Clinical Features and Outcomes of Patients with Non-Iron Nutritional Deficiency Anemia in an In-Patient Setting at Siriraj Hospital: A 10-Year Retrospective Study

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Background: *Anemia is a major public health issue despite preventive interventions. Data on non-iron nutritional deficiency anemia in hospitalized patients are limited.*
Objective: *This study explored the incidence, clinical features, and outcomes of hospitalized patients diagnosed with non-iron nutritional deficiency anemia at a major teaching hospital in Thailand.*
Material and Method: *Medical records of in-patient departments dated between January 2001 and June 2011 were retrospectively reviewed.*
Results: *One hundred and two cases were identified, including 40 patients with vitamin B12 deficiency, 46 with folate deficiency, and 16 with other nutritional deficiency anemias; corresponding incidence rates were 0.4, 0.6, and 0.2 cases per 100,000 per year, respectively. Patients with vitamin B12 deficiency were mostly female, while patients with folate deficiency were preponderantly male. Glossitis and pancytopenia were common characteristics of vitamin B12 deficiency cases, whereas alcohol abuse and cirrhosis were more frequent in folate deficiency cases, as expected. Serum ferritin levels were relatively high across all categories. A significant proportion of anemia cases across all subgroups presented concomitantly with anorexia or poor food intake, which indicates underlying nutritional problems in these patients. Survival of patients with folate and other types of nutritional deficiency anemia was lower than for patients with vitamin B12 deficiency anemia (hazard ratio [HR] and p-values were 2.65, 0.001 and 2.35, 0.023, respectively). Hemoglobin normalization in patients with vitamin B12 deficiency anemia could be achieved by intramuscular injection and oral vitamin B12 treatment in 55.56% and 33.33% (p = 0.248), with a median response time of 9 and 86 weeks (p = 0.151), respectively.*
Conclusion: *Non-iron nutritional deficiency anemia was not common in hospitalized patients in this study. Vitamin B12 injections resulted in faster responses, but with similar efficacy compared with oral treatments. Survival of patients with vitamin B12 deficiency anemia was significantly better than that of those with folate or other types of nutritional anemia.*

Keywords: *Nutritional deficiency anemia, Megaloblastic anemia, B12 deficiency, Clinical outcome, Thailand*

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Anemia is one of the most common disorders in the world and a major public health problem, both in developed and developing countries. Anemia affects one-quarter of the world's population and is concentrated in preschool-aged children and women, making it a global public health concern[1]. Despite preventive interventions, this health issue has not been resolved and continues to affect the health, quality of life, and working capacity of people globally[2]. Anemia is defined as a deficiency in red blood cell concentration or hemoglobin concentration with a concomitant impaired capacity to transport oxygen. Major nutrients involved in adequate erythropoiesis are iron, folate, and cobalamin (vitamin B12)[3]. Deficiencies in these nutrients, either with or without malnutrition, result in anemia. Prevalence of anemia in Thailand varies according to population and geographical distribution and has been reported to range from 5.0 to 56.2%[4]. The major cause of anemia worldwide is iron deficiency, which often occurs concomitantly with folate deficiency and/or vitamin B12 deficiency, as well as with infections[2]. However, there is a paucity of published data regarding prevalence of nutritional anemia, other than anemia secondary to iron deficiency, in Thailand. The majority of reports are based on surveillance studies in small subgroups of asymptomatic

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subjects[5-10]. Thus, the true prevalence status of nutritional anemia in Thailand remains unknown. Furthermore, it has been reported that hospitalized patients, especially elderly patients aged 60 years or more, have a high prevalence of anemia with concomitant malnutrition[11]. Therefore, the present study aimed to determine the incidence, clinical characteristics, and outcomes of patients with non-iron nutritional deficiency anemia in in-patient departments at our institution during a 10-year period.

Material and Method

After review and approval of the study design by the Siriraj Institutional Review Board (SIRB), electronic medical records specific to the in-patient departments at Siriraj Hospital were retrieved from the hospital database by the Medical Records Unit. Search criteria were based on the International Classification of Diseases (ICD)-10 coding system, for which we included disease codes ranging from D50.0 to D53.9 (corresponding diagnoses were: D50, iron deficiency anemia; D51, cobalamin deficiency anemia; D52, folate deficiency anemia; and D53, other nutritional anemia) dated between January 2001 and July 2011. The ICD-10 code could be principle diagnosis, co-morbidity, or complication category. Cases were included if the diagnosis was done within seven days before admission or occurring during the admission. After excluding cases of iron deficiency anemia, charts were reviewed for purposes of accurately classifying anemia cases. Prevalence of anemia was determined and cases of nutritional anemia (other than iron deficiency anemia) were further studied regarding characteristics, etiology, treatment, and outcomes.

Anemia was defined for male patients as hemoglobin level less than 13 g/dL and for female patients as hemoglobin level less than 12 g/dL. In gestating women coursing the second trimester, patients with hemoglobin level less than 10.5 g/dL were considered as having anemia. Iron deficiency anemia was defined as anemia with mean corpuscular volume (MCV) less than 80 femtoliters (fL), serum transferrin saturation less than 15%, serum ferritin less than 12 ng/mL, or anemia that responded to iron supplementation (evidenced by increased reticulocyte count within one to two weeks or normalized hemoglobin level within one to two months after treatment)[12]. Anemia secondary to vitamin B12 deficiency was defined as macrocytic anemia with MCV more than 100 fL, posterior spinal cord abnormalities resulting in ataxia, loss of proprioceptive sensation, and a serum B12 level less than 200 pg/mL[13]. Folate deficiency anemia was defined as macrocytic anemia with MCV more than 100 fL, without neurological abnormalities, and a serum folate level less than 3 ng/mL[13]. It should be noted that serum folate rises rapidly following intake; thus, diagnosis of folate deficiency anemia may be considered depending on the clinical setting and other accompanying investigations. Other nutritional deficiency anemia includes protein deficiency anemia, pyrimidine deficiency anemia, scorbutic anemia, and other megaloblastic anemia not responding to B12 and folate treatment.

Demographic data and baseline patient characteristics were described using descriptive statistics. Comparison of descriptive data between each nutritional anemia subtype and statistical significance were determined using Pearson Chi-square test. Incidence of anemia subgroups was calculated using the total number of hospital admissions each year as denominator. Average incidences were then calculated. Comparisons of continuous non-parametric data were determined using Kruskal-Wallis test. Time to treatment response was analyzed using Kaplan-Meier and log-rank test. Survival analysis was performed using the Cox proportional hazards model. All reported *p*-values were 2-sided and were considered statistically significant if less than 0.05. All statistical analyses were done using Stata® version 12.0 (StataCorp LP, Texas, USA).

Results

According to the ICD-10 coding parameters we defined for our search, 6,943 medical records were

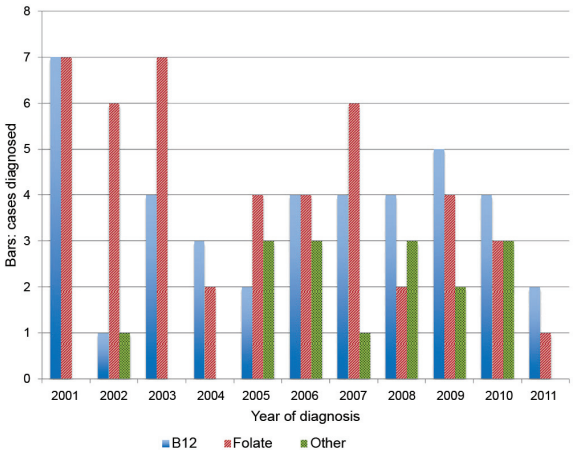

Fig. 1 Annual distribution of non-iron nutritional deficiency anemia diagnosis.

identified and retrieved. Iron deficiency anemia (ICD-10 code D50.0-50.9) was identified in 5,831 cases, all of which were excluded from further analysis. The remaining 622 cases were reviewed and re-classified. True non-iron nutritional anemia was identified in 102 cases, which include 40 cases of B12 deficiency, 46 cases of folate deficiency, and 16 other nutritional deficiency anemia cases. The annual case distribution of non-iron nutritional anemia diagnosis is shown in Fig. 1. Prevalence and incidence corresponding to the annual case distribution of non-iron nutritional anemia diagnosis are presented in Table 1.

Table 1. Prevalence and incidence of anemia in in-patient departments during the 10-year study period

	Iron deficiency anemia	B12 deficiency anemia	Folate deficiency anemia	Other nutritional anemia
Total cases identified	5,891	40	46	16
Prevalence (/100,000)	N/A	9.17	2.62	1.31
Average incidence (/100,000/year)	N/A	0.40	0.60	0.20

N/A = not available

Table 2. Clinical features of patients with non-iron nutritional deficiency anemia

Parameters	B12 deficiency anemia	Folate deficiency anemia	Other nutritional deficiency anemia	*p*-value
Total number	40	46	16	
Male sex	15 (37.50)	28 (60.87)	6 (37.50)	0.063
Median age at diagnosis (years), (range)	69 (1-97)	54 (18-93)	56.5 (11-90)	0.198
Vegan	8 (20.00)	1 (2.17)	0 (0.0)	0.006
Poor intake or anorexia	27 (67.50)	22 (47.83)	11 (68.75)	0.123
Alcoholism	8 (20.00)	32 (69.57)	2 (12.50)	<0.001
Cirrhosis	1 (2.50)	14 (30.43)	2 (12.50)	0.002
History of gastrectomy	6 (15.00)	0 (0.0)	0 (0.0)	0.007
Usage of proton pump inhibitor more than 1 year	3 (7.50)	0 (0.0)	1 (6.25)	0.177
HIV infection	0 (0.0)	2 (4.35)	4 (25.00)	0.001
TB infection	0 (0.0)	6 (13.04)	1 (6.25)	0.058
Presenting symptoms				
Asymptomatic	5 (12.5)	6 (13.0)	6 (37.5)	0.051
Lightheadedness	10 (25.0)	5 (10.9)	2 (12.5)	0.191
Vertigo	5 (12.5)	3 (6.5)	1 (6.2)	0.575
Dyspnea on exertion	22 (55.0)	6 (13.0)	4 (25.0)	<0.001
Fever	8 (20.0)	17 (37.0)	5 (31.2)	0.224
Syncope	8 (20.0)	1 (2.2)	0 (0.0)	0.006
Fatigue	25 (62.5)	14 (30.4)	6 (37.5)	0.01
Paresthesia	4 (10.0)	2 (4.3)	1 (6.2)	0.583
Metallic taste	5 (12.5)	0 (0.0)	1 (6.2)	0.049
Dementia	7 (17.5)	2 (4.3)	0 (0.0)	0.04
Physical examination				
Pallor	37 (92.5)	42 (91.3)	14 (87.5)	0.837
Jaundice	8 (20.0)	14 (30.4)	3 (18.8)	0.449
Glossitis	16 (40.0)	2 (4.3)	2 (12.5)	<0.001
Chronic liver stigmata	0 (0.0)	11 (23.9)	0 (0.0)	0.001
Hepatomegaly	4 (10.0)	7 (15.2)	0 (0.0)	0.235
Splenomegaly	0 (0.0)	2 (4.3)	1 (6.2)	0.342
Disorientation	4 (10.0)	15 (32.6)	5 (31.2)	0.035
Weakness	6 (15.0)	5 (10.9)	4 (25.0)	0.388
Numbness	8 (20.0)	2 (4.3)	1 (6.2)	0.054

HIV = human immunodeficiency virus; TB = tuberculosis
Data are presented as n or n (%), except where otherwise indicated

Patient characteristics are described in Table 2. There was a trend of male preponderance in folate deficiency anemia. Median age of diagnosis was significantly higher in B12 deficiency anemia. Strict vegetarian practice and history of gastrectomy were found to be the cause of B12 deficiency anemia in a minor population. Poor food intake and anorexia were important etiologic factors across the three subgroups. Alcohol abuse and cirrhosis were more prevalent in cases of folate deficiency anemia than in any other subgroup. Fatigue and dyspnea on exertion were the two most common presenting symptoms of non-iron nutritional deficiency anemia. Metallic taste and dementia were more prevalent in B12 deficiency anemia. Glossitis and peripheral numbness were predominant in the B12 deficiency anemia subgroup, while chronic liver stigmata were detected only in the folate deficiency anemia subgroup.

Laboratory parameters are shown in Table 3. Hemoglobin and absolute neutrophil count were significantly lower in B12 deficiency anemia than in other subgroups. Pancytopenia was commonly found in B12 deficiency anemia. Data on hemoglobin typing and bone marrow studies were available in only nine cases and 20 cases, respectively. As such, further analyses on these laboratory parameters could not be performed.

Treatment was given according to the diagnoses; however, iron supplementation was still given despite the overall high serum ferritin levels

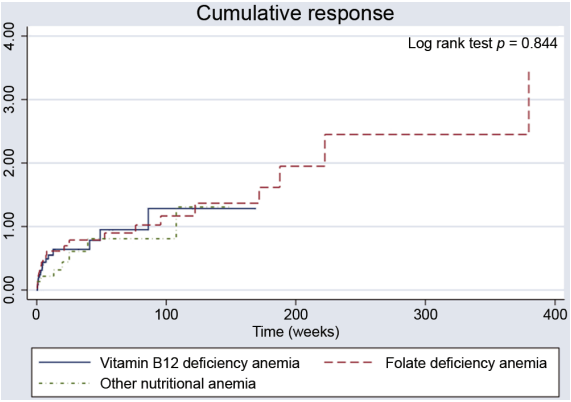

Fig. 2 Cumulative incidence of treatment response in each subgroup.

of the patients (35.00%, 39.3%, and 43.75% for B12, folate, and other nutritional deficiency anemias, respectively, p = 0.819). The majority of patients achieved hemoglobin normalization (50.0%, 65.2%, and 56.3% for B12, folate, and other nutritional deficiency anemias, respectively, p = 0.359). Median time and interquartile range [IQR] to response was 41 (IQR 3-86) weeks for B12 deficiency anemia, 21 (IQR 2-122) weeks for folate deficiency anemia, and 39 (IQR 13-108) weeks for other nutritional deficiency anemias (p = 0.844), as shown in Fig. 2.

Median survival for each subgroup was, as follows: B12, 70.3 (95% confidence interval [CI] 10.9-not reached) months; folate, 3.8 (95% CI 0.9-17.8)

Table 3. Laboratory values of patients with non-iron nutritional deficiency anemia

Parameters	B12 deficiency anemia	Folate deficiency anemia	Other nutritional deficiency anemia	*p*-value
Total number (n)	40	46	16	
Median hemoglobin (g/dL)	6.9 (2.7-11.6)	8.75 (1.9-11.6)	8.9 (7.1-11.9)	0.036
Median MCV (fL)	108.95 (69-139)	103 (73.8-125)	100.7 (77-122.8)	0.059
Median white blood cell count (x10^3 cells/uL)	5.1 (2.03-36)	8.5 (1.0-22.9)	6.2 (2.5-38.62)	0.008
Median absolute neutrophil count (x10^3 cells/uL)	2.74 (0.51-30.6)	5.98 (0.58-19.94)	4.14 (1.05-36.07)	0.002
Median platelet count (x10^3/uL)	118.5 (8-448)	137 (10-742)	149 (73-426)	0.368
Median reticulocyte count (%)	1.4 (0.38-9)	0.98 (0.06-8.7)	1.49 (0.78-5.45)	0.616
Pancytopenia, n (%)	12 (30.0)	3 (6.52)	1 (6.25)	0.006
Macro-ovalocytosis, n (%)	10 (25.0)	3 (6.52)	0 (0.0)	0.009
Macrocytosis, n (%)	17 (42.5)	24 (52.2)	6 (37.5)	0.505
Hypersegmented neutrophil, n (%)	18 (45.0)	12 (26.1)	4 (25.0)	0.133
Median ferritin (ng/mL)	508.0 (7.7-2,049.0)	569.0 (43.0-5,798.0)	153.4 (26.5-671.0)	0.771
Median serum B12 (pg/mL)	78.0 (29.0-950.0)	569.0 (110.0-1,880.0)	876.5 (308.0-2,001.0)	<0.001
Median serum folate (ng/mL)	8.6 (2.6-21.0)	2.6 (0.6-16.6)	11.4 (5.3-21.0)	<0.001

Data are presented as ranges, except where otherwise indicated

months; and other nutritional deficiency anemias, 9.8 (95% CI 0.7-35.1) months as shown in Fig. 3. Folate and other nutritional anemias had significantly worse survival outcome than B12 deficiency anemia (hazard ratio [HR] = 2.65, 95% CI 1.52-4.62, p = 0.001; and HR = 2.35, 95% CI 1.12-4.91, p = 0.023, respectively). All reported mortality cases corresponded to all-cause mortality; anemia-related mortality was rare in our study. Major causes of mortality were infection, cirrhosis, and malignancy.

In the B12 deficiency anemia subgroup, intramuscular (IM) B12 injection was administered to 70% of patients. Hemoglobin normalization was achieved in 53.6% and 37.5% of patients who received IM B12 and oral B12 (p = 0.423), respectively. Median time to response and IQR were 9 (2-49) weeks for IM B12 and 86 (13-86) weeks, respectively (p = 0.151), as shown in Fig. 4. There was no difference in clinical features and etiology between patients who received IM or oral B12 treatment except that the 16 patients with glossitis received IM treatment.

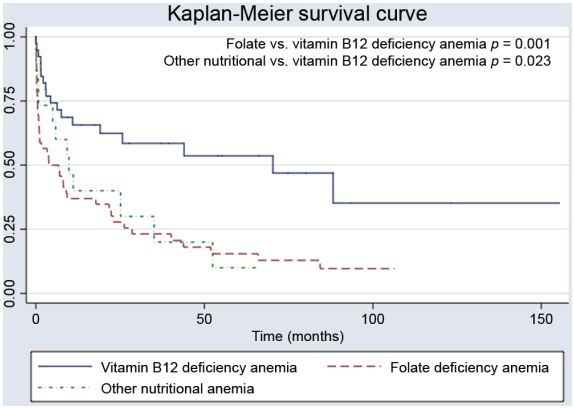

Fig. 3 Kaplan-Meier survival graph for each subgroup.

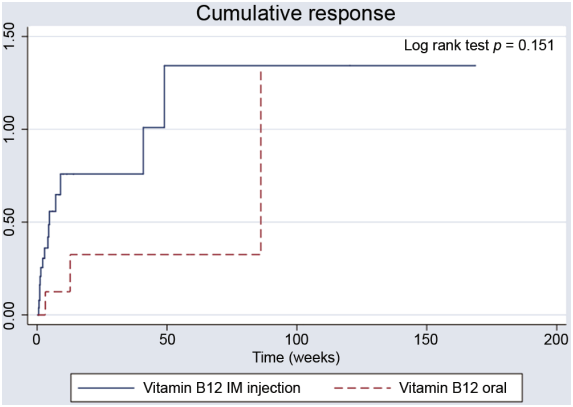

Fig. 4 Cumulative incidence of treatment response in B12 deficiency patients who received intramuscular or oral B12.

Discussion

Based on our review of the literature, the present study is the largest study to describe patients with anemia secondary to nutritional deficiency other than iron deficiency in an in-patient setting in Thailand. Previous studies analyzed subgroups of patients, such as vegetarians[8] or elderly patients in geriatric clinics[10], and those studies were conducted more than 10 years ago. Worldwide, many studies have focused on the biochemical testing of these important nutrients and found no correlation with hemoglobin value, as reported in a recent review article[14]. Incidence of B12 deficiency anemia in this study was 0.4 per 100,000 persons per year, which is in concordance with a recent report from Korea[15]. Notably, this result is much lower than incidence rates found in Caucasian populations[16], which can be as high as 25 per 100,000 persons per year[13]. Incidence of folate deficiency anemia was 0.6 per 100,000 persons per year. We could not compare the incidence of folate deficiency anemia observed in this study to incidence rates found in other populations, due to the paucity of relevant comparative data. The higher incidence of folate deficiency anemia and the preponderance of this condition among men and patients with cirrhosis may be explained by the high intake of alcohol in Thai men. The effect of alcohol in the reduction of folate absorption was described a priori[17]. Interestingly, even in an era of development in Thailand, malnutrition, poor food intake, and anorexia were still found to be the most prevalent etiologies in all anemia subgroups.

Treatment response was comparable in all anemia subgroups, including percentage of hemoglobin normalization and median time to response. However, overall survival was significantly better in B12 deficiency anemia than in folate or other nutritional anemia subgroups. Anemia-related mortality was rare in our study population. In comparison to patients with B12 deficiency anemia, folate deficiency anemia and other nutritional anemias presented a significantly higher risk of death. B12 deficiency anemia patients also had the longest survival after diagnosis. Altogether, these results suggest that folate and other nutritional anemias may have other associated causes, like alcoholism and cirrhosis. As a result, patients with these conditions are at a higher risk for associated disease-related complications.

Prevalence of poor food intake and anorexia in the B12 deficiency anemia subgroup was higher than that reported in the Korean study[15], with median age, clinical manifestations, and laboratory results being similar in both studies. The results of these two studies confirm that B12 deficiency is uncommon in the Asian population. B12 treatment was given intramuscularly in 70.0% of the patients in our study and in 94.3% of the patients in the Korean study, resulting in a longer median time to response in our study (10 months vs. 3 months). However, if we consider only B12 deficiency anemia patients who received IM treatment, median time to response was similar to the corresponding result reported by the Korean study (9 weeks). Whether the treatment for vitamin B12 deficiency anemia should be administered by IM injection or orally is still being debated. A systematic review of randomized controlled trials was recently undertaken, but it was unable to answer this question given the current paucity of data on the matter and given the different definitions of diagnosis applied among the trials evaluated[18]. However, the results of this study demonstrated that IM and oral B12 treatment in patients with B12 deficiency anemia achieved similar hemoglobin response, but the median time to response appeared to be lower in the IM injection group than in the oral group. Differential time to response between IM and oral B12 treatment could be explained by the higher bioavailability of IM treatment over that of oral treatment. In the presence of glossitis, diagnosis of megaloblastic anemia was more confidently made by treating physicians, thus IM B12 was given to all 16 patients with glossitis. Admittedly, the sample size in our study was not adequately large enough to draw definitive conclusions. The strength of this retrospective study was the long follow-up realized by most of the patients that we evaluated. A study with a larger sample size is needed to compare treatment response and outcomes between IM and oral B12 treatment in patients with vitamin B12 deficiency anemia.

Conclusion

B12, folate, and other nutritional deficiency anemias are uncommon in Asian patients. Incidence of folate deficiency anemia was highest among non-iron nutritional deficiency anemias and is associated with alcohol abuse. A significant portion of anemia cases across all subgroups presented concomitantly with anorexia or poor food intake, which indicates underlying nutritional problems in these patients. Survival of patients with vitamin B12 deficiency anemia was significantly better than that of those with folate or other nutritional anemias.

What is already known in this topic?

Nutritional deficiency anemia is common worldwide, with iron deficiency anemia being the most prevalent. Hospitalized patients in developed countries, especially elderly patients aged 60 years or more, have been reported to have a concomitant malnutrition resulting in anemia. Nutritional deficiency anemias other than iron deficiency anemia, particularly megaloblastic anemia, are not well elucidated in developing countries.

What this study adds?

This study reveals that B12, folate, and other nutritional deficiency anemias are uncommon in an in-patient setting in Thailand. Clinical and laboratory features of non-iron nutritional deficiency anemia were identified and should be useful for the identification and recognition of such patients on the wards. This study also shows that survival of hospitalized patients with vitamin B12 deficiency anemia was significantly better than that of patients with folate or other nutritional anemias.

Author contributions

Limvorapitak W designed the study, collected data, performed statistical analysis, and drafted the manuscript. Auewarakul CU initiated and supervised the study and critically revised the manuscript. Both authors read and approved the final manuscript.

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Potential conflicts of interest

None.

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ลักษณะทางคลินิกและผลการรักษาผู้ป่วยโรคโลหิตจางจากการขาดสารอาหารที่ไม่ใช่ธาตุเหล็กในแผนกผู้ป่วยใน โรงพยาบาลศิริราช: การศึกษาย้อนหลัง 10 ปี

วศิเทพ ลิ้มวรพิทักษ์, จิรายุ เอื้อวรากุล

ภูมิหลัง: *ภาวะโลหิตจางเป็นภาวะที่มีความสำคัญในทางสาธารณสุข ใช้เป็นตัวชี้วัดพัฒนาการด้านสาธารณสุขของประเทศ ภาวะนี้ยังคงเป็นปัญหาที่สำคัญของประเทศไทย ข้อมูลของภาวะโลหิตจางที่ไม่ใช่การขาดธาตุเหล็กในแผนกผู้ป่วยในของประเทศไทยยังไม่มีการศึกษาชัดเจนมาก่อน*

วัตถุประสงค์: *เพื่อศึกษาอุบัติการณ์ ลักษณะทางคลินิก และผลการรักษาของผู้ป่วยภาวะโลหิตจางจากการขาดสารอาหารที่ไม่ใช่ธาตุเหล็กในโรงพยาบาลศิริราช*

วัสดุและวิธีการ: *การศึกษาย้อนหลัง 10 ปี โดยการทบทวนเวชระเบียนผู้ป่วยในที่เข้ารับการรักษาในโรงพยาบาล ตั้งแต่ เดือนมกราคม พ.ศ. 2544 ถึง ธันวาคม พ.ศ. 2554*

ผลการศึกษา: *พบผู้ป่วยที่มีภาวะโลหิตจางจากการขาดสารอาหารที่ไม่ใช่ธาตุเหล็ก 102 ราย แบ่งเป็นโรคโลหิตจางจากการขาดวิตามินบี 12 ทั้งหมด 40 ราย จากการขาดโฟเลท 46 ราย และจากการขาดสารอาหารอื่น 46 ราย คิดเป็นอุบัติการณ์เท่ากับ 0.4, 0.6 และ 0.2 รายต่อประชากรแสนรายต่อปี ตามลำดับ ผู้ป่วยโลหิตจางจากการขาดวิตามินบี 12 ส่วนใหญ่เป็นผู้หญิงมีภาวะลิ้นเลี่ยนและมีภาวะเม็ดเลือดต่ำลงทุกประเภทได้บ่อย ในขณะที่ผู้ป่วยโรคโลหิตจางจากการขาดโฟเลทมักเป็นเพศชายมีประวัติดื่มเหล้าเรื้อรังร่วมกับภาวะตับแข็ง ผู้ป่วยทุกกลุ่มที่ทำการศึกษาพบว่ามีระดับเหล็กสะสมเฟอร์ไรตินสูงขึ้น ผู้ป่วยโลหิตจางจากการขาดสารอาหารส่วนหนึ่งมีปัญหาเบื่ออาหารหรือรับประทานอาหารได้น้อยบ่งชี้ถึงภาวะทุพโภชนาการ อัตราการรอดชีวิตของผู้ป่วยโลหิตจางจากการขาดโฟเลทและสารอาหารอื่นต่ำกว่ากลุ่มโลหิตจางจากการขาดวิตามินบี 12 อย่างมีนัยสำคัญ (อัตราความเสี่ยง 2.65 และ 2.35 เท่าเมื่อเทียบกับกลุ่มขาดวิตามินบี 12) การรักษาโลหิตจางจากการขาดวิตามินบี 12 ในรูปแบบรับประทานให้ผลลัพธ์การรักษาไม่แตกต่างจากการฉีดยาเข้ากล้ามเนื้อ แต่การฉีดยาให้การตอบสนองที่เร็วกว่า คือ 9 สัปดาห์ เมื่อเทียบกับ 86 สัปดาห์ หากรักษาด้วยการรับประทานวิตามินบี 12*

สรุป: *ภาวะโลหิตจางจากการขาดสารอาหารที่ไม่ใช่ธาตุเหล็ก เป็นภาวะที่พบได้ไม่บ่อยในผู้ป่วยในที่ได้รับการรักษาในโรงพยาบาล การรักษาภาวะขาดวิตามินบี 12 ด้วยวิธีฉีดให้ผลการตอบสนองที่เท่าเทียมแต่เร็วกว่าวิธีรับประทาน อัตราการรอดชีวิตของผู้ป่วยโรคโลหิตจางจากการขาดวิตามินบี 12 ดีกว่ากลุ่มที่ขาดโฟเลทหรือสารอาหารอื่น*