Red Cell Indices and Therapeutic Trial of Iron in Diagnostic Work-Up for Anemic Thai Females

ISSARANG NUCHPRAYOON, MD, PhD, FAAP*,
BOONRUEN SUKTHAWEE, BNS**,
THASSANEE NUCHPRAYOON, MD, DTM&H, MPH**

Abstract

Anemia is common among Thai females. Thalassemia and iron deficiency are highly prevalent in the Thai population. A therapeutic trial of iron has been used to differentiate between the two conditions, however, no previous study on its usefulness in a Thai population has been reported. Otherwise healthy persons who had complete blood count (CBC) as routine 'check-up' and found to be anemic (Hb < 12 g/dl) at a preventive medicine clinic were tested for hemoglobin typing, serum ferritin, serum iron, and were given oral iron sulfate (120 mg elemental iron per day for at least 2 months) and a repeat CBC on a follow-up visit. Sixty-six individuals, all females, with pre-treatment hemoglobin (Hb) level of 9.5 ± 1.7 g/dl (mean ± SD), had complete data for analysis. Final diagnoses were isolated iron deficiency in 23 (34.8%), iron deficient thalassemia traits in 6 (9.1%) and iron-sufficient thalassemia syndromes in 29 (43.9%) anemic subjects. After a therapeutic trial of iron, Hb rose to 12.8 ± 1.0 g/dl ($n = 16$, $p = 2 \times 10^{-8}$) among the iron deficient group, but not in thalassemia. The authors have identified that the most useful red cell indices that will discriminate between iron deficiency and thalassemia is a combination of red blood cell counts (RBC) > 4.4 x $10^6/\mu l$ and mean corpuscular volume (MCV) < 69 fl. High RBC (> 4.4 x $10^6/\mu l$) and very low MCV (< 69 fl) is a sensitive (92.9%) and highly specific (100%) criteria for diagnosis of mild thalassemia diseases (Hemoglobin H (HbH), Hemoglobin H-Constant Spring (HbH-CS), and homozygous Hemoglobin E (HbEE)). Conversely, a low RBC (> 4.4 x $10^6/\mu l$) and/or low to normal MCV (69-85 fl) is highly sensitive (91.3%) but not specific (60%) for the diagnosis of iron deficiency. The authors conclude that a therapeutic trial of iron is useful as a diagnostic test in anemic females except those with high RBC (> 4.4 x $10^6/\mu l$) and very low MCV (< 69 fl), a subgroup which most likely has thalassemia and are least likely to benefit from iron treatment.

Key word : Anemia, Red Cell Indices, Iron Deficiency, Thalassemia, Therapeutic Trial of Iron

NUCHPRAYOON I, SUKTHAWEE B, NUCHPRAYOON T
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* Department of Pediatrics,
** Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Anemia is common among Thai females [1,2]. Complete blood count (CBC) is the most commonly used laboratory test to detect anemia. The most common causes of microcytic anemia in the Thai population are iron deficiency and thalassemia traits[1].

Several laboratory tests are available to make the diagnosis of iron deficiency[2,3]. These include serum ferritin, serum iron and total iron binding capacity, bone marrow examination for iron store, and serum transferrin receptor[4]. These tests, however, are costly or not widely available. Moreover, iron deficiency often coexists in thalassemia traits[5]. A therapeutic trial of iron can be given to diagnose or exclude iron deficiency without the need for a laboratory test[2,6]. Diagnosis of thalassemia trait, including alpha-thalassemia-1 trait, can then be made by hemoglobin electrophoresis after exclusion of iron deficiency[7]. Many types of thalassemia, such as hemoglobin H and hemozygous hemoglobin E, cause mild anemia and a tendency for iron overload. Iron therapy should be avoided in these cases. These cases could be distinguished from iron deficiency by their red cell indices from automated CBC. The authors report here the effect of a therapeutic trial of iron on otherwise healthy females who were discovered to be anemic by 'routine' check-up visits, and propose a scheme of diagnostic work-up based on automated CBC, therapeutic trial of iron, and hemoglobin electrophoresis.

MATERIAL AND METHOD

Anemia was defined by the World Health Organization (WHO) criteria, which is hemoglobin < 13 g/dl in males and < 12 g/dl in females[8]. Individuals who came for routine physical check-up at the Preventive Medicine Clinic, King Chulalongkorn Memorial Hospital (KCMH), Bangkok, had complete blood count (CBC), and were found to be anemic by this criteria were further tested for serum ferritin, serum iron, and hemoglobin typing. CBC was performed by automated methods by the department of Laboratory Medicine, KCMH. Serum ferritin was determined by an automated electro-chemiluminescent assay (Roche diagnostics, Thailand), the normal range of which was 15-400 ng/ml. Serum iron was determined by the spectrophotometric method (serum iron TIBC kit, Roche diagnostics, Thailand), the normal range of which was 80-170 mg/dl. Attention was paid to collecting blood samples for serum iron determination in iron-free tubes and the assays were performed at the division of Nuclear Medicine, department of Radiology, KCMH. Total iron binding capacity was not determined in the present study. Hemoglobin typing was performed by an isoelectrofocusing (IEF) method at the division of Hematology, department of Medicine, KCMH.

All anemic individuals were prescribed iron sulfate (40 mg elemental per tablet, 1 tablet three times daily) for three months before the results of any laboratory test were known. On the return visit, another CBC was repeated. Laboratory results were informed to each individual, and counseling for thalassemia was given, if appropriate.

Patients who had CBC, iron studies and hemoglobin typing done were included in the analysis. Patients who did not have available data for any of the tests were excluded from the analysis. For comparisons of CBC data between the follow-up and initial visit, individuals whose interval between visits was less than 4 weeks were excluded.

Specific diagnoses of thalassemia diseases and traits were made based on the results of hemoglobin electrophoresis[7], except for alpha-thalassemia-1 trait, which was diagnosed when the subject had low mean corpuscular volume (MCV) < 80 fl, normal hemoglobin typing, and lack of iron deficiency. Alpha-thalassemia-2 trait could not be diagnosed and was considered 'normal'.

Iron deficiency was diagnosed when serum ferritin was less than 20 ng/ml or a significant hemoglobin increase (> 1.5 g/dl) after therapeutic trial of iron treatment, regardless of serum iron level. Data were recorded and analysed on Excel 6.0®. Continuous data between patients groups were compared using the unpaired *t*-test.

RESULTS

Patient characteristics

Between January and December, 2000, 72 individuals, all female, were included in this study, 6 were excluded from the analysis because of incomplete data. The average age of the patients was 36.5 years (Table 1). Of 66 patients with complete data, 31 patients (47%) came for follow-up visits and had available CBC data for comparisons. The median follow-up time was 14 weeks (8-30 weeks). The average hemoglobin level on the initial visit was 9.5 g/dl and most (50 cases, 75.7%) had microcytic anemia (mean corpuscular volume (MCV) < 80 fl) on the initial visit.

Table 1. Patient characteristics, CBC, and red cell indices on the initial visit of the studied patients (total), and comparison between patients who came for follow-up visit or did not come (single visit). The statistical tests used was unpaired *t*-test.

Patient's characteristics, CBC and red cell indices on initial visit	Total (n = 66)	Follow-up (n = 31)	Single visit (n = 35)	P
Age (yr)	36.5 ± 12.6	38.45 ± 12.7	33.4 ± 12.3	0.17
White cell count (x $10^3/\mu l$)	6.66 ± 2.15	6.50 ± 1.48	6.79 ± 2.58	0.58
Red cell count (x $10^6/\mu l$)	4.33 ± 0.67	4.19 ± 0.51	4.44 ± 0.78	0.13
Hemoglobin (g/dl)	9.5 ± 1.7	9.3 ± 1.5	9.6 ± 1.9	0.45
Hematocrit (%)	30.0 ± 5.0	29.8 ± 3.6	30.3 ± 5.9	0.68
Mean corpuscular volume (fl)	71.5 ± 10.4	71.6 ± 9.4	71.4 ± 11.3	0.96
Mean corpuscular hemoglobin (pg)	22.7 ± 4.2	22.4 ± 4.0	22.9 ± 4.3	0.64
Mean corpuscular hemoglobin concentration (g/dl)	31.6 ± 2.4	31.2 ± 2.7	32.0 ± 2.1	0.24
Red cell distribution width (%)	18.3 ± 6.2	19.0 ± 6.5	17.7 ± 5.9	0.43
Platelet count (x $10^3/\mu l$)	298 ± 89	294 ± 97	301 ± 83	0.78

There was no significant difference in age, or initial CBC data between patients who did or did not come for follow-up.

Iron deficiency and thalassemia among anemic females

Iron deficiency was defined by 2 criteria: serum ferritin below 20 ng/ml and/or significant response to iron therapy. Iron deficiency was present in 29 (43.5%), and thalassemia trait and iron deficiency coexisted in 6 (9.1%) subjects. In 8 normocytic anemic subjects, iron deficiency and thalassemia traits were excluded, thus, considered to be anemia from other causes (Table 2). Of 16 iron- deficient non-thalassemic subjects who had available follow-up CBC data, all but one had low serum ferritin and 14 had increased hemoglobin > 1.5 g/dl over the follow-up period. In this group, hemoglobin increased 3.7 g/dl on average, ranging from 0.7 to 8.9 g/dl (Table 2). Serum iron values were variable. Most (20 of 23) iron-deficient non-thalassemic and all 6 iron-deficient thalassemic individuals had low serum iron (< 80 mg/dl). Serum iron levels were higher in the iron-sufficient group (Table 2); however, around half (12 of 25 thalassemic and 2 of 5 non-thalassemic) of iron-sufficient individuals also had low serum iron levels. Therefore, serum iron alone was not a specific test to diagnose iron deficiency.

The most common type of thalassemia found in anemic but otherwise healthy females were homozygous HbE, HbH diseases (HbH and HbH-constant spring (CS)), and alpha-thalassemia-1 trait (Table 2). Half of HbE trait (4 of 8), but none of thalassemia intermedia (homozygous HbE and HbH diseases) individuals, were also iron deficient.

Red cell indices and response to therapeutic iron

In 16 iron-deficient non-thalassemic females who had available CBC on the follow-up visit, hemoglobin had increased 3.7 g/dl (Table 2), from 9.1 to 12.8 g/dl on average (Table 3). Red cell count also increased with iron therapy (from 4.0 x $10^6/\mu l$ to 4.5 x $10^6/\mu l$), and so did red cell size (MCV from 71.1 to 86.8 fl) and hemoglobin (mean corpuscular hemoglobin (MCH) from 22.5 to 27.8 pg). All red cell indices, except for mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW), were highly significantly increased (Table 3).

In contrast, red cell indices of iron-sufficient thalassemic subjects remained unchanged after iron supplement; hemoglobin increased 0.4 g/dl on average, ranging from a decrease of 0.4 to an increase of 1.5 g/dl (Table 2). The initial hemoglobin values of the thalassemic group (average 9.2 g/dl) were similar to the iron-deficient group (average 9.1 g/dl). The initial red blood cell counts (RBC) in the thalassemic group were slightly higher (average 4.5 x $10^6/\mu l$), but the MCV and MCH were relatively lower than the iron-deficient group. After iron treatment, none of the thalassemic red cell indices significantly increased (Table 3). There were too few subjects with post-treatment data in the other two groups (iron-deficient thalassemic and normal groups) to make any meaningful conclusions.

Since CBC is the only test that has an available result within the same day of visit, it is a chal-

Table 2. Patient were categorized by iron status and thalassemia diagnoses. Number of patients in each category and response to therapeutic trial of iron is shown.

Iron status	Thalassemia type	Total number	%	Average serum ferritin†	Range (ng/ml)	Average serum iron	Range (μg/dl)	Hemoglobin increase after iron treatment	Range (g/dl)
Deficient	Normal*	23	34.8	6.2	1-310	45.9	11-183	3.7 ± 2.2	0.7 to 8.9
Deficient	Thalassemia traits	6	9.1	4.9	3-8	40.0	26-73	0.9 ± 2.2	-1.6 to 2.5
	• Alpha-thal trait	1							
	• HbE trait	4							
	• HbJ trait	1							
Normal	Normal*	8	12.1	67.1	30-204	77.2	46-100	0.45	0.3, 0.6
Normal	Thalassemia syndromes	29	43.9	91.2	20-635	92.2	37-238	0.4 ± 0.8	-0.4 to 1.5
	• HbE trait	4							
	• Homozygous HbE	6							
	• Beta-thalassemia trait	2							
	• HbH disease	7							
	• HbH-CS diseases	2							
	• Homozygous HbCS	1							
	• Alpha-thal-1 trait	7							
Total	All patients	66	100	-	-	-	-	1.8 ± 2.2	-1.6 to 8.9
	• Iron deficient	29	43.9						
	• Thalassemics	35	53.0						

† Average number shown is geometric mean value.

* Normal = normal hemoglobin typing, alpha-thalassemia-2 trait cannot be excluded.

Table 3. Response of red cell indices to a therapeutic trial with iron (Rx). Numbers shown is mean ± standard deviation. In the group where n = 2, only the mean value is shown. P-value was derived from the paired *t*-test.

Red cell indices	Iron and thalassemia status									
	Iron-deficient non-thalassemic (n = 16)			Iron-deficient thalassemia trait (n = 3)		Normal (iron-sufficient non-thalassemic) (n = 2)		Thalassemia syndrome, iron-sufficient (n = 10)		
	Pre-Rx	Post-Rx	P-value	Pre-Rx	Post-Rx	Pre-Rx	Post-Rx	Pre-Rx	Post-Rx	P-value
Red cell count (x 10^6/µl)	4.0 ± 0.4	4.5 ± 0.4	9 x 10^{-4}	4.4 ± 0.2	4.5 ± 0.6	3.4	3.7	4.5 ± 0.6	4.5 ± 0.8	0.44
Hemoglobin (g/dl)	9.1 ± 1.2	12.8 ± 1.0	2 x 10^{-8}	10.0 ± 0.7	10.9 ± 1.9	10.4	10.9	9.2 ± 1.4	9.6 ± 1.4	0.27
Hematocrit (%)	28.8 ± 4.2	39.2 ± 4.1	2 x 10^{-7}	31.9 ± 4.1	35.1 ± 4.7	31.8	34.9	30.2 ± 2.7	30.7 ± 3.4	0.38
Mean corpuscular volume (fl)	71.1 ± 8.8	86.8 ± 2.8	4 x 10^{-7}	73.2 ± 7.5	78.0 ± 3.6	92.8	95.7	67.5 ± 5.6	67.3 ± 6.4	0.48
Mean corpuscular hemoglobin (pg)	22.5 ± 4.1	27.8 ± 1.9	9 x 10^{-5}	23.0 ± 2.3	23.4 ± 1.0	30.6	29.6	20.4 ± 2.1	21.7 ± 2.3	0.13
Mean corpuscular hemoglobin concentration (g/dl)	31.5 ± 2.5	32.5 ± 1.2	0.09	31.6 ± 1.4	31.0 ± 1.6	33.0	31.0	31.5 ± 3.2	32.3 ± 0.8	0.08
Red cell distribution width (%)	19.3 ± 6.7	17.5 ± 6.5	0.23	15.3 ± 1.4	17.0 ± 5.9	12.6	14.2	20.8 ± 6.8	20.9 ± 9.0	0.49

lenge whether one could make a diagnosis of thalassemia or iron deficiency based on red cell indices alone. After final diagnoses of iron deficiency and thalassemia were made, a combination of red cell indices were retrospectively analysed to find a simple set of criteria that could most reliably distinguish between the two problems. The authors found that a combination of red cell count (RBC) and MCV criteria were most helpful. Most iron-deficient individuals had RBC below 4.4 x 10^6/µl and/or MCV between 69-85 fl. In contrast, most thalassemic individuals had RBC above 4.4 x 10^6/µl and MCV below 69 fl (Fig. 1).

Using such criteria, the authors found that all but two (n = 29) iron deficient females had either low RBC (< 4.4 x 10^6/µl) and/or low to normal MCV (69-85 fl), a 93.1 per cent sensitivity. The two iron-deficient cases who had high RBC (> 4.4 x 10^6/µl) and very low MCV (< 69 fl) also had HbE trait (1 case) or α-thalassemia-1 trait (1 case). However, 6 of 28 iron-sufficient thalassemic and all 8 iron-sufficient non-thalassemic individuals had a similar RBC-MCV profile, thus, making specificity of this criteria low (60%). But despite its low specificity, the predictive value of high RBC and very low MCV to exclude iron deficiency was good (21 of 23, 91.3%, Fig. 1).

For the diagnosis of thalassemia diseases (HbH, HbH-CS & HbEE), a combination of high RBC (> 4.4 x 10^6/µl) and very low MCV (< 69 fl) was a sensitive (92.9%, n = 14) and specific set of criteria (100%, n = 15). These cases could be identified so that iron supplement is not given initially. The sensitivity to diagnose thalassemia traits, however, was low (52.4%) because 10 cases of thalassemia traits (6 cases of HbE trait and 1 case each of HbCS, HbJ trait, α-thalassemia trait, β-thalassemia-1 trait, n = 21) had low RBC, and/or MCV > 69 fl. The positive predictive value for this criteria to diagnose thalassemia was 100 per cent (n = 23).

DISCUSSION

Iron deficiency and thalassemia traits are prevalent in the Thai population. Iron deficiency is more common in females than in males[1-3,9]. The symptoms and physical signs of iron deficiency are often subtle and non-specific. Many cases of anemia were detected by a complete blood count as part of a routine physical check-up[3].

Therapeutic trial of iron deficiency is one of the most cost-effective test to diagnose iron defi-

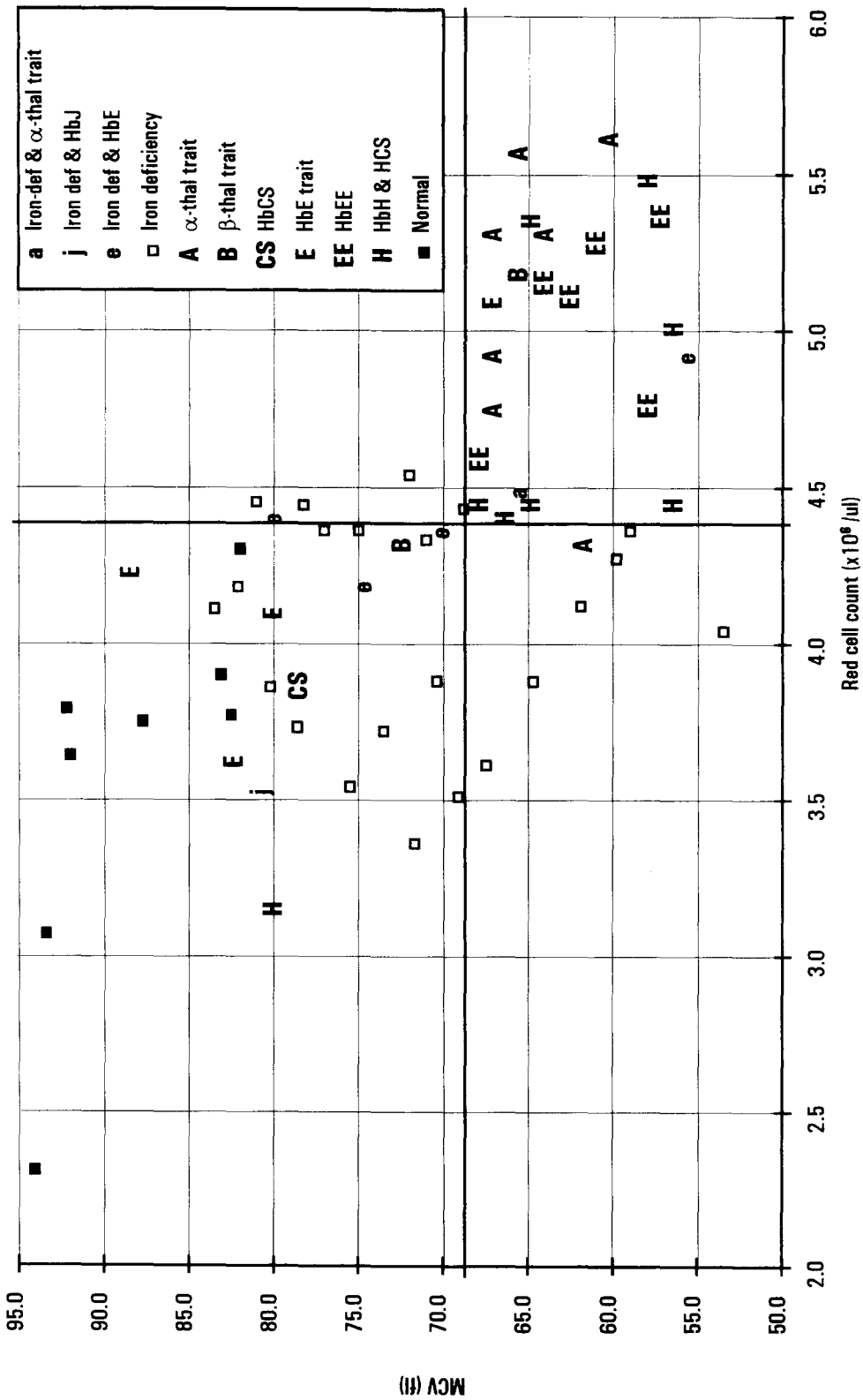

Fig. 1. Scattergram showing red cell count (RBC) and MCV in cases with iron deficiency (iron def) and various thalassemia syndromes, or a combination. Solid lines denote cut-off points for red cell indices (RBC 4.4 x 10^6/μl and MCV 69 fl).

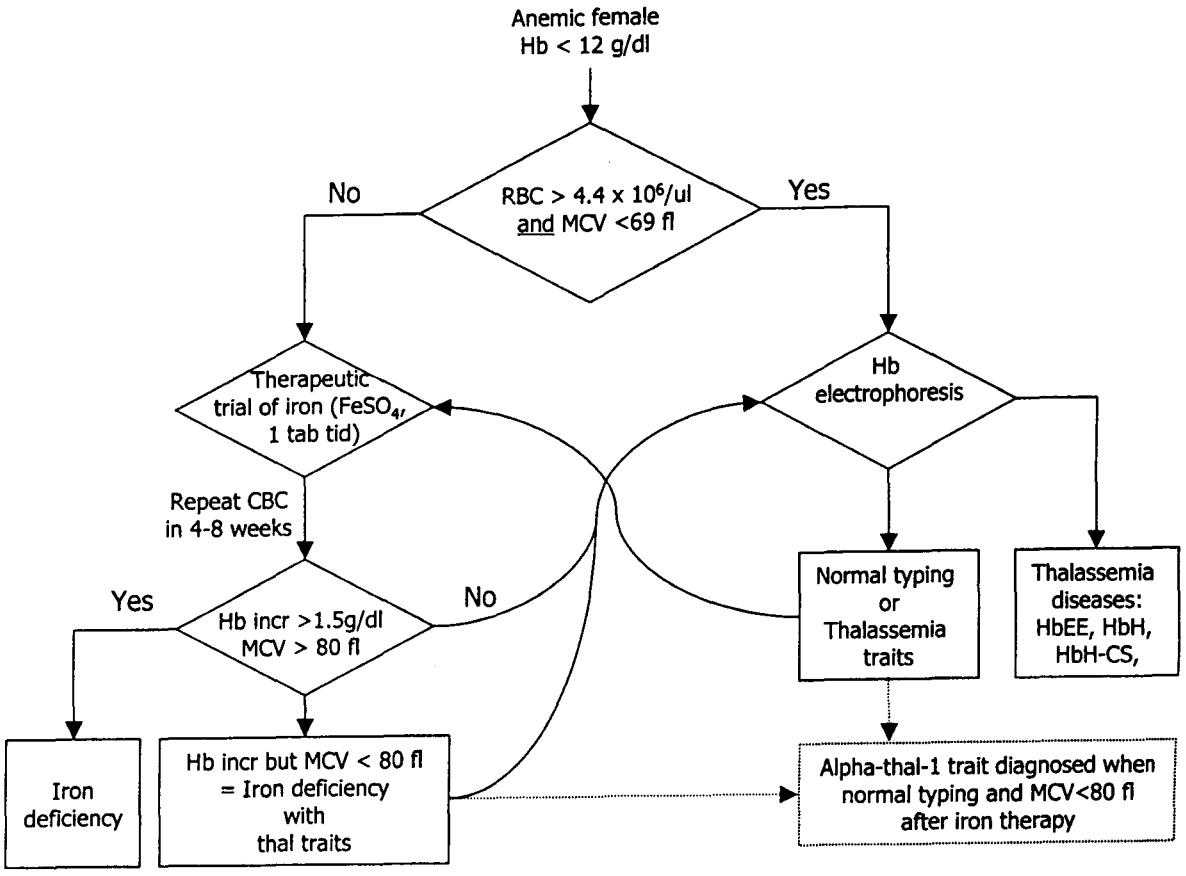

Fig. 2. Suggested algorithm for diagnostic work-up of anemic Thai females, using automated CBC parameters, therapeutic trial of iron, and hemoglobin electrophoresis.

ciency worldwide[3,7]. In Thailand, the types and prevalence of thalassemia is different from that of Western countries. Alpha-thalassemia-1 trait, hemoglobin H, and hemoglobin E syndromes are unique in this region[10,11]. Therapeutic trials of iron have been adopted by the Thai Society of Hematology as a way to diagnose or rule-out iron deficiency[7]. The present finding that both iron deficiency and thalassemia can coexist in the same individual, as high as 9 per cent in the present series, supports the use of a therapeutic trial to exclude iron deficiency before diagnosis of thalassemia in anemic subjects.

A therapeutic trial of iron requires follow-up visits for CBC, which was a problem in the present study as well as in clinical practice[12]. Despite a 47 per cent follow-up rate, the authors believe that the presented data is unbiased because the initial CBC values in subjects with follow-up visits were not statistically different from those without (Table 1). The treatment duration of 8-16 weeks in the present study was adequate to show significant changes in blood cells after sufficient iron supply, but a shorter (4-6 weeks) therapeutic trial could be used, and is recommended by the Thai Society of Hematology[7].

Although thalassemia traits can have co-existing iron deficiency, several types of thalassemia minor and thalassemia intermedia had a tendency for iron overload. The authors found that hemoglobin H and H-CS had high ferritin levels, therefore, unnecessary iron treatment should be avoided. The authors identified a simple set of criteria that would most likely exclude iron deficiency: a high red cell count (> 4.4 x 10^6/μl) and very low MCV (< 69 fl). If a therapeutic trial of iron was given to anemic females

except those who had such high RBC and very low MCV, it would successfully avoid unnecessary iron supplement to most cases of HbH diseases.

The cut-off RBC value for thalassemia in the present study is lower than other reports[13], which is probably due to the subjects being exclusively female. In addition, the types of thalassemia in the present study include both alpha- and beta-thalassemia traits and a mild form of the diseases. In an Indian study ia which only beta-thalassemia traits were included, their cut-off point for RBC count was 4.9 x $10^6/\mu l$[13]. In a U.S. study[14], both alpha- and beta-thalassemia were included, however, HbE syndromes were under-represented.

Several discrimination functions have been developed from red cell indices to differentiate iron deficiency from thalassemia traits[15-20]. The MCV/RBC ratio has been proposed by Mentzer[16], where MCV/RBC > 15 suggests iron deficiency. In the presented data, the sensitivity of Mentzer index to diagnose iron deficiency would be 82.8 per cent (24 of 29), a lower sensitivity than the authors' RBC & MCV criteria (93%). Three cases of HbH would also have Mentzer index > 15 and thus been mistaken as iron-deficiency. Red cell distribution width (RDW) has been observed to be wide (> 15%) among iron-deficient patients[19]. A discrimination function based on RDW was shown to be useful to differentiate iron deficiency from thalassemia traits[20]. However, the authors did not find RDW to be useful in anemic Thais because RDW values were higher than 15 per cent in most iron deficient subjects as well as thalassemic subjects, particularly with HbH diseases (Table 3). The difficulty in applying discrimination functions in a Thai population may be related to a high prevalence of HbE traits, which is known to have less pronounced change in red cell indices[21-23].

The authors found that a combination of high red cell count (> 4.4 x $10^6/\mu l$) and very low MCV (< 69 fl) is useful to identify thalassemia and exclude iron deficiency in anemic females, the group which would not benefit from a therapeutic trial of iron. The high specificity of this criteria suggests that a hemoglobin electrophoresis, rather than iron supplement, is the most helpful initial work-up for this subgroup. Therefore, a recommendation of diagnostic work-up of anemic females could be made (Fig. 2). In anemic females with high RBC and very low MCV, a hemoglobin typing should be performed first, which revealed a specific type of thalassemia in 16 of 23 cases (right lower quadrant, Fig. 1). If a thalassemia trait or normal hemoglobin typing is found, a therapeutic trial of iron is then needed to exclude coexisting iron deficiency. For cases with normal typing, lack of iron response (6 of 7) would then allow us to make the diagnosis of alpha-thalassemia-1 trait.

For anemic subjects with low RBC count (< 4.4 x $10^6/\mu l$) and/or low MCV (69-85 fl), an initial therapeutic trial of iron would be most useful (Fig. 2). Twenty-four of 33 responded to iron treatment (hemoglobin increased > 1.5 g/dl). Most iron-deficient individuals will also have an MCV above 80 fl at the follow-up visits. For subjects whose MCV does not reach 80 fl, an electrophoresis would identify a specific thalassemia diagnosis. Around 5 per cent of HbE trait would also have MCV > 80 fl[21] and could be screened by a low-cost dichlorophenol indolphenol (DCIP) test if counselling is needed[24].

This scheme of work-up would result in significant cost saving over the conventional use of serum ferritin and Hb electrophoresis to make the diagnosis of iron deficiency and thalassemia. Considering the current estimated cost of CBC to be 50 baht, ferritin level is 200 baht, and Hb electrophoresis is 200 baht, and treatment with iron sulfate is 54 baht per month (1 tablet three times daily for 4 weeks at 0.6 baht per tablet), the cost of conventional diagnostic work-up for each anemic female with serum ferritin and hemoglobin electrophoresis would cost 450 baht plus an average treatment cost of 71.3 baht (44% would be iron-deficiency and need 3-month oral iron therapy) per case, a total cost of 521.3 baht per case. If algorithm (Fig. 2) was used, all cases would need an initial CBC, 23/64 would have initial Hb electrophoresis, 18 of which would have a normal result or trait and need a therapeutic trial of iron. Forty-one of 64 would be given initial therapeutic trial of iron, and after a second CBC, 15 would not respond and need Hb electrophoresis. Of 26 iron responders, 4 would still have MCV< 80 fl and need Hb electrophoresis. The overall cost of therapeutic diagnosis, therefore, would be 256.50 baht per case, a 51 per cent cost reduction over the conventional diagnostic scheme.

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การตรวจหาสาเหตุของภาวะโลหิตจางในสตรีไทยโดยใช้ดัชนีเม็ดเลือดแดงและการรักษาด้วยธาตุเหล็ก

อิศรางค์ นุชประยูร, พบ, ปรด,*
*บุญรื่น สุขทวี, พยบ**, ทัสสนี นุชประยูร, พบ***

ภาวะซีดพบได้บ่อยในสตรีไทย มักเกิดจากการขาดธาตุเหล็กหรือธาลัสซีเมีย ซึ่งสามารถแยกจากกันด้วยการรักษาด้วยยาเสริมธาตุเหล็ก ผู้วิจัยทำการศึกษาผู้มาตรวจสุขภาพประจำปี หญิงที่ได้รับการตรวจเลือดและพบว่าซีด คือระดับฮีโมโกลบินต่ำกว่า 12 กรัม/ดล โดยตรวจเลือด (CBC) ฮีโมโกลบินทัยป์ ระดับเฟอริตินและระดับธาตุเหล็กในซีรัม และให้การรักษาด้วยยาเสริมธาตุเหล็ก 120 มก ต่อวันเป็นเวลาสองเดือน และนัดตรวจเลือด CBC ซ้ำ พบว่าในผู้หญิงที่ซีด 72 ราย อายุเฉลี่ย 36 ปี ระดับฮีโมโกลบิน 9.5 $\pm$ 1.7 กรัม/ดล มีสาเหตุจากขาดธาตุเหล็ก 23 ราย (34.8%), ทั้งขาดธาตุเหล็กและมีธาลัสซีเมียแฝง 6 ราย (9.1%), ธาลัสซีเมียแต่ไม่ขาดธาตุเหล็ก 29 ราย (43.9%) เมื่อรักษาด้วยยาเสริมธาตุเหล็กแล้วผู้ที่ขาดธาตุเหล็กจะมีระดับฮีโมโกลบินสูงขึ้นเป็น 12.8 $\pm$ 1.0 กรัม/ดล อย่างมีนัยสำคัญทางสถิติ ($n = 16$, $p = 2 \times 10^{-8}$) ค่าดัชนีเม็ดเลือดแดงที่จะช่วยวินิจฉัยภาวะขาดธาตุเหล็กและธาลัสซีเมีย คือ จำนวนเม็ดเลือดแดง (RBC) ที่มากกว่า 4.4 ล้านเซลล์ต่อไมโครลิตร (มคล) ร่วมกับขนาดเม็ดเลือดแดง (MCV) ที่เล็กกว่า 69 เฟมโตลิตร (ฟล) โดยพบว่าภาวะจำนวนเม็ดเลือดแดงมาก (> 4.4 ล้าน/มคล) และขนาดเล็กมาก (< 69 ฟล) มีความไวสูง (92.9%) และความจำเพาะสูง (100%) ในการวินิจฉัยธาลัสซีเมียประเภท HbH, HbH-CS, และ HbEE, ส่วนภาวะจำนวนเม็ดเลือดแดงต่ำ (< 4.4 ล้าน/มคล) และขนาดเล็กหรือปกติ (69-85 ฟล) มีความไวสูง (91.3%) แต่ความจำเพาะต่ำ (60%) ในการวินิจฉัยภาวะการขาดธาตุเหล็ก โดยสรุป การรักษาผู้ที่ซีดด้วยยาเสริมธาตุเหล็กเป็นวิธีการวินิจฉัยแยกโรคที่ดี เราควรให้การรักษาด้วยยาเสริมธาตุเหล็กในสตรีที่ซีดทุกราย ยกเว้นในรายที่จำนวนเม็ดเลือดแดงมาก (> 4.4 ล้าน/มคล) และขนาดเล็กมาก (< 69 ฟล) ซึ่งมักจะพบว่าเป็นธาลัสซีเมียแต่ไม่ขาดธาตุเหล็ก

คำสำคัญ : ภาวะซีด, ดัชนีเม็ดเลือดแดง, การขาดธาตุเหล็ก, ธาลัสซีเมีย, การรักษาด้วยธาตุเหล็ก

อิศรางค์ นุชประยูร, บุญรื่น สุขทวี, ทัสสนี นุชประยูร
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* ภาควิชากุมารเวชศาสตร์,
** ภาควิชาเวชศาสตร์ป้องกันและสังคม, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330