CHAPTER I

INTRODUCTION

Anemia is one of the major public health problems especially in developing countries. The most common cause of anemia is iron deficiency. It has been estimated that more than 500 million people suffer from this disease(De Maeyer and Adiels-Tegman,1985).

According to several surveys of hematologic value among Thais in various parts of Thailand, the prevalence of anemia varies from 11 to 67 percent depending on age groups, sex, location of survey, laboratory used and criteria for diagnosis.(Areekul et.al.,1972,1976 ; Charoenlarp et. al.,1988 ; Chaturachinda , 1972 ; Korananta-kul , 1984 ; Na-Nakorn , Wasi and Pootrakul ,1984 ; Panich and Pompatkul , 1981 ; Ratanabanangkoon et.al. ,1980 ; rimdusit , 1975 ; Sirijerachai , 1989 ; Sundharagiati ,1967 ; Suwanik et.al. ,1981 ; Tintara , Kor-anantakul and Pompatkul , 1988 ; Vachananda ,1963 ; Valyasevi , Benchakarn and Dhamamitta , 1974 ; Wasi , 1972)

The etiology of anemia in Thailand had not been systematically surveyed but it is believed that the most common cause is iron deficiency. The study of Ratanabangkoon, et al. about the prevalence and etiology of anemia in children in 1980 showed that 23% of the subjects had anemia and majority of that subjects had low serum iron while serum vitamin B12 and serum folate were normal. Although, those subjects can not represent Thai children population since they all

lived in Bangkok and had higher socioeconomic status than most of the children who lived in rural area. Therefore, it still can be assumed from the results of this study that the major cause of anemia among Thai children is iron deficiency. In adults, the study of Areekul, et al. in 1976. and Tintara, et al. in 1988 about anemia and its etiology among pregnant women showed that 75-82% of anemic cases in those studies were caused by iron deficiency.

Most of the studies about anemia in adult in Thailand used hematocrit or hemoglobin level as the criteria for diagnosis, only some also used serum ferritin or serum iron to detect the prevalence of iron deficiency(Areekul et.al.,1976 ; Ratanabanangkoon et.al.,1980 ; Sunndharagiati,1967 ; Tintara et.al.,1988).Most of them studied the pregnant women. Very few studies used non pregnant women as the subjects. Na-Nakorn, et al. studied hematocrit value and prevalence of iron deficiency anemia among 877 women in reproductive age group in 1973, using therapeutic trial as the gold standard for iron deficiency. The subjects in this study were medical and nursing students, doctors and nurses who generally have had higher education and higher socioeconomic status than the majority of Thai women. They found that 12% had anemia but only 1% responded to iron supplementation. However, from 877 subjects only 236 cases took iron supplement regularly and came back for re-evaluation. The doses of ferrous sulfate given to them was low, (60 mg/d). Therefore the prevalence of iron deficiency anemia among this group of population may be underestimated. Since iron deficiency depended on iron food intake which varied according to economic status, therefore we can assume that among the major population of the same age and sex, who have lower socioeconomic status, the problem is even more serious.

The Northeastern part of Thailand is the poorest part of the country. The people in the rural area of the Northeast has lower socioeconomic status compared

to the people in other parts of Thailand. The dryness of the weather in summer leads to difficulty of finding enough food especially protein from animal which is also the major source of iron. Hook worm infestation, which is one of the causes of chronic blood loss that can lead to iron deficiency anemia, is also common in this area, although the prevalence rate and severity is not as high as that of the southern part of Thailand. From the reason previously mentioned, the rural area of the Northeastern part of Thailand especially the underdeveloped area of this part is the high risk area of high prevalence of iron deficiency anemia.

There are two studies about iron content in food of the Northeastern Thailand. The first study was done by Nutacharat, et al. in 1973. They surveye dietary nutrient intake of the villagers in 7 villages of Khon Kaen province by measuring food intake of the subjects's family every meal for 2 days, the dietary nutrient intake was calculated according to food composition table. The average iron intake of the villagers in Khon Kaen province from this study is 12.3 mg/day, 2.5 mg of this is heme iron which is more absorbable. About 40% of iron intake came from rice which contained high phytate, which is the inhibitor of iron absorption. Therefore most of the villagers in Khon Kaen are at risk to have inadequate iron intake because according to the Recommended Dietary Allowance (RDA) of the Thais , only men and menopause women received adequate iron intake. The second study was done by Suwanik, et al. in 1980. By analyzing food iron content of the meals, they found that there was so much difference between food iron content of people from Bangkok and that of the rural area (24.20+7.76 mg/day in Bangkok, 13.17±2.87 mg/day in Ang Thong in central rural area, and 7.37±3.29 mg/day in Si Sa Ket in rural area of Northeastern Thailand) The results of these two studies showed that :

1. Dietary iron content in the food of the people from the rural area of Thailand is significantly lower than in the city .

2. Iron content in the food of people who live in northeastern part of Thailand is lower than the RDA of the Thais.

Pregnant, lactating and menstruating women were the groups at risk of iron deficiency anemia among adults because they require higher iron intake than men and menopause women. There is a recommendation to give iron supplement to every case of pregnant and lactating women. But for the non-pregnant menstruating women who were also at risk especially the one who live in the area where iron content in food is low such as northeastern part of Thailand, there are very few data about the real prevalence of anemia which is caused by iron deficiency. Most of the surveys used hemoglobin or hematocrit as the criteria for the diagnosis of anemia. Since mild cases of iron deficiency may have no anemia and anemic cases may be caused by the other disease, therefore there is an overlapping between the two problems.

In the northeastern part of Thailand where prevalence of thalassemia and hemoglobinopathies is high (about 40% of the population are hemoglobin E heterozygote) and average iron content in food is low, the overlapping of the two problems may be more. Suwanik, et al. studied iron status of Thai population in Bangkok and one village at Si Sa Ket province in 1981. They found that serum ferritin values in both males and females from the village were definitely lower than those of Bangkok with the mean value of 32 and 15 ng/ml for males and females respectively compared to 81 and 48 ng/ml of those from Bangkok ($P < 0.001$). It was noted that especially in females, transferrin saturation among the villagers was also lower than those of Bangkok group ($P < 0.005$). When anemia was determined by hemoglobin level, there are 23.6% of male and 34.3%

of female anemic cases . When iron deficiency status was determined by serum ferritin level, there are 31.1% of males and 46.0% of females, who live in the rural area, haveing iron deficiency. However they did not show how many percent of anemic cases having low serum ferritin. Since the female subjects from the rural area in this study were in their reproductive ages (27-42 years old), therefore we can conclude from this study that :

1. Iron deficiency is still a problem in the rural area especially in the poor areas of the Northeastern Thailand.

2. The problem is more prominent in reproductive age group females than males

The clinical manifestations of iron deficiency may be quite subtle. Most individuals with mild iron deficiency anemia have no complaints that are dramatic enough to make them seek medical attention. Nevertheless, several manifestations of iron deficiency have been recognized that are clinically and economically meaningful, particularly in view of the continuing high prevalence of this disorder.[21] The studies of Gardner , et al. in 1977., Viteri and Torun in 1974, Basta, et al. in 1979 and Edgerton, et al. in 1979 showed the impairment of work performance of the anemic agricultural laborers which improved after iron supplementation. Therefore improvement of iron status can lead to improvement of work performance and productivity , and subsequently improve the economic status of the population.

Iron fortification in salt and fish sauce was used as an intervention to improve the iron status of the people in rural areas in the studies of Charoenlarp in 1983 and Suwanik, et al. in 1986. There were improvements in the mean hemoglobin level of subjects in both studies. Thus, iron fortification in salt and fish sauce was recommended by the two authors to be a national policy to solve

this problem. The problems of iron fortification in salt and fish sauce are : first, the production of salt and fish sauce in Thailand is in the small factory houses and there are many difficulties in controlling them especially the production of low quality fish sauce which most of the poor people consume; second, Thailand has many cases of patients who are diseased form of homozygote or compound heterozygote thalassemia and hemoglobinopathies. There are about 500,000 cases of thalassemia patients in Thailand and about 16 million of Thai population have abnormal gene of thalassemia or hemoglobinopathies. As we know iron overload is the major complication of thalassemia. Using iron fortification to supplement iron for the entire population may have a harmful effect to a certain number of Thalassemic patients. To identify the high risk group of iron-deficiency anemia and give iron supplement is the safer way to solve this problem.

In summary, the problems that lead to this study are :

1. high prevalence of anemia among the female in reproductive age group especially in the underdeveloped and low socioeconomic area, even though they are not pregnant.

2. high prevalence of thalassemic and hemoglobinopathic genes among the Thais leads to the problem of identifying the true prevalence of iron deficiency anemia and the problem of solving iron deficiency by iron fortification methods.

3. no available present data about this high risk group population (female in reproductive age group who live in the underdeveloped area and do not pregnant). Since economic growth in the last 5 years is high and the available data were done more than 10 years ago, therefore the present prevalence of iron deficiency anemia and iron status of these population may change.

4. to know the true prevalence of iron deficiency anemia and iron status of this high risk group and its associated factors may help us justify the suitable method to solve the problem.

LITERATURE REVIEW

PREVALENCE OF ANEMIA IN REPRODUCTIVE AGE GROUP FEMALE

The prevalence of anemia among female reproductive age group from several surveys are showed on Table 1.

The data showed high prevalence of anemia among these group of population only in the survey that was done in the rural area. From the study of Na-Nakorn in 1973 the prevalence of anemia among females in the reproductive age group in Bangkok was about 12%. Suwanik et. al. was studied in 1981 it was decreased to 2.3%. So among the people who live in big city and have higher socioeconomic status, anemia is not a big problem. In contrast, this group of population in rural, area still have high prevalence as showed by the survey of Sirijerachai in 1988, About 25% of these population have anemia.

However, the prevalence of anemia detected by hematocrit or hemoglobin level alone can not determine the size of iron deficiency among the population, since prevalence of abnormal hemoglobin especially hemoglobin E and prevalence of thalassemia in Thailand is high. Wasi et al. (1973) found that systemically the subject with heterozygote of hemoglobin E had lower hematocrit, approximately 1.5 percent on the average than those with normal hemoglobin. Because of this reason, the overlapping between the cases of iron deficiency anemia and thalassemia or hemoglobinopathies occurs.

The studies about prevalence of iron deficiency anemia in adult were showed on Table 2. Most of them were done in pregnant women, using

TABLE I PREVALENCE OF ANEMIA AMONG FEMALE REPRODUCTIVE AGE GROUP (15-45 YR.)

YEARS	NO	LOCATION	CRITERIA	PREVALENCE	INVESTIGATOR
1972		ALL OVER THAILAND			
	1569	Hb AA	Hb <12 G%	35%	WASI , et al.
	472	Hb AE	Hb <12 G%	44%	WASI , et al.
1973	877	BANGKOK	Hct <36%	12%	NA-NAKORN,et al
1974	553	NAKORN-CHAISREE	Hb <12 G%	48%	NA-NAKORN
1978		CHIENG MAI			
	159	NORMAL DIET	Hct <36%	5%	LINPISARN, S.
	232	VEGETARIAN	Hct <36%	49%	
1981	144	BANGKOK	Hb <12 G%	2.3%	SUWANIK, et al.
	158	SI SA KET	Hb <12 G%	34. 3%	
1988	573	KHON-KAEN	Hct <36%	26.4%	SIRIJERACHAI

TABLE II : PREVALENCE OF IRON DEFICIENCY IN ADULT.

GROUP	NO	LOCATION	CRITERIA	PREVALENCE.	INVESTIGA TOR	YEAR
PREGNANCY	154 241	BANGKOK UBOL	SERUM IRON < 50 ug	6.5 13.65	VALYASEVI	1972
PREGNANCY	216	SIRIRAJ	SERUM IRON < 50 ug	22.6	AREEKUL	1976
PREGNANCY	100	HADYAI	THERAPEUTIC TRIAL	19.3	TINTARA	1988
MALE FEMALE	209 485	SI SA KET	SERUM FERRITIN <21 ng/dl SERUM FERRITIN < 13 ng/dl	31.0 46.0	SUWANIK	1981

therapeutic trial or serum iron as the gold standard. Since there are many physiologic factors that may interfere with serum iron level and this study have high diurnal variation, using serum iron alone to determine iron status is not enough.

The study of Suwanik et.al. (1981) at Si Sa Ket Province showed high prevalence of iron deficiency among the reproductive age groups of both male and female. However, this study was done almost 12 years ago. And it did not show how many percent of the people had anemia secondary to iron deficiency and how many percent of the people who were iron deficient have anemia.

HOOK WORM INFESTATION AND ITS RELATIONSHIPS TO IRON DEFICIENCY

An epidemiological survey made by Vajarasathira and Harinasuta in 1957 showed that hook worm infection was very common in Thailand. The most prevalent species was Necator americanus. Infestation rate among the people in Northeastern area was 19.5%. Although it is not as high as in the Southern area, it is still high.

Heavy infestation of hook worm has relationship with anemia. Areekul et al. (1970) studied blood loss from hook worm by using ^{51}Cr-labelled red blood cells ; they found that blood loss per worm per day is about 0.03-0.08 ml. There is a significant correlation between total blood loss and number of hook worm eggs in stools.

Nateewattana and Sivasomboon (1970) studied the relationship between hook worm infestation and level of serum iron among the inmates of Chiang-

Mai Provincial Prison . They found that the reduction of serum iron directly related with the severity of hook worm infestation.

The effect of hook worm infestation to iron deficiency anemia depends on severity of infestation, iron storage and iron intake of the subjects. In the high risk group only mild infestation might have effect on the iron status of the patients. Therefore hook worm infestation was accounted to be the associate factor of iron deficiency anemia in this study.

EFFECTS OF IRON DEFICIENCY

The major effect of iron deficiency in adult is socioeconomic loss due to decreasing work performance and productivity. There are many studies both in experimental animals and clinical trials in this area.

Gardner, et al. (1977) studied work performance among 75 women who worked on a tea estate in Sri Lanka . The subjects performed a standard, multistage-treadmill test in which speed and grade were gradually increased for a maximum period of 18 minutes. The results were analyzed according to the concentration of hemoglobin in venous blood. They showed the significant difference of performance value among the subjects who have low hematocrit compared to the subjects who have normal hematocrit by means of percentage of subjects who reached the maximum work load of 6.36 km/hr, exercise heart rate, post exercise lactate concentrations and 2,3 -DPG.

Viteri and Torun (1974) evaluated performance in the Harvard Step test among Guatemalan agricultural laborers. The test showed impairment of performance even with the mildest degree of anemia. The performance significantly elevated after treatment with iron compared to the placebo group.

These two studies showed the influence of iron deficiency anemia in decreasing an individual performance in a brief, intense type of exercise. Performance is roughly proportional to the degree of anemia and treatment with iron corrects the abnormality.

Prolonged activity which is more closely related to work performance and productivity was measured by Basta et al. in 1973. They determined the relationship between income and hemoglobin among a group of workers on an Indonesian rubber plantation.

The most interesting study was done by Edgerton, et al. (1979). They studied 199 women who worked on a tea plantation in Sri-Lanka. The quality of tea picked per day was studied before and after treatment with iron supplementation or placebo. There was a significant increase in productivity in association with iron treatment, particularly among those subjects whose initial hemoglobin concentration was between 6 and 8 g/dl. The effect of iron treatment on voluntary activity was also estimated in a subgroup of 18 women by using a small movement sensitive recording device that was strapped to the subjects' body. The women who received iron treatment were found to be about 60% more active than matched subjects who were given a placebo.

From these studies, it was showed that iron deficiency especially when anemia occurred, even in mild form, the work performance and productivity decreased.