Lahu were majority accounting for 27.00%, followed respectively by Akha (25.90%), Shan or Tai Yai (22.40%), and Haw or Chinese Yunnan (10.80%). Yao and Karen did not enroll in this study (Table 1).

Prevalence of thalassemia and hemoglobinopathies by screening tests

According to the results of MCV, OFT and DCIP, the 2,731 pregnant women were divided into 8 groups. The majority of ethnic groups' pregnant women (83.89%) had negative results of MCV/OFT/DCIP. In contrast, 20.10% pregnant women were positive for at least one screening test. Within the latter group, 5.50%, 2.20% and 1.60% of the subjects had positive results of MCV, OFT and DCIP, respectively. Seven point eight percent had positive results of MCV /OFT, 0.70% had positive MCV/ DCIP and 0.20% had positive OFT/DCIP. Finally, 2.10% of the pregnant women had positive results for MCV/OFT/DCIP (Table 2).

The 370 spouses were divided into 8 groups based on screening results. The majority of the spouses (78.40%) had negative results of MCV/OFT/DCIP. In contrast, 21.60% spouses were positive for at least one screening test. Within the latter group, 4.90%, 7.00% and 0.80% of the subjects had positive results of MCV, OFT and

Table 2 Screening results of thalassemia and hemoglobinopathies of ethnic groups' pregnant women. Positive MCV means MCV values were 79.99 fL and less. Negative MCV means MCV values were 80.00 fL and more

Test of screening			N (2,731)	%
MCV	OFT	DCIP		
-	-	-	2,291	83.89
+	-	-	150	5.49
+	+	-	213	7.80
+	+	+	57	2.09
+	-	+	20	0.73
-	+	-	59	2.16
-	+	+	6	0.22
-	-	+	44	1.61

(+) is Positive for screening test and (-) is Negative for screening test

Table 3 Screening results of thalassemia and hemoglobinopathies of spouses. Positive MCV means MCV values were 79.99 fL and less. Negative MCV means MCV values were 80.00 fL and more

Test of screening			N (370)	%
MCV	OFT	DCIP		
-	-	-	290	78.38
+	-	-	18	4.86
+	+	-	26	7.03
+	+	+	4	1.08
+	-	+	1	0.27
-	+	-	26	7.03
-	+	+	2	0.54
-	-	+	3	0.81

(+) is Positive for screening test and (-) is Negative for screening test

Table 4 Prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups' pregnant women and spouses

Types	N (160)	%
1. Pregnant women	80	
1.1 Hemoglobin E trait	12	15.00
1.2 α -thalassemia 1 trait (SEA type)	11	13.75
1.3 β -thalassemia trait	5	6.25
1.4 β -thalassemia trait with α -thalassemia 1 trait	1	1.25
1.5 Hemoglobin H disease	1	1.25
1.6 Normal HP typing by HPLC and PCR	50	62.50
2. Spouses	80	
2.1 Hemoglobin E trait	10	12.50
2.2 α -thalassemia 1 trait (SEA type)	8	10.00
2.3 β -thalassemia trait	5	6.25
2.4 Normal HP typing by HPLC and PCR	57	71.25

DCIP, respectively. Seven percent had positive results of MCV /OFT, 0.30% had positive MCV/DCIP and 0.50% had positive OFT/DCIP. Finally, 1.10% of the spouses had positive results for MCV/OFT/DCIP (Table 3).

Prevalence of carriers of thalassemia and hemoglobinopathies by Hb typing and Southeast Asia- α thalassemia 1 analysis

Analysis of 80 couples (160 samples) having positive screening results showed that HbE were mostly found in both pregnant women and spouses, followed, respectively, by the SEA- α thalassemia 1 and β -thalassemia. However, considerable amount

of samples were not identified in this study and they could be of other types of thalassemia/hemoglobinopathies (Table 4).

Further analysis to determine prevalence of thalassemia/hemoglobinopathies in each ethnic group has shown that thalassemia/hemoglobinopathies were mostly prevalent in Shan ethnicity. The lowest prevalence was observed in Haw or Chinese Yunnan (Table 5).

DISCUSSION AND CONCLUSION

Thalassemia and hemoglobinopathies is an important problem in Thailand, especially in the

Table 5 Prevalence of carriers of thalassemia and hemoglobinopathies in different ethnic groups

Races/Types	N (160)	%
1. Shan or Tai Yai		19.38
- Hb E trait	13	
- α -thalassemia 1 trait (SEA)	10	
- β -thalassemia trait	7	
- Hb H disease	1	
- Normal HP typing by HPLC and PCR	17	
2. Lahu		7.50
- α -thalassemia 1 trait (SEA)	6	
- Hb E trait	6	
- Normal HP typing by HPLC and PCR	34	
3. Hmong		1.25
- α -thalassemia 1 trait (SEA)	1	
- Hb E trait	1	
- Normal HP typing by HPLC and PCR	5	
4. Lisu		1.88
- β -thalassemia trait	2	
- β -thalassemia trait with α -thalassemia 1 trait (SEA)	1	
- Normal HP typing by HPLC and PCR	12	
5. Akha		1.88
- α -thalassemia 1 trait (SEA)	1	
- Hb E trait	2	
- Normal HP typing by HPLC and PCR	25	
6. Haw or Chinese Yunnan		1.25
- α -thalassemia 1 trait (SEA)	1	
- β -thalassemia trait	1	
- Normal HP typing by HPLC and PCR	14	

northern area. The prevalence of overall α -thalassemia trait, β -thalassemia trait and hemoglobin E trait in the northern part of Thailand among native Thai people were reported to be as high as 30%, 9% and 13%, respectively [1]. The prevalence of carriers of thalassemia and hemoglobinopathies vary from region to region. Thus, to obtain the best outcome of prevention and control of the thalassemia syndrome, study on the prevalence, appropriate carrier screening strategy and the molecular analysis of thalassemia and hemoglobinopathy types have been conducted in many countries. In Thailand, the Ministry of Public Health promotes the campaign of prevention and control of severe thalassemia by screening and genetic counselling. The aim of thalassemia screening is to identify carriers of SEA- α -thalassemia 1, β -thalassemia and HbE with the ultimate goal to decrease number of the new cases of severe thalassemia disease while included Hb Bart's hydrops fetalis, homozygous β -thalassemia and HbE/ β -thalassemia.

Effective prevention programs for thalassemia have been demonstrated in many European countries where the numbers of carriers of abnormal genes are high, such as Cyprus, Greece and Italy, and now also in the Middle East [1, 12, 13]. Premarital screening for thalassemia is standard practice and national audit

data are available. Most at-risk couples are identified early for prenatal diagnosis in the first pregnancy and the majority uses this service and produce healthy offspring. Screening program need to be supported by public education and regulatory structures empowering individuals to make informed decisions and to ensure that people are protected against discrimination as a result of their test results. A nationwide campaign of public education about thalassemia and the risk of having thalassemia children, especially targeted towards school children, couples who intend to marry, and pregnant women, should be continuously carried out. The campaign should include the total health care of family members and provide knowledge of the relevant services available. Public education should be carried out through all means of mass media in appropriate language through newspaper, television, radio, workshops, with exhibitions at the village levels.

This study was designed as a retrospective descriptive study to determine the prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups' pregnant women and their spouses who attended ANC clinic at Mae Fah Luang Hospital, Mae Fah Luang District, Chiang Rai Province, Thailand during 1st January 2552 to 31st December 2556 B.E. The subjects consisted of eight

ethnic groups; Akha, Lahu, Lisu, Hmong, Karen, Shan or Tai Yai, Yao and Haw or Chinese Yunnan. Screening results have shown a considerable number of subjects possibly carrying the genes for thalassemia and hemoglobinopathies. This result should raise awareness of health care personnel about this disorder in these ethnic groups. Unfortunately, only 80 samples from spouses were available for confirmatory tests. This was due to the difficulty in calling the spouses to join the study and many also dropped out. However, this was the first survey conducted among eight ethnic groups in Chiang Rai Province and Thailand. The information emerged from this study would pave the way to future insight into the real situation of thalassemia and hemoglobinopathies in ethnic people.

This study also found that the prevalences of common thalassemia carriers varied from types of thalassemia and races. This emerging fact should be made use in the planning of prevention and control program customized for different area. However, only 160 samples were confirmed in this study. The small sample size of confirmed tests may not be enough to substantially declare the real prevalence of specific types of thalassemia and hemoglobinopathies in each ethnic group. Further survey is strongly encouraged to figure out the real prevalence. The prevalence observed in the present study is useful as it demonstrates the existence of thalassemia and hemoglobinopathies in the ethnic groups of people residing in this part of Thailand.

In the light of prevalence of thalassemia and hemoglobinopathies carriers, the study of Tienthavorn, et al. [14] in the public health area of Chiang Mai Province found that Hb E trait was the highest prevalence, followed by SEA- α -thalassemia 1 trait and β -thalassemia trait, respectively. This study had the estimated overall prevalence of carriers of thalassemia and hemoglobinopathies in ethnic groups' pregnant women and spouses as 37.50% and 28.75%, respectively which was higher than that observed in the study of Wanapirak, et al. [15] that reported the overall prevalence of thalassemia carriers in pregnant women at Maharaj Nakorn Chiang Mai Hospital to be 25.40%. This difference in the prevalence may be due to the different ethnic origins and amount of samples analyzed. However, when considering the mixture of thalassemia types, the finding raised in this study and that found by Wanapirak, et al. [15] did not much differ. This figure of almost identical thalassemia types leads to the assumption that the people in Chiang Mai might have the same racial background as those of the Mae Fah Luang District, Chiang Rai. This notion certainly needed further elucidation.

The overall prevalence of thalassemia trait in ethnic groups' pregnant women and spouses at Mae Fah Luang Hospital in the present study was 37.50% and 28.75% which were classified to be HbE trait, α -thalassemia-1 (SEA type) trait, β -thalassemia trait, the combination of a thalassemia-1 (SEA type) and β -thalassemia trait and Hemoglobin H disease. These results are in the same figure as those reported for other Southeast Asian populations [1]. The prevalence of the present study may not represent the prevalence of thalassemia and hemoglobinopathies in the Chiang Rai Province because most of the samples were from Mae Fah Luang Hospital, Mae Fah Luang District. Similar studies should be conducted in other parts where ethnic people live to represent the true prevalence. The limitation of the present study is that the authors did not determine the prevalence of other types of thalassemia and hemoglobinopathies, such as α -thalassemia-2, Hb constant spring etc. This study focused on only the types causing severe thalassemia syndrome, which need prenatal control in a large scale. This others is not clear for more information, we need to study the details or types of their characteristic of others.

It has been proven that one of the most effective prevention and control methods are the prospective screening program [16-20]. The program consists of the screening pregnant women and/or their spouses to identify carrier status followed by offering prenatal diagnosis to the couples at risk of severe thalassemia syndrome, i.e. Hb Bart's disease, β -thalassemia major, and β -thalassemia/HbE disease. The prevalence of thalassemia carrier demonstrated in the present study probably suggests the cost-effectiveness of a prospective screening program in prevention and control strategy of this disease in Mae Fah Luang Hospital. However, further gathering and analyzing more data is strongly recommended and should be study in detail for finding out the specific types of the other types of thalassemia and hemoglobinopathies.

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CONFLICT OF INTERESTS

There is no conflict of interests to be declared.

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