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EFFECTS OF IRON STATUS ON PLATELET COUNT IN ADULT POPULATION OF DHAKA CITY

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ABSTRACT

Background: Platelet count is altered with alteration of body iron status. Both thrombocytosis and thrombocytopenia have been observed in iron deficiency anemia. Iron deficiency anemia is a common form of nutritional anemia in Bangladesh. Changes in platelet count in iron depleted conditions may increase the future risk of thromboembolic complications. **Aim:** This study aimed to assess the platelet count in relation to iron status in adult in Dhaka city. **Materials and Method:** This cross-sectional study was conducted to assess platelet count in relation to iron status in adult population of Dhaka city. A total number of 108 study subjects of both sexes (40 male and 68 female) aged 18 – 45 years were selected. Study subjects were divided into three groups on the basis of hemoglobin (Hb) concentration. In group A (Hb. 8 – 10.9 gm/dl), 31 study subjects were included. In group B (Hb. 11- 11.9 gm/dl), 34 study subjects were included and in group C (Hb. ≥12 gm/dl), 43 study subjects were included. Hematological parameters (hemoglobin concentration, platelet count) were measured by the automated hematology analyzer and iron parameters (serum iron, serum ferritin, total iron binding capacity [TIBC]) were measured by automated biochemistry analyzer in the Department of Laboratory Medicine, Dhaka Medical College, Dhaka. For statistical analysis one way ANOVA followed by Bonferroni test and Pearson's correlation coefficient ® test were performed as applicable using SPSS for Windows version 25. **Results:** In this study, serum iron showed statistically significant negative correlation with platelet count (r= -0.645, p<0.001) and serum ferritin showed statistically significant negative correlation with platelet count (r= -0.572, p<0.001) and total iron binding capacity showed statistically significant positive correlation with platelet count (r= 0.555, p<0.001). **Conclusion:** This study concluded that lower serum iron, serum ferritin and higher total iron binding capacity cause increase in platelet count. The changes in platelet count negatively correlated with iron status and positively correlated with severity of iron deficiency anemia.

Keywords: Platelet count, Serum iron, Serum ferritin, Iron deficiency.

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INTRODUCTION

Platelets are originated from megakaryocytes which are less in number but largest cells in the bone marrow. Megakaryocytes are derived from the common pluripotent hematopoietic stem cells which further differentiate into mature platelets by several complex sequence of events[1].

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The prime function of platelet is hemostasis, thrombosis and wound healing through a complex activation process. Other functions include immunity and communication with other cells and tissue in the vessel[2].

In recent times, platelets have appeared as an important clinical target for various disease pathophysiology[3]. Thrombocytosis is a known laboratory finding that is related with many diseases. Primary thrombocytosis is a proliferative disease of the bone marrow that occurs due to specific mutations of megakaryopoietic stem cells in the bone marrow[4]. Secondary thrombocytosis is also known as reactive thrombocytosis that is nonspecific and related with various conditions such as iron deficiency, blood loss, hyposplenism or asplenism, malignant disease, acute or chronic inflammation[5].

A study reported that iron deficiency anemia developed when inadequate iron supply failed to maintain normal level of hemoglobin[6]. According to the World Health Organization, hemoglobin level below 13gm/dl in case of men and below 12 gm/dl in case of women is known as anemia. The estimated prevalence of anemia in developing countries is 42% in women and 30% in men of 15- 59 years[7]. Since Bangladesh is a developing country, it is likely for the prevalence of anemia to be high[8].

Both thrombocytosis and thrombo-cytopenia have been noted in iron deficiency anemia. Thrombocytopenia was found in severely anemic individuals and it may be due to depletion of several factors like transient thrombopoietin deficiency, depletion of iron enzymes. Thrombocytosis was noted in individuals with less severe iron deficiency anemia and it occurs due to increase in erythropoietin stimulated platelet production in anemic states[9].

Thrombocytosis have also been observed in some cases of severe iron deficiency anemia. Due to thrombocytosis, thromboembolic events such as carotid artery thrombus, retinal vein occlusion and cerebral venous thrombosis, stroke were reported in some cases of severe iron deficiency anemia[10-12]. Therefore, iron deficiency may increase the risk of thromboembolic events[13].

Some authors suggested that platelet count in iron deficiency anemia usually remain normal unless or otherwise the situation is complicated by active blood loss which produces thrombocytosis or hypersplenism leading to thrombocytopenia[14].

This study is designed to assess the effect of iron status on platelet count in adult Bangladeshi population of Dhaka city.

MATERIALS AND METHOD

Study design
Cross- sectional study was carried out.

Study place
The department of Physiology, Dhaka Medical College.

Study period
From July 2018 to June 2019

Ethical Approval

Ethical clearance was obtained from the Research Review committee of the concerned department and ethical review committee of Dhaka Medical College, Dhaka.

Study Population

A total 108 Bangladeshi adult male and female were included in this study. Age range of the participants was 18 years to 45 years. The individuals selected belonged to middle class to ensure similar financial and dietary pattern among the participants. The socioeconomic condition of the subjects was determined by modified Kuppuswamy socioeconomic scale[15].

Selection Criteria

Included into the study were participants of both sexes in the age range of 18 years to 45 years belonging to the middle socioeconomic status. Individuals with history of acute infection, chronic inflammatory disorder, hematological disorder, hypertension, diabetes mellitus, history of taking medications (antiplatelet drugs, iron supplement, multivitamin), alcohol, tobacco were excluded from this study. Subjects with pregnancy, lactation, body mass index of more than 30kg/m^2 and blood doner were also excluded from this study.

Data Collection

All the information were recorded in a prefixed data collection form. This was done after receiving the informed written consent from those who volunteered to participate in the study.

Sample Collection

With all aseptic precautions, 7 ml blood was collected from ante-cubital vein by 10 cc disposable plastic syringe from each subject. From the sample, 2 ml blood was taken in a Complete Blood Count (CBC) tube with Ethylenediaminetetraacetic acid (EDTA) anticoagulant, 2ml blood was taken in a glucose tube with sodium fluoride anticoagulant and remaining 3ml blood was taken in another tube without any anticoagulant for biochemical tests. The blood samples were sent to the department of laboratory Medicine, Dhaka Medical College Hospital.

Sample Analysis Procedure

CBC tube containing blood was analyzed for estimation of hemoglobin concentration, total count of white blood cells (WBC) and platelet parameters. The tube containing 3 ml blood sample for biochemical tests was centrifuged at a rate of 3000-4000 rpm for 10-15 minutes for separation of serum and then the serum was analyzed for estimation of biochemical parameters (serum iron, serum ferritin, total iron binding capacity, serum creatinine, SGPT). Glucose tube containing blood was also centrifuged to separate plasma and plasma was analyzed for estimation of random blood glucose.

Grouping of study subjects

After determining the hemoglobin concentration, individuals were divided into 3 groups (on the basis of their hemoglobin level)[16].

Group A: Hemoglobin concentration 8-10.9 gm/dl (Moderate anemia)

Group B: Hemoglobin concentration 11-11.9 gm/dl (Mild anemia)

Group C: Hemoglobin concentration ≥ 12 gm/dl (Normal)

Blood sample collection was continued until each group consisted of at least 30 subjects. Eventually, 31 study subjects were included in group A, 34 study subjects were included in group B and 43 study subjects were included in group C. This unequal distribution of study subjects among the groups resulted from the attempt made to achieve a minimum of 30 subjects in each group leading to more participants being enrolled to fulfill the goal.

Statistical Analysis

Statistical analysis was performed by using a computer based statistical program SPSS version 25.0. For statistical analysis one way ANOVA followed by Bonferroni test and Pearson's correlation coefficient (r) test were performed as applicable.

RESULTS

A total number of 108 adult subjects were selected for this study. In this study, the age range of the study population was 18 years to 45 years. The mean (±SD) age of the study subjects was 30.42 ± 7.45 years. There were 40 (37%) males and 68 (63%) females. Table 1 displays the sociodemographic characteristics of the study participants.

Table 1 : Sociodemographic characteristics of study subjects (N=108)

Parameters	Mean ± SD
Age (Years)	30.42±7.45 (18 – 45)
Sex	
Male	40 (37%)
Female	68 (63%)
Socio- economic condition	Middle class
BMI (Kg/m^2)	23.81±2.71 (18.9 – 27.6)
Systolic pressure (mmHg)	109.31±8.92 (100 – 120)
Diastolic pressure (mmHg)	69.17±7.75 (60 – 80)

Results were expressed as mean ± SD, frequency and percentage. Figures in parenthesis Indicate range. N = total number of subjects, BMI= Body mass index

Table 2: Study parameters (serum iron, serum ferritin and total iron binding capacity) of the subjects in different groups (N=108)

Parameters	Groups		
	Group A (n_1=31)	Group B (n_2=34)	Group C (n_3=43)
S. Iron (µg/dl)	22.04±14.86	36.96±13.30	48.07±16.14
S. Ferritin (ng/ml)	48.81±24.00	83.11±35.39	138.41±38.81
TIBC (mcg/dl)	393.15±46.86	305.74±62.82	287.78±67.69
Total platelet count (×10^3/ µl)	412.26±83.09	311.37±89.89	247.48±62.73

Statistical analysis

Parameters	*p* value			
	A vs B vs C	A vs B	A vs C	B vs C
S. iron	<0.001***	0.001***	<0.001***	0.007**
S. ferritin	<0.001***	0.345^{ns}	<0.001***	0.031*
TIBC	<0.001***	<0.001***	<0.001***	0.438^{ns}
Total count of platelet	<0.001***	0.001***	<0.001***	0.002***

Results were expressed as mean ± SD,***=Highly significant,**/*=Significant, p<0.05 is the level of significance,. N = total number of subjects

Table 2 shows the various parameters pertaining to iron in the body and total platelet count of the study subjects. These parameters have been compared among the 3 groups and details of the outcome of each parameter is as follows:

Serum iron level

The mean (±SD) serum iron level was 22.04 ± 14.86, 36.96 ± 13.30 and 48.07 ± 16.14 µg/dl in group A, group B and group C respectively. The mean (±SD) serum iron level in group A was lower than that of group B which was statistically significant (p= 0.001). The mean (±SD) serum iron level in group A was lower than that of group C which was statistically significant (p<0.001). The mean (±SD) serum iron level in group B was lower than that of group C which was statistically significant (p= 0.007).

Serum ferritin level

The mean (±SD) serum ferritin level was 48.81± 24.00, 83.11±35.39, 138.41±38.81 ng/ml in group A, group B and group C respectively. The mean (±SD) serum ferritin level was lower in group A than that in group B but was not statistically significant (p= 0.345). The mean (±SD) of serum ferritin was lower in group A than that in group C which was statistically significant (p<0.001). The mean (±SD) serum ferritin in group B was lower than that of group C which was statistically significant (p= 0.031).

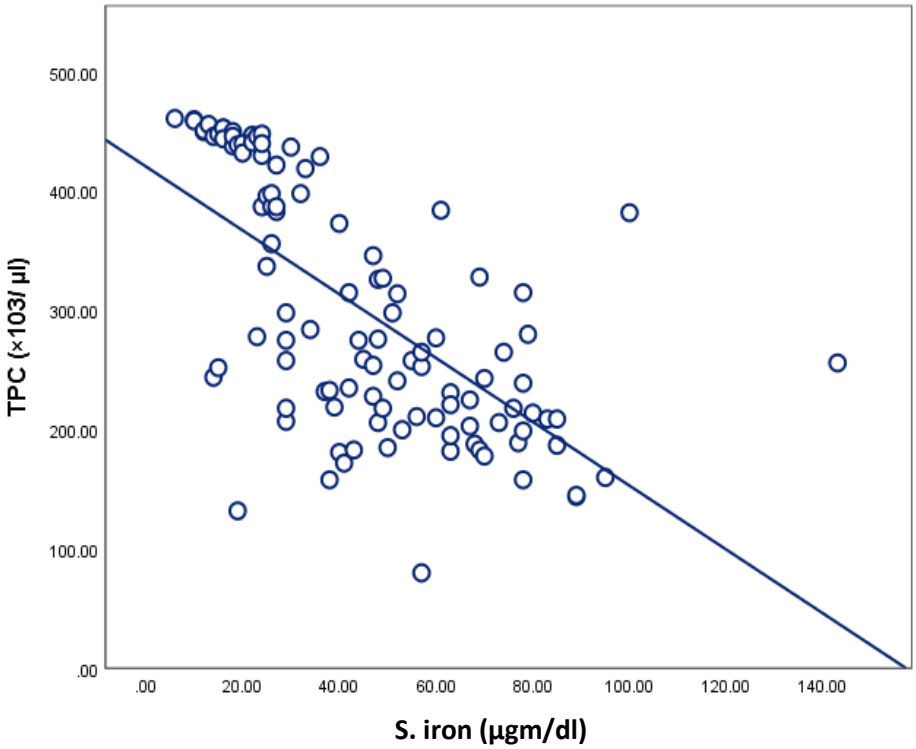
Total iron binding capacity

The mean (±SD) total iron binding capacity level was 393.15±46.86, 305.74±62.82, 287.78±67.69 µg/dl in group A, group B and group C respectively. The mean (±SD) of serum iron binding capacity level was higher in group A than that of group B which was statistically significant (p< 0.001). The mean (±SD) of total iron binding capacity was higher in group A than that of group C which was statistically significant (p<0.001). The mean (±SD) of total iron binding capacity was higher in group B than that of group C but was not statistically significant (p= 0.438).

Total count of platelet

The mean (±SD) total count of platelet level was 412.26±83.09, 311.37±89.89, 247.48±62.73 $\times 10^3/\mu l$ in group A, group B and group C respectively. The mean (±SD) of the total count of platelet in group A was higher than that of group B which was statistically significant (p<0.001). The mean (±SD) of the total count of platelet in group A was higher than that of group C which was statistically significant (p<0.001). The mean (±SD) of the total count of platelet in group B was higher than that of group C which was statistically significant (p= 0.002).

Figure 1: Correlation of serum iron with Total Platelet Count in the study subjects (N=108)



TPC = Total count of platelet

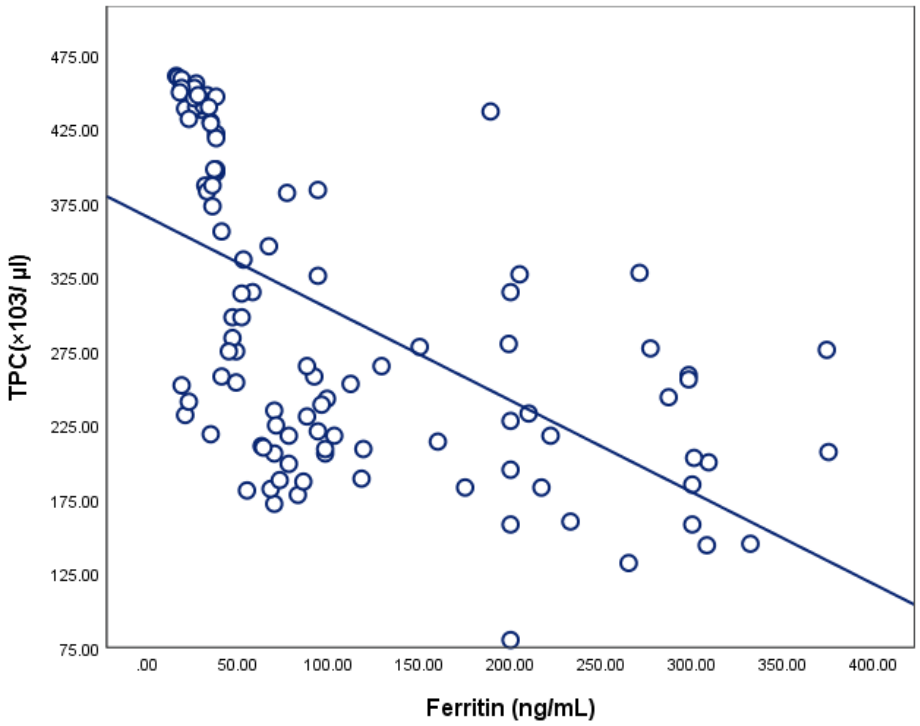
N = Total number of study subjects

Study subjects: Bangladeshi adult male and female

r = -0.645, p = <0.001***

Serum iron showed negative correlation (r= -0.645) with platelet count which was statistically significant (p<0.001) (Figure-1)

Figure 2 : Correlation of serum ferritin with TPC in study subjects (N=108)



TPC = Total count of platelet

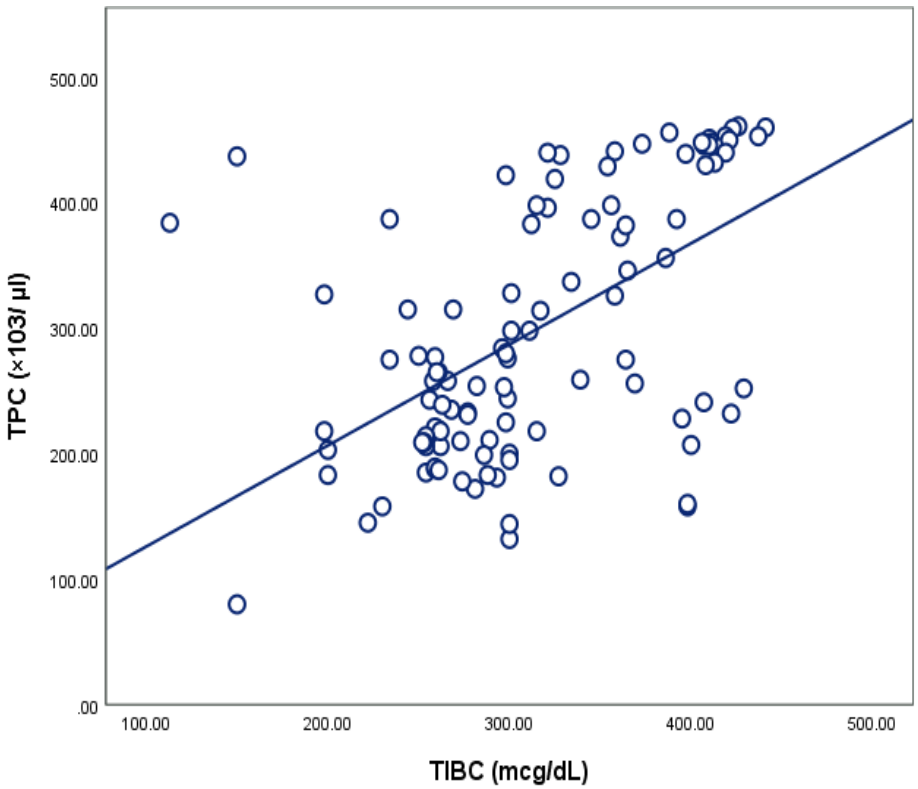
N = Total number of study subjects

Study subjects: Bangladeshi adult male and female

r = -0.572, p = <0.001***

Serum ferritin showed negative correlation (r= -0.572) with platelet count which was statistically significant (p<0.001) (Figure-2).

Figure 3 : Correlation of serum TIBC with TPC in study subjects (N=108)



TPC = Total count of platelet

TIBC= Total iron binding capacity

N = Total number of study subjects

Study subjects: Bangladeshi adult male and female

r = 0.555, p = <0.001***

Total iron binding capacity showed positive correlation (r= 0.555) with platelet count which was statistically significant (p<0.001) (Figure 3).

DISCUSSION

The present study was undertaken to assess the platelet count in relation to iron status in adult population residing in different areas of Dhaka city. In the present study, mean serum iron level in all groups were lower than normal range. The mean serum iron in group A was lower than those of group B and group C. Mean serum iron level of group B was also lower than that of group C. Similar observations were found by other researchers of different countries[14,17,18].

The mean serum ferritin level in group A was lower than that of group C. Mean serum ferritin level of group B was also lower than that of group C. In the present study, mean serum ferritin level in all groups were within normal range but serum ferritin level in group A and B were closer to the lower limit of normal level. Similar findings were observed by other studies[17-19].

The mean total iron binding capacity in group A was higher than those of group B and group C. In the present study, the mean serum total iron binding capacity level in all groups were within normal range but serum TIBC level in group A was closer to the higher limit of normal level. Cahskan et al. reported similar results in their study[17].

The mean total count of platelet in group A was higher than those of group B and C. The mean total count of platelet in group B was also higher than that of group C. In the present study, mean total platelet count in all groups were within normal range but platelet count in group A and B were closer to the higher limit of normal level. In Pearson's correlation test, platelet count showed significant negative correlation with serum iron, serum ferritin and positive correlation with TIBC.

Similarly, Cahskan et al. and Rajagopal et al. found higher platelet count in iron deficiency anemic group compared to non-anemic group[17,18]. Kadikoylu et al. found significant negative correlation of serum iron with platelet count[20]. Kuku et al. found negative correlation of serum ferritin with platelet count which was statistically not significant and positive correlation with TIBC which was statistically significant[21].

On the other hand, Dincol and Aksoy found no rise of platelet count in their study group of uncomplicated iron deficiency anemia. The etiological factor in most cases was malnutrition. They also included patients with iron deficiency anemia complicated with hepatosplenomegaly and active blood loss in their study. They found thrombocytosis in active blood loss and thrombocytopenia in hepatosplenomegaly. They suggested that, in iron deficiency anemia platelet count remain at normal level unless the situation is complicated with active blood loss or hepatosplenomegaly[14]. The present study result also contradicts with that of Holbro et al. [22]. They found no significant change of platelet count in their study group of healthy blood donor. They observed low ferritin level does not correlate with higher platelet count in iron deficiency in absence of inflammation. They suggested that factors other than iron may influence platelet count and probably degree of iron deficiency in their study population might not be strong enough to stimulate platelet production. Most of them were mildly anemic.

In iron deficiency, increased platelet production is caused by stem cell shunt mechanism. According to some researchers, the pluripotent stem cells can differentiate into erythroid, myeloid or megakaryocytic cell line. In iron deficiency, normal erythropoiesis is inhibited by blocking maturation but stimulation for erythropoiesis continues. By an unknown feedback mechanism, committed erythroid cells stimulate proliferation of pluripotent stem cells. As erythroid maturation is

already blocked, pluripotent stem cells differentiated to other cell line like platelets and or granulocytes. Therefore, there is increase in production of platelets and /or granulocytes. Due to short life span of granulocyte in comparison to platelets, leukocytes failed to show any significant change in counts[23].

In the present study, lower serum iron, serum ferritin and TIBC cause increase in platelet count. This may be due to increased commitment of the hematopoietic progenitor cells into megakaryocyte lineage in iron deficiency. However, the exact mechanism cannot be elucidated from the present study as bone marrow study were not assessed.

Furthermore, in the present study, platelet count showed negative correlation with serum iron, serum ferritin and positive correlation with total iron binding capacity. Such correlation further support the findings of the present study.

CONCLUSION

After analyzing the results of the study, it can be concluded that lower serum iron, serum ferritin and higher total iron binding capacity cause increase in platelet count. The change in platelet count is negatively correlated with iron status and positively correlated with severity of iron deficiency anemia.

LIMITATIONS

Male and female were not taken in equal ratio in study groups. Grouping of the subjects were done on the basis of WHO recommended hemoglobin concentration range only for the female although both male and female subjects were included in this study. Sample was collected from middle class socioeconomic group of Dhaka city only which does not represent all the socioeconomic group of Dhaka city.

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CONFLICT OF INTEREST

There is no conflict of interest.

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