ORIGINAL ARTICLE

The importance of plasma ferritin values in blood donors for the evaluation of body iron store in a five-month period

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ABSTRACT

Aim To present haemoglobin and ferritin parameters in donors to highlight the importance of serum ferritin testing for the purpose of evaluating iron depots in order to make recommendations for preserving a population of blood donors.

Method A prospective study was conducted on 80 blood donors divided in two groups: group I (regular donors, n =40) and group II (irregular donors, n=40). Haemoglobin and ferritin were measured twice every 45 days, before two consecutive blood donations.

Results By measuring haemoglobin and ferritin values before donation in both groups, a decrease of initial ferritin value in Group I relative to Group II was observed (without statistical significance). A significant decrease was found between repeated measurements for both parameters in both groups, indicating equal intensity of the decline in value regardless of a donor status. Measurement of ferritin before and after donation revealed statistically significant loss of ferritin in all examinees (p=0.011). The decline in haemoglobin after donation, although significant, did not fall below the reference value for donation in either women or men.

Conclusion Results indicate the need for periodic monitoring of the plasma value of ferritin in voluntary donors who donate blood more than twice a year and the possible oral supplementation with iron.

Key word: anaemia, blood, donors, haemoglobin

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INTRODUCTION

The development of modern medicine, diagnostic and therapeutic procedures have imposed increased demands of blood and blood products. The donor selection process aims to determine general health of a donor in order to be convenient to donate a single dose of 450 ml of blood not affecting donor health as well as providing a safe dose of blood for a patient. In addition to the general requirements for donation that the donor must meet according to the World Health Organisation (WHO) recommendations (1), screening of voluntary donors routinely determines the concentration of haemoglobin. The values of haemoglobin required for blood donation for females are >125 g/L and 135 g/L for males with a minimum period of 4 and 3 months pause, respectively, since the last donation (1). A large number of studies have shown that frequent blood donations lead to depletion of iron reserves (2). Decreased iron reserves in the blood are a well-known risk factor in multiple blood donations. Each 1 mL of blood contains approximately 0.5 mg of iron, donating a single dose of blood, an average of 242 mg of iron is lost (3-5). An increase in the frequency of blood donation among the donor population may result in excessive iron loss and the development of iron deficiency with or without symptoms, as well as anaemia. Low serum ferritin values are accurate indicators of the assessment of iron depot status in an individual (6). Testing of ferritin concentration in voluntary donors is not a routine test and it is recommended only when the haemoglobin level does not meet the donation limit, according to the WHO recommendations (1).

Transfusion medicine is on the margins of the health care system. Blood as a medicine obtained from voluntary donors is taken for granted, and no account is taken of how much effort is required to produce it. Voluntary donors are people with a strong sense of altruism. In today's society, this is not recognized, there are numerous obstacles that make it difficult to reach donors and can negatively affect their attitude for blood donation. By taking care of the health of voluntary donors, we can influence their positive attitude with the aim of preserving them. Although several studies have shown that repeated blood donation causes depletion of iron depots and iron deficiency, all transfusion centres still do only haemoglobin as an indirect indicator of iron status in the screening of voluntary donors (4,5,7). We want to show that in our population a haemoglobin estimate may not be sufficient to assess donor safety prior to phlebotomy, so we can point to the need to review donor acceptance guidelines.

The aim of this study was to examine haemoglobin and ferritin concentration of voluntary blood donors before donating blood in two consecutive measurements (45 days apart) to examine the need for the introduction of additional ferritin concentration screening.

EXAMINEES AND METHODS

Examinees and study design

A prospective study was conducted on 80 blood donors, aged 22-55 years, both genders, at the Blood Transfusion Institute of the Federation of Bosnia and Herzegovina in the period from 15 April to 30 August 2019. Examinees were classified as regular donors if they donated blood at least three times in the last year for males and twice for females, and irregular donors did not donate blood at all or did not do a donation in the last 3 years.

According to the criteria, two groups were formed: group I – 40 regular donors, both genders, aged 22-55 years, and group II – 40 non-regular donors. Group I and group II were designated as Ia and Ib / IIa and IIb, depending on whether it was the first or repeated measurement.

Inclusion criteria were: voluntary blood donors between 22-55 years of age, haemoglobin value of >125 g/L before donation for females and 135 g/L for males, and a minimum period of 4 and 3 months from the last donation depending on examinees' gender. Exclusion criteria were all criteria for exclusion of voluntary blood donors according to WHO (1).

Voluntary donors were informed of the aim of the study and signed an informative consent form. The study was approved by the Ethics Committee of the School of Medicine, University of Sarajevo, as well as the Blood Transfusion Institute of the Federation of Bosnia and Herzegovina.

Methods

Haemoglobin and ferritin were determined in regular and irregular blood donors twice at 45-day intervals, every time before blood donations. Determination of haemoglobin was performed

using capillary blood collected by puncturing the fingertip of one hand (HemoQue Hb 301, Ängelholm, Sweden). Blood sample (3mL) for ferritin measurement (Architect i2000sr, Illinois, USA) was collected in a tube with ethylenediaminetetraacetic acid (EDTA) from the donation bag. Haemoglobin and ferritin values were expressed in g/L and ng/mL. A decrease in iron stores was defined as plasma ferritin values below 20 ng/mL; value of 15 ng/mL was the cut off for iron deficiency that leads to the decreased erythropoiesis (7). An iron deficiency anaemia was defined as serum haemoglobin and ferritin below 13 g/dL and 15 mg/ mL, respectively (2).

The Body Mass Index (BMI) was calculated according to the formula for the ratio of body weight to the square of a person's height (9,10).

Statistical analysis

The normality of data distribution was tested with the Shapiro-Wilk test. Numerical variables were presented as the mean or median with 25th to 75th percentile depending on the normality of data distribution. If assumption of data normality was met, the difference in the mean values of two groups was tested using the independent t-test, while the difference in repeated-measures was tested by the dependent t-test. Otherwise, Mann Whitney and the Wilcoxon rank test were used, respectively. The frequency of the categorical variables was presented by the absolute number and percentage. The $p<0.05$ was taken as statistically significant.

RESULTS

The study involved 26 female and 54 male examinees, with an equal ratio in both groups. The age of the examinees ranged from 22 to 55 years. In the Group I the average age was 35.33±9.6 years, and in the Group II 33.20±6.22 years (p=0.2). The difference in the BMI between groups I and II was not statistically significant (p=0.46) (Table 1).

Table 1. Average age, gender and body mass index (BMI) distribution of regular and non-regular blood donor groups

Parameter	Group I (n=40)	Group II (n=40)
Average age (years)	35.33±9.6*	33.20± 6.22
Gender/male (n, %)	27 (67.5)	27 (67.5)
Gender/female (n, %)	13 (32.5)	13 (32.5)
BMI (kg/m2)	26.68±2.758*	27.85 ± 6.255

*non-significant; Group I, regular donors; Group II, non-regular donors;

The mean value of haemoglobin before donation in the Group Ia was 155.5 g/L, and in the Group IIa 155.07 g/L (p=0.861), and the mean value of haemoglobin after donation in the Group Ib was 149.35 g/L and in the Group IIb 149.03 g/L (p=0.916). The analysis of the mean value of two repeated measurements of haemoglobin of the Group I showed a statistically significant difference (p=0.0004), as it was in the Group II (p=0.0001) (Table 2).

Table 2. Haemoglobin and ferritin values of regular and non-regular donor groups according to the first and second measurement

Group	Haemoglobin (mean±SD)	Ferritin (percentile)
Ia	155.55 ±12.19*‡	32.83 (18.03-49.22)*‡
Ib	149.35 ± 13.47†	23.36 (11.15-42.80)†
IIa	155.07 ± 12.04‡	43.1 (20.64-79.41)‡
IIb	149.03 ± 13.76	26.63 (12.50-53.66)

*non-significant difference Ia vs IIa; †non- significant difference IIa vs IIb; ‡significant difference in two repeated measurements; Ia, the first measurement in regular donors; Ib, the second measurement in regular donors; IIa, the first measurement in non-regular donors; IIb, the second measurement in non-regular donors;

Measurement of ferritin values between the Groups Ia and IIa before the donation did not reveal a statistically significant difference (p=0.21). After the donation, there was a decrease in the value of ferritin, but there was no statistically significant difference between the Groups Ib and IIb (p=0.31). By measuring the value of ferritin in the Group Ia compared to the Group IIa, a lower mean value of ferritin was observed in the Group Ia (p=0.106). By measuring the value of ferritin in the Group I before (41.54 ng/mL) and after (29.28 ng/mL) donation, a statistically significant difference was found (p=0.0001), and the same result was shown by measuring the mean value before (56.67 ng/ml) and after donation (38.35 ng/mL) in the Group II (p=0.0001). After donation in both study groups there was a significant decrease in haemoglobin and ferritin (Table 2).

All examinees had haemoglobin reference values before donation (Table 2), while ferritin values in 25% of examinees from the Group I and 22.5% from the Group II had ferritin <20 ng/mL before the donation, and as much as 42.5% and 37.5%, respectively, in the repeated measurement (Table 3). In both groups of examinees after donation there was a decrease in haemoglobin (Table 2), but it was still in the reference values appropriate for donation.

Table 3. Frequency of examinees with plasma ferritin values indicating reduced iron depots

Donor's category	No (%) of donors in the group			
	Ia	Ib	IIa	IIb
Total number	40 (100)		40 (100)	
Ferritin <20 ng/mL	10 (25)	17 (42.5)	9 (22.5)	15 (37.5)
Ferritin <15 ng/mL	8 (20)	13 (32.5)	5 (12.5)	10 (25)

Ia, first measurement in regular donors; Ib, second measurement in regular donors; IIa, first measurement in non-regular donors; II b, second measurement in non-regular donors

DISCUSSION

In this study, we investigated the changes of haemoglobin and ferritin concentrations in blood donors especially to draw attention to the importance of testing serum ferritin for assessing iron depots in order to create recommendations to protect the blood donors. Abdullah SM (4) found a statistically significant difference in plasma ferritin values between first-time donors and regular voluntary donors. The results of our study have shown reduced initial values of ferritin in the Group I compared to the Group II (but without statistical significance), although we expected statistical significance, since multiple donors are more exposed to ferritin loss.

Baseline haemoglobin and ferritin parameters were not significantly different depending on a donor status in our study. A significant decrease was found between repeated measurements for both parameters in both groups indicating an equal intensity of the value decline regardless of the donor status. In contrast, other authors did not perform a control measurement between two blood donations, but monitored the values of ferritin before the donation in the control group and regular blood donors who donated with different intensities; they found (2,4,5) that ferritin values in subjects who had not donated so far were in the reference value and/or higher than in regular voluntary blood donors. In our study it was observed that reduced iron stores were presented in almost the same number of examinees who donated blood for the first time in relation to regular voluntary donors.

By analysing the mean value of the Group I haemoglobin before and after the donation we found a statistically significant difference, as well as when measuring values before and after donation in the Group II; also by measuring the value of ferritin in the Group I before and after donation.

The decrease in haemoglobin after donation, although significant, did not fall below the reference value for donation in either females or males; with such haemoglobin values voluntary donors would be eligible for at the next donation, regardless of the expressed low ferritin value. However, regular donation would lead to depletion of ferritin stores and consequent anaemia, which would cause the voluntary donor to be blocked for an extended period of time (11). A study conducted in 2018 at the Institute for Transfusion Medicine of the FBIH on 330 voluntary donors showed that the increase in the number of donations reduced the concentration of serum ferritin in the blood of voluntary donors, although haemoglobin levels remained acceptable for donations, and negative correlation was observed between the number of donations and the value of serum ferritin (11). In both groups analysed in our study a decrease in haemoglobin values after donation was noticed, but still in the reference values for donation. Other studies (4,5, 12-14) showed that iron deficiency was present in males who had four or more blood donations during 1 year. In addition, Tailor et al. (15) found a significant correlation between the frequency of donations, last donation interval and the serum ferritin measurement. This suggest that ferritin should be included in the assessment of regular blood donors to secure adequate iron reserves in the donor population and a need to modify the donor acceptance criteria. Reddy et al. (5) also showed that the increase in the frequency of blood donation was accompanied by a significant decrease in serum ferritin, iron-deficient erythropoiesis in 11.2% of the regular donors, and accordingly they are at risk of developing iron deficiency anaemia. Saracul et al. (16) have found that the incidence of iron deficiency was higher in male donors with three or more donations per year. The results of many studies were similar to our findings (11-15) and showed the importance of measuring iron stores as an indicator of selection for blood donation. Voluntary donors with low haemoglobin and iron, due to the delays in donating blood for a long period, often express their dissatisfaction and find it difficult to return as voluntary donors. Transfusion facilities should consider counselling and iron supplementation for males as well, and not just for females, in order to keep voluntary donors at the base (17).

According to the WHO recommendation (18), serum ferritin concentrate less than <15 ng/mL indicates depleted iron stores. Haematological recovery after donating a single unit of whole blood or erythrocyte depends on the total iron supply in the body (5,17). Several studies have revealed rapid recovery of haemoglobin in voluntary blood donors with anaemia due to iron deficiency supplemented with a daily dose of 200 mg of iron (17,19).

The main limitation of the study is the small study group. Despite the small number of respondents, the results of the study indicate a mismatch

between the haemoglobin and ferritin levels of voluntary blood donors. We believe that this research will open the question of the need for additional testing of the concentration of ferritin in the blood as a useful laboratory parameter for the assessment of the iron depot of blood donors in Bosnia and Herzegovina. In this way, the possibility would be avoided that donors with satisfactory haemoglobin levels and ferritin values risky for the development of anaemia would donate blood, which would result in them being excluded from donation for a longer period due to developed anaemia. In addition, ferritin analysis would identify at-risk individuals who would be candidates for iron supplementation and thus prevent the development of sideropenic anaemia.

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TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

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