Original Article

The Prevalence and Risk Factors of Iron Deficiency Anemia in Thai Infants by Complete Blood Count at 9-Month-Old

Pussayaban Suwannakeeree, MD[1], Patraporn Jangmeonwai, MD[1]

[1] Department of Pediatrics, Panyananthaphikkhu Chonpratan Medical Center, Srinakharinwirot University, Nonthaburi, Thailand

Background: Infants are the most at risk from iron deficiency (ID) and iron deficiency anemia (IDA), but the prevalence of the latter in this group is unclear. Estimation as to the prevalence of IDA using Hb of less than 11 g/dL may have been exaggerated due to thalassemia and hemoglobinopathies. On the other hand, iron studies are costly and not routinely available in low resource settings. In the present research, the authors estimated the prevalence of IDA in 9-month-old infants at the authors' well-baby clinic by improving the post-iron-treatment criteria of Hb and defined the risk factors of IDA in infants.

Objective: To estimate the prevalence of IDA in 9-month-old infants at the well-baby clinic and to define the risk factors of IDA.

Materials and Methods: A retrospective cohort study of 391 children who had complete blood count (CBC) screening at 9-month-old at the well-baby clinic. Anemia was defined according to the WHO criteria (hemoglobin of 11 g/dL or less for children aged six months to five years). IDA was defined as an increase of at least Hb 1 g/dL after receiving iron treatment for one to two months. Mean levels of hematological parameters were compared between groups using independent samples t-test. The characteristics with potential risk factors for IDA were compared with iron non-responder and normal group. Multivariable adjusted odd ratios and 95% confidence intervals (CIs) of IDA were calculated using multinomial logistic regression with control for risk factors.

Results: One hundred fourteen children (29.1%) were anemic. There was no difference between anemic and non-anemic children in baseline characteristics. Seventy children in the anemic group were diagnosed with IDA. The prevalence of IDA in the present study was 17.9%. The IDA group showed significant improvement in Hb, Hct, MCV, MCH after receiving iron treatment, but there were no significant changes in the iron non-responder group. The risk factor for IDA was exclusive breastfeeding for at least six months (odds ratio 3.14, 95% CI 1.67 to 5.90, p<0.001).

Conclusion: The prevalence of IDA and anemia in the present study was 17.9% and 29.1%, respectively. The risk factor for IDA was exclusive breastfeeding for at least six months.

Keywords: Anemia, Iron deficiency anemia, Prevalence of anemia in infants, Complete blood count screening, Thai infants

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Iron deficiency anemia (IDA) is the most common nutrient deficiency worldwide. Infants are the group most at risk from iron deficiency (ID) and IDA[1-3]. In previous studies, ID in infants is related to brain structure development by impairing the neurotransmitter system and myelination, affecting long-term brain function after iron repletion[1,2,4-6].

The Thai Ministry of Public Health has considered anemia reduction to be a national goal since 1982[7]. Complete blood count (CBC) screening of six to twelve-month-old infants to detect anemia has been a part of the policy. A large amount of CBC data existed on Thai infants but limited data on the prevalence of IDA in infants. According to the World Health Organization (WHO) report in 2011, the prevalence of anemia in Thai children aged 6 to 59 months was 29%, representing a moderate level of public health significance[8]. A recent report from the International Study of Asthma and Allergies in Childhood (SEANUT) project, on the nutritional status of 3,119 Thai children aged from 0.5 to 12.9 years in 2013, shows that the prevalence of anemia in children aged

Correspondence to:

Suwannakeeree P.

Department of Pediatrics, Panyananthaphikkhu Chonprathan Medical Center, Faculty of Medicine, Srinakharinwirot University, 222 Moo 1, Tiwanon Road, Pakkred, Nonthaburi 11120, Thailand.

Phone: +66-2-5122345

Email: psuwannakeeree@outlook.com, pammy060@gmail.com

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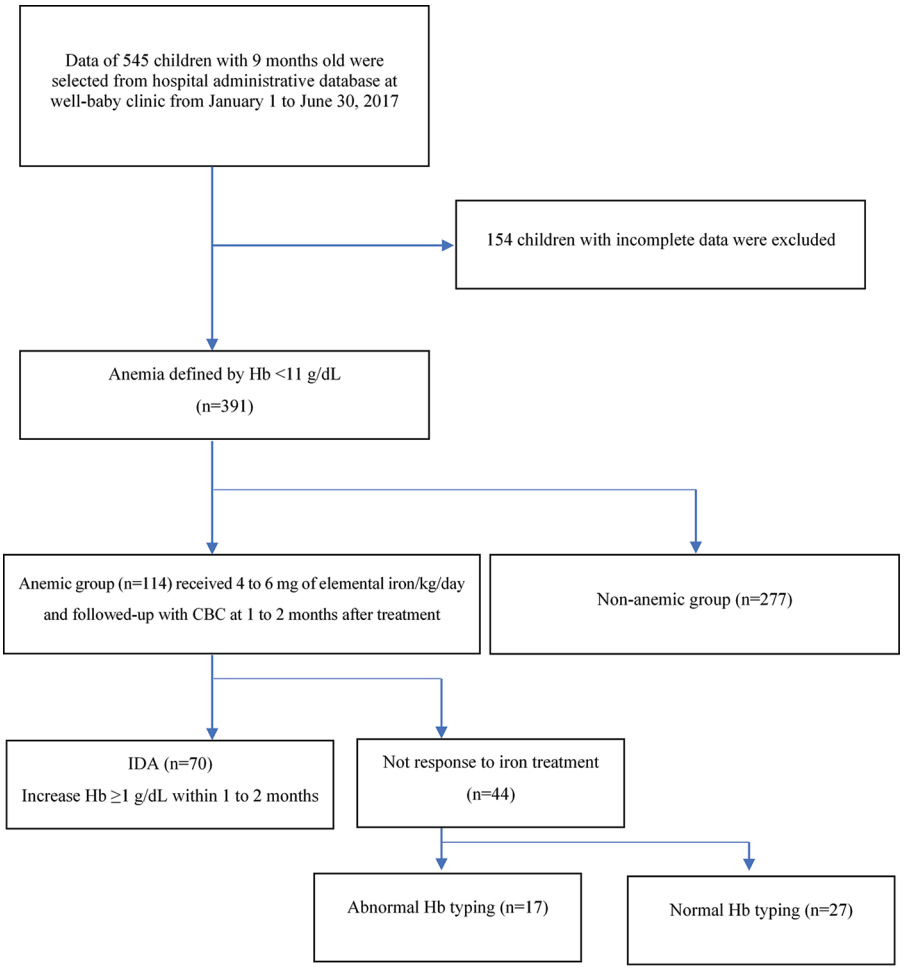

Figure 1. Study flow chart.

IDA=iron deficiency anemia; CBC=complete blood count; Hb=hemoglobin

0.5 to 2.9 years and 3 to 5.9 years in Thai urban areas were 26% and 3.1%, respectively[9]. There was no data on the prevalence of IDA in children aged 0.5 to 2.9 years, although the prevalence of IDA in children aged 3 to 5.9 years was only 2.5%[9]. The prevalence of anemia in infants seems to be greater than in the older group and the prevalence of anemia in children is not represented that of the infants.

Hemoglobin (Hb) less than 11 g/dL or hematocrit (Hct) less than 33% are the cut off values for anemia in this age group, but there is no differentiation between IDA, thalassemia, thalassemia traits, or other hemoglobinopathies. The true prevalence of IDA is difficult to define by Hb or Hct screening among Thai children due to high prevalence of thalassemia disease and hemoglobinopathies[10-12].

In Thailand, children aged from 9 to 12 months diagnosed with anemia are treated with 4 to 6 mg/kg/day with ferrous for one to two months as recommended by the Ministry of Public Health and WHO[8,13]. Anemic children who have increasing Hb of more than 1 g/dL will be diagnosed with IDA, while those showing no improvement in Hb will be investigated further through Hb typing or DNA analysis for thalassemia.

In the present research, the authors estimated the prevalence of IDA in nine-month-old infants at the well-baby clinic by improving the post-iron treatment criteria for Hb and defining the risk factors of IDA in infants.

Materials and Methods

The present research was designed as a retrospective cohort study, using data from a hospital administrative database, as demonstrated by the flow chart in Figure 1. The sample size of at least 300

Table 1. Baseline characteristics of nine-month old infants at the well-baby clinic (n=391)

Characteristics	Anemic group (n=114) Mean±SD	Non-anemic group (n=277) Mean±SD	p-value
Sex; n			0.075
Male	51	152	
Female	63	125	
Body weight (kg)	8.40±0.99	8.52±0.97	0.280
Body length (cm)	70.29± 7.16	70.60±4.91	0.620
Head circumference (cm)	33.50±0.70	33.04±1.04	0.19
Maternal age (years)	25.30±1.40	27.2±1.18	0.38
Exclusive breastfeeding for 6 months after birth; n (%)	46 (40)	48 (17)	<0.001
Hb at 9 months (g/dL)	10.07±0.84	11.88±0.62	<0.001
Hct at 9 months (%)	31.27±2.17	35.57±3.01	<0.001
MCV (fl)	66.02±8.36	73.40±5.00	<0.001
MCH (pg)	21.35±3.02	24.41±1.86	<0.001
MCHC (g/dL)	32.17±1.68	33.23±1.16	<0.001
RDW (%)	15.90±2.65	13.08±1.38	<0.001

SD=standard deviation; Hb=hemoglobin; Hct=hematocrit; MCV=mean corpus volume; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; RDW=red cell distribution width

children was calculated by applying the $n = Z^2 P(1–P)/d^2$ formula and p=0.26, based on the national reported prevalence of anemia in children aged 0.5 to 3 years old in urban areas, which was 26%. The data on children were captured on a computerized database. During the study period between January 1 and June 30, 2017, CBC screening was performed on 545 children aged 9 months old. Of these 545 children, 391 children were term and normal birth history became the present research participants, having complete information (body weight and length, duration of exclusive breastfeeding, CBC at nine months, CBC and red cell indices after iron treatment, and further investigations). Anemia was defined according to the WHO criteria (Hb of 11 g/dL or less for children aged six months to five years). IDA is defined as an Hb increase of at least 1 g/dL after receiving iron treatment (4 to 6 mg of elemental iron/kg/day) for one to two months. Hb typing was performed in children with anemia who did not respond to iron treatment.

Approval to conduct the study was obtained from the Ethics Committee of the Panyananthaphikkhu Chonprathan Medical Center, reference number EC 004/60.

Statistical analysis

Statistical analysis was performed using Stata, version 14 (StataCorp LP, College Station, TX, USA). Continuous data were presented as mean ± standard deviation (SD). Mean levels of hematological parameters were compared between two groups (anemia versus non-anemia, IDA versus iron non-responders or between IDA and others) using compare means with independent samples t-test. Comparisons containing p-values of less than 0.05 were considered statistically significant. The potential risk factor characteristics for IDA: male gender, maternal age, birth weight, body length, and exclusive breastfeeding for six months were compared between the IDA, iron non-responder, and normal groups. Multivariable adjusted odd ratios and 95% confidence intervals (CIs) of IDA, iron non-responder, and normal (control) groups were calculated using multinomial logistic regression with control for risk factors.

Results

One hundred fourteen children (29.1%) were anemic. There was no statistically significant difference between anemic and non-anemic children in male gender, mean body weight, body length, head circumference, and maternal age. Of the children in the anemic group, 40% had a history of exclusive breastfeeding for six months, which was significantly greater than in the non-anemic group, 17% of whom had exclusive breastfeeding (p<0.001). Significant differences in Hb, Hct, and red blood cell indices were observed between the anemic and non-anemic groups, as shown in Table 1.

Table 2. Red blood cell parameters pre- and post-iron therapy (n=114)

	Iron deficiency anemia (n=70); mean±SD			Iron non-responder (n=44); mean±SD		
	Pre-iron treatment	Post-iron treatment	p-value*	Pre-iron treatment	Post-iron treatment	p-value**
Hb (g/dL)	9.93±0.89	11.37±0.64	<0.001	10.09±0.86	10.25±1.14	0.59
Hct (%)	30.76±1.6	35.41±1.8	<0.001	31.17±2.7	31.9±3.2	0.30
MCV (fl)	66.02±8.39	70.08±6.5	0.002	64.59±8.85	64.57±9.2	0.99
MCH (pg)	21.53±3.18	22.72±3.01	0.02	20.85±3.11	20.56±3.21	0.72
MCHC (g/dL)	32.23±1.94	32.02±1.64	0.49	32.39±1.67	31.98±1.56	0.23
RDW (%)	15.81±2.69	16.47±4.23	0.27	16.44±3.21	17.01±3.51	0.42

SD=standard deviation; Hb=hemoglobin; Hct=hematocrit; MCV=mean corpus volume; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; RDW=red cell distribution width

* Comparison parameters between pre-iron treatment and post-iron treatment in the iron deficiency anemia group

** Comparison parameters between pre-iron treatment and post-iron treatment in the iron non-responder group

Table 3. Multivariable logistic regression for risk factors of IDA (n=391)

Risk factors	IDA group			Iron non-responder			Non-anemic group	
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI
Sex: male	1.10	0.57 to 2.13	0.76	0.45	0.19 to 1.07	0.08	1	Reference
Exclusive BF for 6 months	3.14	1.67 to 5.90	<0.001	0.64	0.23 to 1.81	0.40	1	Reference
Body weight	0.87	0.59 to 1.28	0.49	0.88	0.56 to 1.37	0.57	1	Reference
Body length	1.03	0.93 to 1.14	0.53	0.96	0.92 to 1.01	0.14	1	Reference
Maternal age	0.99	0.94 to 1.04	0.79	0.92	0.85 to 1.01	0.19	1	Reference

IDA=iron deficiency anemia; OR=odds ratio; CI=confidence interval; BF=breastfeeding

Seventy children in the anemic group showed an increase in Hb of at least 1 g/dL after iron treatment were diagnosed with IDA according to the WHO definition. IDA in the present study was prevalent in 70 out of 391 children (17.9%). Children who showed no increase in Hb after iron treatment were defined as being in the iron non-responder group. All of them were tested for thalassemia by Hb typing, and 17 out of 44 (40%) were found to have abnormal Hb typing such as beta-thalassemia with Hb E, homozygous Hb E, and Hb H disease. The IDA group showed significant improvement in Hb, Hct, mean corpus volume (MCV), and mean corpuscular hemoglobin (MCH) after receiving iron treatment, although there were no significant changes in the average Hb, Hct, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW) in the iron non-responder group as shown in Table 2.

The children were grouped into three levels, normal, IDA, and iron non-responder, based on CBC screening at the well-baby clinic, and CBC for follow up after receiving 4 to 6 mg of elemental iron/kg/day for one to two months. The risk factors for IDA were analyzed using multinomial logistic regression and presented with odds ratios. The three groups were similar in gender, body weight, and body length at age 9 months, and maternal age (Table 3). The risk factor for IDA was exclusive breastfeeding for at least six months (odds ratio 3.14, 95% CI 1.67 to 5.90, p<0.001) (Table 3).

Discussion

Iron studies are costly and not routinely available in low resource settings. The methods used are expensive and time-consuming. Furthermore, multiple venous blood sampling in infants causes significant pain and stress for children and their parents. For these reasons, the prevalence of IDA in Thai children under one year old is not actually known. In the present study, the authors estimated the prevalence of IDA in infants using a therapeutic iron trial.

In the present study, the prevalence of anemia (Hb of less than 11 g/dL) was 29.1%, similar to the report in children aged between 0.5 to 2.9 years of

the SEANUT (26%)[9]. More than half of the anemic infants had IDA (70 out of 114, 61.4%), and the prevalence of IDA in the present study was 17.9%. The prevalence of IDA in the present study was lower than that contained in a 2007 study in South-East Asia, which reported a prevalence of 26%[14] but higher than those in South Korea (11%)(3), Japan (4%), and New Zealand (4.3%)[15,16]. Improving Maternal-child health care system might be an important factor for decreasing the prevalence of IDA compared with the last decade. Pregnant women have free access to continuum of care including antenatal care, delivery, and postpartum care at public hospitals. Once the child is born, these well-child checks will begin at well-baby clinic. Each child receives regular check-ups from health personnel, and their parents is educated in breastfeeding and nutrition.

In anemic infants, the red cell indices are unable to differentiate between the IDA and iron non-responder groups. There are no discrimination indices that can differentiate between IDA and thalassemia traits[17-19]. IDA infants in the present study might be IDA alone or coexisting with the thalassemia trait. They also have lower means MCV and MCH after iron treatment than reference range red blood cells indices in normal Thai children (reference range versus the study, MCV 80 versus 70 fl, and MCH 27 versus 23 pg)[20]. In post-iron treatment, red cell indices were not significant changed in the iron non-responder group while significant MCV and MCH increased were observed in the IDA group.

The present study data showed that more infants in the anemic group were exclusively breastfed for six months than in the normal group (40% versus 17%, $p<0.001$) as shown in Table 1. The risk factor for IDA in the present study was exclusive breastfeeding for at least six months (odds ratio 3.14). This result is similar to that of a study conducted in 2005 on 140 Thai infants aged from 9 to 12 months, in which the adjusted risk ratio of IDA for exclusive breastfeeding was 6.3 (95% CI 1.5 to 25.0)[21]. Many previous studies have shown that exclusive breastfeeding for infants aged over six months to be associated with an increased risk of IDA, especially in developing countries such as Brazil[22], Nigeria[23], and Iran[24]. An observational study in 2007 investigated the relationship between iron status in infancy and type of milk. The present study reported breastfed infants had a greater risk of anemia and low levels of ferritin at 8 and 12 months of age (risk ratio 1.55, $p=0.009$ and 1.73, $p=0.006$ at 8 and 12 months, respectively)[25]. Excessive feeding of any kind of milk, which is more than 600 mL/day or six breastfeeds or more, in the second six months of life could decrease the energy and iron intake from solid food.

The limitations of the present study involved a lack of standards and confirmation of iron present in blood tests for nine-month-old infants. However, the prevalence of IDA in infants has been estimated by a therapeutic trial of iron and considered sufficient to evaluate the magnitude of the problem.

Furthermore, the present study was based on a retrospective survey of medical records, and consequently, there is lack of information regarding prenatal maternal anemia status, maternal gravida, as well as the amount and type of complementary food. The iron-taking compliance in anemic group who were prescribed 4 to 6 mg of elemental iron/kg/day, was probably not evaluated precisely. For this reason, some of iron non-responder children might be IDA with poor iron-taking compliance.

Most infants in the present study were considered to be in the low to medium socioeconomic family status, with their medical expenses covered by universal health care by the Thai government. Therefore, the results of the present study may not be applicable to all socioeconomic groups. A prospective and well-planned risk assessment study of IDA in infants and young children is important to control its prevalence.

Conclusion

The prevalence of IDA in the present study was 17% (70 out of 391 children). The risk factor for IDA was exclusive breastfeeding for at least six months (odds ratio 3.14, 95% CI 1.67 to 5.90, $p<0.001$).

What is already known on this topic?

ID in infants relates to developing brain structures and affects long-term brain function. Infants are the most at risk from ID and IDA.

What this study adds?

In this study, the prevalence of IDA in infants is much more than of the older children. The risk factor for IDA is exclusive breastfeeding for at least six months.

Conflicts of interest

The authors declare no conflict of interest.

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