Iron Deficiency, Ferritin and Total Iron Binding Capacity Among Bangladeshi Children: Urban and Rural Settings

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Plasma transferrin, the most important physiological source of iron, is a glycoprotein synthesized in the liver and together with ferritin binds essentially all circulating plasma iron [2]. Under physiologic conditions, this chelation renders iron soluble, prevents iron-mediated free-radical toxicity, and facilitates iron transport into cells. The total iron binding capacity (TIBC) of plasma is dependent on the totality of all iron binding sites on transferrin. Transferrin binds tightly to the cell receptor and is drawn into the cell to release its iron. Once in the cytoplasm, iron is delivered to various intracellular locations including mitochondria for heme biosynthesis and to ferritin for storage. The receptor releases the "empty" transferrin to the cell exterior to continue gathering iron.

Abstract

In iron deficiency (ID) body tries to compensate by producing more transferrin to increase iron transport and thus transferrin and TIBC increase. This cross-sectional study was conducted among 274 children from two primary schools; one urban (Dhaka city) and one rural (Gazipur district). By sex and area of residence ratio was equal with mean age 8.86 ± 2.035 years. Phlebotomist collected venous blood with all aseptic precaution. Estimation of serum Hemoglobin, serum Iron, serum and Total Iron Binding Capacity (TIBC) were done in a reference laboratory. Serum iron level was found below 50 µg/dl among all the subjects. Only mean hemoglobin was found statistically significant difference between the age group of within and above 10 years of subjects, hemoglobin and Ferritin were found significantly more among male over female subjects and hemoglobin and Ferritin were found significantly more among male over female subjects and hemoglobin, iron, and Ferritin among rural subjects over urban subjects (p<0.05). Higher serum Ferritin was found associated with higher serum iron and serum TIBC was found negatively correspond with serum iron (p<0.05). Plant-based foods containing non-heme iron may also suggested for Bangladeshi children.

Keywords: Serum Vitamin D; Children; Urban and Rural Settings; Bangladesh

Introduction

Iron deficiency anemia is considered as one of the serious public health problems in Bangladesh. Nutritional anemia is an acquired problem due to consumption of inadequate diet and also of insufficient bio-available essential nutrients to meet the need for hemoglobin and red blood cell synthesis. Ferritin is an intracellular iron storage protein and a marker of iron stores. Iron deficiency can be detected seeing the low ferritin values. Elevated levels of ferritin frequently indicate iron overload caused by damaged hepatocytes; inflammatory disorders; liver disease; alcohol excess; or malignancy [1].
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Metabolically inactive iron is stored in ferritin and hemosiderin, and is in equilibrium with exchangeable iron bound to carrier molecules. TIBC quantitatively measures serum transferrin and can be useful in diagnosis of iron deficiency anemia, iron overload and chronic inflammatory disorders [3].

Increased levels of TIBC suggest that total iron body stores are low, increased concentrations may be a sign of iron deficiency anemia [4]. Decreased levels of TIBC may indicate anemia of chronic disease such as hemolytic anemia, hemochromatosis, chronic liver disease, hypoproteinemia, malnutrition, pernicious anemia, and sickle cell anemia [5]. Therefore, iron deficiency can be defined as a low serum iron and ferritin with an raised TIBC whereas, a low serum ferritin is virtually diagnostic of iron deficiency alone, on the other hand, a normal serum ferritin can be reported in patients with co-existent diseases (Hepatitis, anaemia of chronic disorders) in spite of deficient in iron [6].

If iron deficiency continues, all of the stored iron is used and the body tries to compensate by producing more transferrin to increase iron transport. The serum iron level continues to decrease and transferrin and TIBC increase [7].

Use of iron status as biomarker in diagnosing anemia may make confusion as this is sometimes influenced by inflammation [8]. This cross-sectional study is an attempt to explore the association of Ferritin and TIBC with iron deficiency among school going anemic children in Bangladesh.

Materials and Methods

This was a community based cross-sectional study which was conducted among 274 primary school children during March 2018 to February 2019. Two primary schools were selected purposively (one from Dhaka city and one from Gazipur district). After taking assent from guardians all required data were collected. At the time of enrollment, trained research assistants administered a pretested socio-demographic questionnaire of each participating subject. Socio-demographic information including age, household size, education of parents or caregiver, income, employment of the head of the households and housing condition were recorded. Venous blood was collected in the morning taking after a 4 - 6 hour overnight fast by trained phlebotomist. Samples were taken in the red-top tube for serum separator. Then the tubes were kept in cold box and sent to the reference laboratory within 4-h. For Hemoglobin estimation, blood was diluted in a solution containing potassium cyanide and potassium ferricyanide. The absorbance of the solution was then measured in a spectrophotometer at a wavelength of 540 nm. For serum Iron analysis, the sample volume for the red-top tube for serum separator. Then the tubes were kept overnight fast by trained phlebotomist. Samples were taken in glass containers were used to store samples. The Serum Iron was tested through using Beckman Synchron LX20, serum ferritin was analyzed using immunoradiometric procedure (Ramco Laboratories, Stafford, TX USA) and Total iron binding capacity (TIBC) was analyzed using BioLis24i Clinical Analyzer (Carolina Liquid Chemistries Corp., Winston-Salem, NC, USA) in a reference laboratory. Data was analyzed using SPSS software version 20. Student t-test, One-way ANOVA were done to see the effect of ferritin and TIBC on serum iron. This study received ethical approval from Bangladesh University of Professional and all the ethical issues related the biomedical research were maintained strictly.

Results

| Characteristics | Frequency (%) |
|-----------------|--------------|
| Age group       |             |
| 5 to 10         | 202 (73.7)  |
| 10 to 14 years  | 72 (26.3)   |
| Mean age        | 8.86 ± 2.035 years |
| Sex of subjects |             |
| Male            | 137 (50.0)  |
| Female          | 137 (50.0)  |
| Class           |             |
| Class I         | 79 (28.8)   |
| Class II        | 55 (20.1)   |
| Class III       | 45 (16.4)   |
| Class IV        | 49 (17.9)   |
| Class V         | 46 (16.8)   |
| Family Members  |             |
| Up to 4 members | 148 (54.0)  |
| 5 - 6 members   | 114 (41.6)  |
| More than 6 members | 12 (4.4)  |
| Mean            | 4.55±1.072  |
| Locality        |             |
| Rural           | 132 (48.2)  |
| Urban           | 142 (51.8)  |

Table 1: Socio-demographic distribution of subjects (n=274).

Among the study participants, male female ratio was equal. The mean age of the study subjects was 8.86 ± 2.035 years. Majority of the children were within 5 – 10 years (73.7%) and rest were within 10 – 14 years. The male and female ratio was equal. Among the participants 28.8% were in class I, 20.1% were in class II, and 16.4% were in class III, 17.9% in class IV and rest 16.8% were in class V. Around 48% study participants were of rural areas.

Among the mothers of the subjects, 76.3% were housewife while rest were found engaged with individual profession. Among the fathers 26.3% were service holder, 16.8% were engaged with business and rest were found engaged in different profession. The education level of the mothers was found as 16.4% had no institutional education, 44.9% had primary level, 31.4% had secondary level (up to SSC), 4.7% had up to HSC level and 2.6% were graduate. That of father was found as 14.2% had no institutional education, 38.0% had primary level, 37.6% had secondary level (up to SSC), 5.5% had up to HSC level and 4.7% were graduate.

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The table 5 shows that the mean hemoglobin was 11.606 ± 1.2551 g/dl among the subjects who were under age of 10 years and 12.031 ± 1.3559 µg/dl among the subjects who were over the age of 10 years, the mean serum iron was 10.942 ± 3.1499 µmol/L among the subjects who were under age of 10 years and 11.360 ± 3.1426 µmol/L among the subjects who were over the age of 10 years, the mean serum Ferritin was 23.484 ± 17.2363 µg/L among the subjects who were under age of 10 years and 25.355 ± 17.7307 µg/L among the subjects who were over the age of 10 years, the mean serum TIBC was 58.78 ± 22.990 µmol/L among the subjects who were under age of 10 years and 59.4 ± 33.491 µmol/L among the subjects who were over the age of 10 years. Serum iron level was estimated which shows that all the subjects had below 50 µg/dl. Only mean hemoglobin was found statistically significant difference between the age group of within and above 10 years of subjects (p<0.05).

The mean hemoglobin was 11.873 ± 1.2878 g/dl among the male subjects and 11.562 ± 1.2851 µg/dl among the female subjects, the mean serum iron was 11.277 ± 3.2239 µmol/L among the male subjects and 10.827 ± 3.0647 µmol/L among the female subjects, the mean serum Ferritin was 26.226 ± 18.2698 µg/L among the male subjects and 21.725 ± 16.1426 µg/L among the female subjects, the mean serum TIBC was 58.78 ± 23.825 µmol/L among the male subjects and 59.13 ± 28.270 µmol/L among the female subjects. Statistically significant differences of hemoglobin and Ferritin were found between male and female subjects (p<0.05).

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The mean hemoglobin was 11.894 ± 1.5541 g/dl among the rural subjects and 11.554 ± 0.9692 µg/dl among the urban subjects, the mean serum iron was 12.082 ± 3.4969 µmol/L among the rural subjects and 10.095 ± 2.4303 µmol/L among the urban subjects, the mean serum Ferritin was 26.570 ± 18.8714 µg/l among the rural subjects and 21.564 ± 15.4952 µg/l among the urban subjects, the mean serum TIBC was 56.56 ± 21.554 µmol/L among the rural subjects and 61.19 ± 29.603 µmol/L among the urban subjects. Statistically significant differences of hemoglobin, iron, and Ferritin were found between rural and urban subjects (p<0.05).

| Variable          | Mean        | t           | Sig. (2-tailed) | Mean Difference |
|-------------------|-------------|-------------|-----------------|-----------------|
| Hb (g/dL)         | Rural 11.894 ± 1.5541 | 2.157 | 0.032 | 0.3404 |
|                   | Urban 11.554 ± 0.9692 |     |      |       |
| Iron (µmol/L)     | Rural 12.082 ± 3.4969 | 5.423 | 0.000 | 1.9869 |
|                   | Urban 10.095 ± 2.4303 |     |      |       |
| Ferritin (µg/l)   | Rural 26.570 ± 18.8714 | 2.390 | 0.018 | 5.0060 |
|                   | Urban 21.564 ± 15.4952 |     |      |       |
| TIBC (µmol/L)     | Rural 56.56 ± 21.554 | -1.471 | 0.142 | -4.632 |
|                   | Urban 61.19 ± 29.603 |     |      |       |

Table 5: Serum Hemoglobin, Iron, Ferritin, and TIBC status by area of residence.

The mean hemoglobin was 11.894 ± 1.5541 g/dl among the rural subjects and 11.554 ± 0.9692 µg/dl among the urban subjects, the mean serum iron was 12.082 ± 3.4969 µmol/L among the rural subjects and 10.095 ± 2.4303 µmol/L among the urban subjects, the mean serum Ferritin was 26.570 ± 18.8714 µg/l among the rural subjects and 21.564 ± 15.4952 µg/l among the urban subjects, the mean serum TIBC was 56.56 ± 21.554 µmol/L among the rural subjects and 61.19 ± 29.603 µmol/L among the urban subjects. Statistically significant differences of hemoglobin, iron, and Ferritin were found between rural and urban subjects (p<0.05).

Table 6: Relationship between serum iron on Ferritin and TIBC.

| Model        | Unstandardized Coefficients | Standardized Coefficients | t     | F   | p-value |
|--------------|-----------------------------|---------------------------|-------|-----|---------|
| (Constant)   | 10.18                       |                           | 21.682| 168.810 | 0.000   |
| Ferritin (µg/l) | 0.109                     | 0.600                     | 13.139| 0.000 |         |
| TIBC (µmol/L) | -0.029                    | -0.244                    | -5.352| 0.000 |         |

Dependent Variable: Iron (µmol/L)
One-way ANOVA

Statistically we can say that, 1-point increase of the serum Ferritin corresponds to 0.11 points increase of serum Iron. Again 1-point decrease of the serum TIBC corresponds to 0.03 points increase of serum Iron. Serum Iron and serum Ferritin (b coefficients) are positive numbers except TIBC; higher Ferritin is associated with higher iron (p<0.05).

Discussion
The present study was conducted among the primary school students of rural and urban settings in Bangladesh and included a total 274 children (132 rural and 142 urban children with equal sex). The mean age of the respondents was around nine years whereas, majority (74%) of them were in the age group of 5 to 10 years. Among the mothers of the children, seventy six percent were housewife while rest were found engaged with other profession. Among the fathers more than one-fourth were service holder, and rest were found engaged in other profession including business. The education level of the mothers, around sixteen percent were illiterate, whereas, rest of them were literate. Besides that, among the father, fourteen percent were illiterate, whereas, rest of them were literate.

The all the study subjects had Serum iron level below 50 µg/dl. This study tried to explore any mean differences of hemoglobin, serum iron, serum ferritin and TIBC among the subjects by age group, gender and by residence. Only mean hemoglobin was found statistically significant difference between the age group of within and above 10 years of subjects, significant differences of hemoglobin and Ferritin were found between male and female subjects and significant differences of hemoglobin, iron, and Ferritin were found between rural and urban subjects (p<0.05). On One-way ANOVA, it was found that higher Ferritin is associated with higher iron and TIBC was negatively correspond with serum iron, which where are statistically significant (p<0.05). Similar findings were reported from the studies conducted among university students in Hodeida Province, Yemen [9] and among rural women of reproductive age in Ethiopia [10].

Conclusion and Recommendation
Prevalence of anemia and insufficiency serum iron among the school going children is marked. Serum Ferritin and TIBC were found having significantly associated with serum iron deficiency. Instead of recommending only iron rich food as counter measure for anemia, plant-based foods containing non-heme iron but building ferritin levels may also suggested for Bangladeshi children.
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