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Relationship of iron deficiency anaemia with folic acid and vitamin B12 deficiency in children

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Abstract
Paediatric anaemia refers to a hemoglobin or haematocrit level lower than the age-adjusted reference range for healthy children. Physiologically, anaemia is a condition in which reduced haematocrit or haemoglobin levels lead to diminished oxygen-carrying capacity that does not optimally meet the metabolic demands of the body. There are several studies done to find out the prevalence of iron deficiency anaemia in paediatric population in India and other developing countries. But there is lack of studies using laboratory depths to find out the particular origin of nutritional anaemia. Hence there was a need tostudy the relationship of folic acid and vitamin B12 deficiency in patients with iron deficiency anaemia in Indian children.
The children's admitted to paediatric ward in Patna Medical College and Hospital were considered in the study. The approval of the Ethical Committee is taken from the Hospital. The written consent from the parents was taken. All patients acknowledged in paediatric ward of this hospital for any complaints were assessed for anaemia
The Anaemia is the major health disease in the Indian children. The Iron deficiency is the major cause of the Anaemia. The other nutrients also contributes to the cause of anaemia. Iron deficiency in found the 59% patients. The nutritional anaemia is seen in the 15% of the selected population due to deficiency of Folic acid. Also it can be concluded that the 30% of the Vitamin B12 deficiency children's had anaemia.

Keywords: iron deficiency anaemia, folic acid and vitamin B12, nutritional anaemia

Introduction
Paediatric anaemia refers to a hemoglobin or haematocrit level lower than the age-adjusted reference range for healthy children. Physiologically, anaemia is a condition in which reduced haematocrit or haemoglobin levels lead to diminished oxygen-carrying capacity that does not optimally meet the metabolic demands of the body.
Anaemia is not a specific disease entity but is a condition caused by various underlying pathologic processes. It may be acute or chronic. The combination of anaemia with leukopenia, neutropenia, or thrombocytopenia may suggest a more global failure of haematopoiesis, caused by conditions such as aplastic anaemia, Fanconi anaemia, myelofibrosis, or leukaemia, or may suggest a rapid destruction or trapping of all blood elements, such as hypersplenism, localized coagulopathy in a large heamangioma, or heamophagoctic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS).
The main physiologic role of red blood cells (RBCs) is to deliver oxygen to the tissues. Certain physiologic adjustments can occur in an individual with anaemia to compensate for the lack of oxygen delivery. These include (1) increased cardiac output; (2) shunting of blood to vital organs; (3) increased 2,3-diphosphoglycerate (DPG) in the RBCs, which causes reduced oxygen affinity, shifting the oxygen dissociation curve to the right and thereby enhancing oxygen release to the tissues; and (4) increased erythropoietin to stimulate RBC production.
The clinical effects of anaemia depend on its duration and severity. When anaemia is acute, the body does not have enough time to make the necessary physiologic adjustments, and the symptoms are more likely to be pronounced and dramatic. In contrast, when anaemia develops gradually, the body is able to adjust, using all 4 mechanisms mentioned above (1, 3, and 4 in most cases), ameliorating the symptoms relative to the degree of the anaemia [1].
The three main types of anaemia are due to blood loss, decreased red blood cell production, and increased red blood cell breakdown. Causes of blood loss include trauma and gastrointestinal bleeding, among others. Causes of decreased production include iron deficiency, a lack of vitamin B12, thalassemia, and a number of neoplasms of the bone marrow. Causes of increased breakdown include a number of genetic conditions such as sickle cell anaemia, infections like malaria, and certain autoimmune diseases. It can also be classified based on the size of red blood cells and amount of hemoglobin in each cell. If the cells are small, it is microcytic anaemia. If they are large, it is macrocytic anaemia while if they are normal sized, it is normocytic anaemia. Further testing is then required to determine the cause [2].
Certain groups of individuals, such as pregnant women, benefit from the use of iron pills for prevention [2-4]. Dietary supplementation, without determining the specific cause, is not recommended. The use of blood transfusions is typically based on a person's signs and symptoms [2]. In those without symptoms, they are not recommended unless hemoglobin levels are less than 60 to 80 g/L (6 to 8 g/dL) [1]. These recommendations may also apply to some people with acute bleeding [2]. Erythropoiesis-stimulating medications are only recommended in those with severe anaemia.
The term 'nutritional anaemia' comprises all pathological situations in which the blood haemoglobin concentration changed to an abnormally low level. This may be owed to a deficit in one or numerous nutrients. The foremost nutrients responsible in the production of haemoglobin are iron, folic acid, and vitamin B12. In communal health relations, iron

deficiency is by far the principalreason of nutritional anaemia global. Folic acid deficiency is less prevalent and is regularly perceived with iron deficiency. Vitamin B12 deficiency is far infrequent and it arises mostly in vegetarians [5]. There are several studies done to find out the prevalence of iron deficiency anaemia in paediatric population in India and other developing countries [6, 7, 8, 9]. But there is lack of studies using laboratory depths to find out the particular origin of nutritional anaemia. Hence there was a need to study the relationship of folic acid and vitamin B12 deficiency in patients with iron deficiency anaemia in Indian children.

Methodology

The children's admitted to paediatric ward in Patna Medical College and Hospital were considered in the study. The approval of the Ethical Committee is taken from the Hospital. The written consent from the parents was taken. All patients aged 6 months to 10 years acknowledged in paediatric ward of this hospital for any complaints were assessed for anaemia. WHO Expert group suggested that anaemia should be considered to exist when Haemoglobin is below the following levels in venous blood.

- 6 months to 6 years 11 gm / dl,
- less than 12 g/dL for girls from 6 to 18yrs and boys from 6 to 14 years, and
- less than 13 g/dl for boys from 15 to 18 yrs of age [10].

Exclusion Criteria

- Children's less than 6 months of age,
- Sick patients and
- Children's who are diagnosed with Thrombosis/Leukaemia
- Children's having diseases causing bone marrow suppression

Inclusion Criteria

Children's s with Haemoglobin levels less than the WHO cut off levels for anaemia

In those patients found to have anaemia, the following laboratory investigations were done like mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), serum ferritin, serum iron, total iron binding capacity (TIBC), serum transferrin (TRF), serum folate assay and serum vitamin B12 assay. 5 ml of blood was collected in a EDTA tube for the study. Serum haemoglobin was estimated by spectrophotometric method by automated machine, serum ferritin by Chemiluminescent immunoassay, serum iron by Ferrozine_no deproteinization, TIBC by ion exchange resin ferrozine method, serum transferrin (TRF) by rate nephelometry, serum folate assay and vitamin B12 assay by Chemiluminescent immunoassay. In case they were suffering from acute infective or inflammatory conditions [12] the above investigations were done after 3 afebrile days. The normal values for various study parameters in this study were considered from Nelson Text Book of Pediatrics [13].

Results

Total 100 children's admitted to paediatric ward in Patna Medical College and Hospital were considered for the study. The following are the observations in all the children's. Various lab tests were performed in the study group.

Table 1: Age of the patient and number of cases

Patients age in years	No. of cases	Percentage
Less than 1 year	8	8
1 – 2 years	18	18
2 – 4 years	24	24
4 – 6	28	28
6 – 8	14	14
8 – 10	8	8
Total	100	100

The Table number 1 indicates the age group of the patients and number of the cases. Upto 1 year of age group had 8 % of cases. 1 to 2 years of age group had 18% of cases. 2 to 4 years of age group had 24% of cases. In 4 to 6 years of the children's 28% of cases were found. In 6 to 8 years age group of the children's 14% and in 8 to 10 years 8% cases were observed.

Table 2: Haemoglobin Levels

Hemoglobin levels in gms/dl	No. of cases	Percentage
Less than 7	4	4
7 – 8	6	6
8 - 9	8	8
9 -10	14	14
10 - 12	68	68
Total	100	100

Table 2 compiled the Haemoglobin levels in the study group patients. 9-12 Hb is found in 14% of populations whereas 10-12 Hb is seen the 68% of population. The Hb level of the 7-9 is also found in the few percentage of population.

Table 3: Observed Value of the Serum Markers

Marker	Observed Value
Blood Folatepg/ml	2.2 - 21.2
Serum B12 ng/ml	42 - 1500
Serum Iron mcg / dl	12 – 284
TIBC mcg/dl	175 – 636
Serum Ferritin mcg / l	110-711
Serum Transferrin mg/dl	170 – 578

The Table 3 compiles the laboratory findings in the selected study group. The level of the Blood Folate is seen as 2.2 - 21.2pg/ml. The level of the Serum B12 is observed as 11 – 1500 ng/ml. The Iron level is also detected as 12 – 284 mcg/dl.

Table 4: Incidence of Iron deficiency, Folic Acid levels, and Vitamin B12 levels of patients studied

Iron deficiency	Percent
Yes	59
No	41
Total	100
Folic Acid deficiency	
Yes	15
No	85
Total	100
Vitamin B_{12}deficiency	
Yes	30
No	70
Total	100

Table number 4 compiles the Iron deficiency in the 59% patients. The nutritional anaemia is seen in the 15% of the selected population due to deficiency of Folic acid. Also it can be concluded that the 30% of the Vitamin B12 deficiency children's had anaemia.

Pasricha *et al.* [14] in 2011, calculated the micronutrients such as vitamin B12, folate, iron and vitamin A concentrations of 396 children in the age group of 12 – 23 months in rural Karnataka in south India. They found that 65.6% had at least one micronutrient deficiency and those children between 1-2 years who are breast feeding should be targeted during micronutrient supplementation programs. Ahmed F *et al.* [15] in 2008 studied the prevalence of selected micronutrient deficiencies amongst anaemic adolescent school girls in rural Bangladesh, and they found that 28% of the girls had depleted iron stores, 25% had folic acid deficiency, 89% had vitamin B12and 7% had vitamin B12 deficiencies. They concluded that there is coexistence of micronutrient deficiencies among anaemic adolescent girls in rural Bangladesh, although they do not suffer from energy deficiency. Of all micronutrients only iron and vitamin B2 concentrations were found to be related to the Hb concentration. In this study conducted 100 anaemic patients were studied and in this population 59% Iron deficiency is seen.

Conclusion

The Anaemia is the major health disease in the Indian children. The Iron deficiency is the major cause of the Anaemia. The other nutrients also contributes to the cause of anaemia. Iron deficiency in found the 59% patients. The nutritional anaemia is seen in the 15% of the selected population due to deficiency of Folic acid. Also it can be concluded that the 30% of the Vitamin B12 deficiency children's had anaemia.

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