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IRON METABOLISM PARAMETERS IN REGULAR BLOOD DONORS – A GENDER RELATED ANALYSIS*

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ABSTRACT

The aim of the study was to assess iron metabolism parameters in response to frequent blood donations in Polish blood donors, highlighting gender-related differences. The study comprised 170 whole blood donors (44 females and 126 males) in the age range of 19-60 years, admitted to the Regional Blood Transfusion Center in Bydgoszcz. The control group consisted of 36 age- and sex-matched non-donors. The peripheral blood cell count and iron status parameters, such as: serum iron, ferritin, total- and unsaturated binding capacities, erythropoietin and transferrin saturation were assessed. There were no statistical differences in basic hematological parameters between regular blood donors and non-donors. Ferritin concentrations in male as well as in female blood donors were significantly lower than in male and female non-donors. Moreover, total- and unsaturated iron binding in capacities were significantly increased in male donors compared with male non-donors. The ferritin concentration in males donating blood once a year was significantly higher than observed in women donating blood once a year. Unsaturated iron binding capacity was significantly decreased in male compared with female donors (1 blood donation/year). No statistical differences in iron metabolism parameters were found between male and female blood donors who donated blood 2-3 times per year. High-frequency blood donors, both males and females, are particularly exposed to iron deficiency. Serum ferritin concentration in males donating blood 2-3 times a year was similar to ferritin levels observed in females. Inclusion of ferritin testing in pre-donation qualification of regular donors should be considered to detect subclinical iron deficiency.

Keywords: iron metabolism, blood donors, anemia.

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INTRODUCTION

During the last couple years, much attention has paid to iron deficiency as a frequent adverse event observed in regular blood donors (BAART et al. 2013, AMREIN et al. 2017, RIGAS et al. 2017.). Single whole blood donation leads to a loss of approximately 250 mg of iron. This amount is relatively high when compared to the average body iron stores, estimated at 600-1000 mg in adult males and 200-300 mg in females. Body iron balance is regulated mainly at the point of absorption because of the limited capacity for iron excretion (except menstruation). Iron absorption varies from 1 mg day⁻¹ for men to 1.5 mg day⁻¹ for women, but increases with iron deficiency up to 4-5 mg day⁻¹ in repeated donors (KISS 2015). Taking into account the limited iron absorption with a diet and the loss of iron with a single donation unit, a high incidence of iron deficiency among regular blood donors, especially women, is expected.

Iron deficiency, if not counteracted, causes anemia and diminishes the quality of life of volunteer blood donors. Moreover, a decreased hemoglobin concentration, which reflects iron-restricted erythropoiesis, results in temporary disqualification from donating blood. According to the study of CUSTER et al. (2004), 15% of iron depleted blood donors never return to donate blood, and about 14% return only once. In the face of a high demand for blood and blood products, maintaining a large population of regular donors has become an overriding goal.

Blood centers worldwide differ in policy and there is no consensus concerning the optimal donation frequency as well as inter-donation intervals. According to the data from the international forum (2017), the maximum number of donations that can be collected from males and females is legally sanctioned in European countries at completely different levels (VUK et al. 2017). Females can give blood in a 1-year period 2 times (Italy, Cyprus), 3 times (Croatia, Portugal, Slovakia, Sweden) or even 4 times (Belgium, Bulgaria, France, Germany, Latvia, Poland) with different intervals between donations (from 56 days to 4 months). The maximum number of donations per year for men is also 'country-dependent' (4-6 times year⁻¹; interval: 56 days- 3 months) (VUK et al. 2017).

Pre-donation qualification of donors is based on general criteria such as a questionnaire, physical examination, and complete blood cell count testing before each blood donation (BAART et al. 2013, RIGAS et al. 2017, VUK et al. 2017). However, the procedures do not allow for detailed analysis of iron metabolism and early detection of iron deficiency. Hemoglobin is a late-stage marker of iron deficiency, having a limited value as a preventive screening tool (ARCHER, BRUGNARA 2015).

The aim of the study has been to assess iron metabolism parameters in response to frequent blood donations among Polish blood donors, highlighting gender-related differences.

MATERIAL AND METHODS

Patients

The study comprised 170 regular whole blood donors (44 females and 126 males) in the age range of 19-60 years (mean age 35.43 ± 10.49), admitted to the Regional Blood Transfusion Center in Bydgoszcz, Poland. Eligible donors fulfilled all routine criteria for donation, namely they completed a detailed questionnaire, underwent clinical examination and hemoglobin screening (complete blood cell count). The minimum hemoglobin concentration to donate was $>13.50 \text{ g dl}^{-1}$ for males and $>12.5 \text{ g dl}^{-1}$ for females. Blood donors who were taking any iron or iron-containing vitamin supplements or being on a vegetarian diet were excluded from the study. Based on the blood donation frequency in the last year, blood donors were divided into three subgroups:

I group – donors who gave blood once in the last year (M/30, F/18);

II group – donors who gave blood 2-3 times in the last year (M/56, F/22);

III group – donors who gave blood 4-5 times in the last year (M/40, F/4).

The control group consisted of 36 volunteers (non-donors), who were qualified to the first blood donation procedure in the Regional Blood Transfusion Center in Bydgoszcz, Poland. The control group comprised 26 males and 10 females in the age range of 18- 52 (mean age 25.86 ± 8.930).

All blood samples from repeated donors (study group) and first-time donors (control group) were taken during pre-donation qualification.

The study was approved by the Bioethics Committee of Collegium Medicum in Bydgoszcz, the Nicolaus Copernicus University in Toruń, Poland (KB/427/2005). A written informed consent was obtained from all participants.

Analytical methods

Blood samples were taken from the elbow vein, into 3 tubes containing: 1) sodium citrate, 2) dipotassium ethylenediaminetetraacetic acid (K₂ EDTA) and 3) clot activator. Samples were centrifuged at $1500 \times g$ for 15 min at 4°C (citrate plasma) and $1000 \times g$ for 10 min at 4°C (serum). The plasma and serum obtained were divided into aliquots and stored at -80°C until analysis, but no longer than 6 months.

Peripheral blood counts were performed on Advia 120 Hematology System (Siemens Healthineers, Germany). Serum iron (Fe), total iron binding capacity (TIBC) and unsaturated iron binding capacity (UIBC) were measured on the Architect c8000 clinical chemistry analyzer (Abbott, Abbot Park, Illinois, USA). Transferrin saturation was calculated by dividing the serum iron level by total iron-binding capacity. Serum ferritin concentration was measured using DRG Ferritin kit (EIA-1872, DRG International Inc., USA).

Soluble transferrin receptor (sTfR) was quantified using the Human sTfR ELISA (BioVendor Laboratory Medicine Inc., Czech Republic). Plasma erythropoietin (Epo) concentration was examined by an ELISA (Roche Diagnostics GmbH, Germany).

Statistical analysis

The statistical analysis was performed with the use of Statistica 13.0 software (StatSoft® Cracow, Poland). The Shapiro-Wilk test was applied to assess the normality of distribution. For the parameters with a normal distribution, an arithmetic mean and standard deviation were determined, and the parameters with an abnormal distribution were presented as a median and interquartile ranges. An independent sample t-test for parametric continuous variables and the Mann Whitney *U* test for nonparametric continuous variables were used to compare the differences between the two subject groups. The chi-square test was used to compare frequency of iron-depleted male and female blood donors. Correlation coefficients were determined by the Spearman's test. The *p*-values less than 0.050 were considered statistically significant.

RESULTS

As shown in Table 1, there were no statistical differences in basic hematological parameters such as red blood cells (RBCs), hemoglobin concentration, hematocrit and red blood cell indices between regular blood donors and non-donors. However, iron and ferritin concentrations as well as transferrin saturation were significantly decreased in whole blood donors when compared to non-donors.

There are significant differences in the reference values for males and females for the majority of basic hematological and biochemical parameters. For this reason, a detailed analysis was performed in subgroups divided according to the sex (Table 2).

Hematological parameters were significantly decreased in female compared with male blood donors (Table 2). There were no differences in complete blood cell counts (CBCs) when compared male/female donors and male /female non-donors (respectively). Notably, all of the obtained hematological results were within normal reference ranges.

However, the statistical analysis revealed significant differences in iron metabolism parameters between the gender subgroups. The ferritin concentration in female blood donors was significantly lower than in male donors. On the other hand, UIBC was significantly increased in female as compared with male blood donors. Furthermore, the ferritin concentration in male donors as well as female blood donors were significantly lower as com-

Table 1

Hematological parameters and laboratory indicators of iron status in donors and non-donors

Parameters	Blood donors <i>N</i> = 170		Non-donors <i>N</i> = 36		<i>p</i>
RBC ($\times 10^{12} \text{ l}^{-1}$)	4.960 \pm 0.390		4.910 \pm 0.430		NS
Hemoglobin (g dl ⁻¹)	14.91 \pm 1.120		14.76 \pm 1.300		NS
Hematocrit (%)	42.93 \pm 3.170		43.04 \pm 3.560		NS
MCV (fl)	86.78 \pm 4.580		87.65 \pm 3.910		NS
MCH (pg)	30.01 \pm 1.890		30.13 \pm 1.830		NS
MCHC (mg dl ⁻¹)	34.59 \pm 0.750		34.52 \pm 0.800		NS
Iron ($\mu\text{g dl}^{-1}$)	88.00	64.00; 111.0	97.00	74.00; 140.0	0.049
Ferritin (ng ml ⁻¹)	9.010	5.550; 15.82	18.60	7.290; 30.73	<0.005
sTfR ($\mu\text{g ml}^{-1}$)	1.110	0.720; 1.660	1.280	0.780; 1.560	NS
TIBC ($\mu\text{g dl}^{-1}$)	318.1 \pm 42.97		303.8 \pm 46.39		NS
UIBC ($\mu\text{g dl}^{-1}$)	222.6 \pm 62.48		197.5 \pm 71.49		NS
EPO (mIU ml ⁻¹)	3.680	2.080; 5.670	3.950	2.350; 5.910	NS
TfS (%)	26.39	19.29; 35.39	29.15	24.53; 46.77	0.048

Data are expressed as a median and interquartile ranges or mean \pm standard deviation; NS – not significant, RBC – red blood cells, MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, sTfR – soluble transferrin receptor, TIBC – total iron binding capacity, UIBC – unsaturated iron binding capacity, EPO – erythropoietin, TfS – transferrin saturation

pared with male/female non-donors ($p = 0.007$ and $p = 0.047$, respectively). Moreover, total- and unsaturated iron binding capacities were significantly increased in male donors compared with male non-donors ($p = 0.011$ and $p = 0.022$, respectively).

Serum iron, soluble transferrin receptor, erythropoietin and transferrin saturation did not differ between blood donors and non-donors in the gender subgroups.

Detailed analysis of iron metabolism parameters in blood donors and non-donors according to gender

Parameters	Blood donors		Non-donors		<i>p</i>
	males <i>N</i> = 126	females <i>N</i> = 44	males <i>N</i> = 26	females <i>N</i> = 10	
RBC ($\times 10^{12} \text{ l}^{-1}$)	5.070 \pm 0.370	4.660 \pm 0.270	5.060 \pm 0.390	4.530 \pm 0.220	<0.001^{&}
Hemoglobin (g dl ⁻¹)	15.37 \pm 0.830	13.53 \pm 0.600	15.38 \pm 0.960	13.41 \pm 0.780	<0.001^{&}
Hematocrit (%)	44.13 \pm 2.450	39.46 \pm 2.320	44.59 \pm 2.750	39.00 \pm 1.760	<0.001^{&}
MCV (fl)	87.33 \pm 4.600	85.16 \pm 4.160	88.23 \pm 3.800	86.22 \pm 4.010	0.007^{&}
MCH (pg)	30.33 \pm 1.860	28.96 \pm 1.570	30.44 \pm 1.730	29.53 \pm 1.950	<0.001^{&}
MCHC (mg dl ⁻¹)	34.72 \pm 0.740	34.18 \pm 0.620	34.66 \pm 0.790	34.26 \pm 0.810	<0.001^{&}
Iron ($\mu\text{g dl}^{-1}$)	88.00 66.00;118.5	89.00 59.00;108.0	97.00 78.00;140.0	102.0 74.00;129.0	NS
Ferritin (ng ml ⁻¹)	9.260 6.030;17.63	7.600 4.000;10.72	18.72 9.65;41.16	18.62 11.40;22.87	0.047* 0.007** 0.048^{&}
sTfR ($\mu\text{g ml}^{-1}$)	1.070 0.660;1.630	1.250 0.780;1.780	1.130 0.710;1.490	1.440 1.110;1.680	NS
TIBC ($\mu\text{g dl}^{-1}$)	314.4 \pm 41.41	329.5 \pm 46.17	289.0 \pm 31.02	332.1 \pm 58.43	0.011**
UIBC ($\mu\text{g dl}^{-1}$)	216.3 \pm 61.93	242.0 \pm 60.92	181.1 \pm 58.31	228.7 \pm 86.32	0.022** 0.026^{&}
EPO (mIU ml ⁻¹)	3.450 1.900;5.670	4.350 2.610;5.510	2.970 1.100;5.510	4.040 3.950;6.640	NS
TfS (%)	27.76 19.59;35.56	25.71 17.40;34.73	31.47 25.16;47.63	25.67 24.10;45.91	NS

NS – not significant; sTfR – soluble transferrin receptor, TIBC – total iron binding capacity, UIBC – unsaturated iron binding capacity, EPO – erythropoietin.

Data are expressed as a median and interquartile ranges or mean \pm standard deviation;

* female donors to female non-donors, ** male donors to male non-donors, & female to male blood donors

Table 3 shows the distribution of iron status variables among male and female blood donors according to the frequency of blood donation per year. RBCs, hemoglobin, hematocrit and MCHC were significantly increased in male compared with female blood donors, regardless of donation frequency. The ferritin concentration in males donating blood once a year was signifi-

Table 3

Iron metabolism parameters in males and females according to blood donation frequency per year

Parameters	Blood donors 1 donation year ⁻¹		<i>p</i>	Blood donors 2-3 donations year ⁻¹		<i>p</i>
	males <i>N</i> = 30	females <i>N</i> = 18		males <i>N</i> = 56	females <i>N</i> = 22	
RBC ($\times 10^{12} \text{ l}^{-1}$)	5.030 \pm 0.480	4.630 \pm 0.300	<0.005	5.040 \pm 0.340	4.690 \pm 0.270	<0.001
Hemoglobin (g dl ⁻¹)	15.32 \pm 0.750	13.57 \pm 0.640	<0.001	15.46 \pm 0.810	13.53 \pm 0.610	<0.001
Hematocrit (%)	43.82 \pm 2.630	39.78 \pm 2.120	<0.001	44.31 \pm 2.320	39.35 \pm 2.690	<0.001
MCV (fl)	87.51 \pm 5.320	86.81 \pm 3.120	NS	88.14 \pm 4.080	84.04 \pm 4.470	<0.001
MCH (pg)	30.41 \pm 2.090	29.69 \pm 1.070	NS	30.68 \pm 1.570	28.43 \pm 1.690	<0.001
MCHC (mg dl ⁻¹)	34.76 \pm 0.700	34.21 \pm 0.510	0.014	34.81 \pm 0.760	34.09 \pm 0.650	<0.001
Iron ($\mu\text{g dl}^{-1}$)	78.00 64.00;112.5	74.00 63.00;93.00	NS	92.50 65.00;123.0	90.00 53.00;108.0	NS
Ferritin (ng ml ⁻¹)	17.74 10.02;25.09	7.840 3.880;11.33	0.045	8.850 6.020;14.18	7.650 3.870; 10.72	NS
sTfR ($\mu\text{g ml}^{-1}$)	1.220 0.350;1.630	1.170 0.800;1.440	NS	1.020 0.640;1.500	1.330 0.790; 2.200	NS
TIBC ($\mu\text{g dl}^{-1}$)	296.4 \pm 42.23	326.5 \pm 60.32	NS	317.8 \pm 41.18	329.8 \pm 39.54	NS
UIBC ($\mu\text{g dl}^{-1}$)	201.3 \pm 60.39	243.8 \pm 58.85	0.042	218.1 \pm 65.37	241.8 \pm 68.40	NS
EPO (mIU ml ⁻¹)	2.970 1.760;4.600	2.790 1.990;4.570	NS	3.560 2.060;5.670	4.440 3.410;5.230	NS
TfS (%)	27.27 20.13;35.56	24.61 19.70;28.18	NS	27.22 18.44; 35.04	26.93 14.67;34.77	NS

Data are expressed as a median and interquartile ranges or mean \pm standard deviation; NS – not significant, MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, sTfR – soluble transferrin receptor, TIBC – total iron binding capacity, UIBC – unsaturated iron binding capacity, EPO – erythropoietin, TfS – transferrin saturation

cantly higher than observed in women donating blood once a year ($p = 0.045$). Unsaturated iron binding capacity was significantly decreased in male compared with female donors (1 blood donation year⁻¹).

Interestingly, no statistical differences in iron metabolism parameters

were found between male and female blood donors who donated blood 2-3 times per year. Serum ferritin in males donating 2-3 blood units per year was only 8.850 ng ml⁻¹ and was similar to the ferritin concentration observed in females donating blood with the same frequency (7.650 ng ml⁻¹, $p = \text{NS}$).

The lowest iron storage pool was observed in blood donors donating blood with the highest donation frequency (4-5 units year⁻¹). Ferritin concentrations in these males and females were 8.230 ng ml⁻¹ and 5.150 ng ml⁻¹, respectively. However, a small number of women donating blood 4 times a year (N=4) makes the statistical analysis meaningless (data not shown).

Depletion of body iron stores, defined as serum ferritin below 12 ng ml⁻¹, was observed in 80 males (63%) and 37 females (84%) from the whole study group.

As shown in Table 4, the percentage of male and female iron-depleted donors was increasing with donation frequency per year. There was a signifi-

Table 4

The prevalence of iron depletion depending on the donation frequency and gender

Donors	1 donation year ⁻¹		2-3 donations year ⁻¹		4-5 donations year ⁻¹	
	M	F	M	F	M	F
No.of donors with ferritin <12 (ng ml ⁻¹)	12 (30.00%)	13 (72.00%)	39 (69.60%)	21 (95.50%)	29 (72.50%)	3 (75.00%)
chi	4.680		5.930		0.010	
<i>p</i>	0.031		0.015		0.915	

M – males, F – females

cant difference in the prevalence of iron depletion between males and females donating blood once and 2-3 times a year. However, the percentage of iron-depleted males donating blood at 2-3 donations a year was more than twice as high as observed in males donating blood one a year (69.60% vs 30%).

DISCUSSION

The present study is one of very few observations comprising a detailed and extensive analysis of iron metabolism parameters in both male and female blood donors. In the majority of previously published research, study groups were restricted to men, which is probably a consequence of a large disproportion of men and women donating blood, with a dominance of the former (BADAR et al. 2002, SZYMCZYK-NUŻKA, WOŁOWIEC 2003, BOINSKA et al. 2010, WAHEED et al. 2018). Moreover, in-depth studies of the iron status in Polish honorary blood donors are scarce and there are no contemporary investigations (SZYMCZYK-NUŻKA, WOŁOWIEC 2003). This makes the present work unique and valuable from the clinical point of view.

When taking into account the whole studied population, the statistical analysis revealed that multiple donations of blood did not significantly affect morphological parameters of peripheral blood. There were no significant differences in RBCs, hemoglobin, hematocrit and RBCs indices between donors and healthy controls. Thus, all blood donors met basic requirements for the next blood donation. Despite the lack of any disturbances in CBCs, blood donors had significantly decreased serum iron and ferritin concentrations as well as decreased transferrin saturation in comparison with non-donors. These results are similar to ones observed by *many different researchers*, who also confirmed iron depletion in regular blood donors, regardless of their *socio-economic* background or nationality (MITTAL et al. 2006, VILSU et al. 2008, ABDULLAH et al. 2011, RIGAS et al. 2014, WAHEED et al. 2018).

Due to the significant difference in iron turnover between males and females, a more detailed analysis was conducted in subgroups of blood donors divided according to the gender. The present study has shown that RBCs, hemoglobin, hematocrit and all RBCs indices were significantly decreased in female compared with male blood donors, which reflects well their physiological condition. Additionally, we did not observe any statistical differences in the peripheral blood count between male donors and male non-donors or between female donors and female non-donors. The hemoglobin concentration, which is a crucial parameter in pre-donation qualification of donors, was above the minimum value of 12.50 g dl⁻¹ for female and 13.50 g dl⁻¹ for male donors in all cases.

Despite the lack of any change in the complete blood cell count, a detailed analysis of iron metabolism parameters revealed subtle, initially unnoticeable differences. Serum ferritin in female donors was significantly lower than in male donors (7.600 ng ml⁻¹ vs 9.260 ng ml⁻¹, $p = 0.047$). Moreover, there were significant differences in serum ferritin levels between males/ females donating blood and males/females from the control group ($p = 0.007$, $p = 0.047$, respectively). Furthermore, male donors had significantly higher total- and unsaturated binding capacities than male non-donors. On the other hand, serum iron, which is of limited diagnostic value because of its high variability, was similar in all divided subgroups. We did not observe any significant differences in EPO concentration and transferrin saturation between donor subgroups.

All these results are in accordance with results from other populations of donors (BADAR et al. 2002, SZYMZYK-NUŻKA, WOŁOWIEC 2003, MITTAL et al. 2006, MAHIDA et al. 2008, ABDULLAH et al. 2011, WAHEED et al. 2018). BOULAHRISS et al. (2008) demonstrated a lower ferritin concentration in women donating blood 3-4 times a year than in non-donors (32 µg l⁻¹ vs 10 µg l⁻¹, $p < 0.001$). According to the authors, regular iron loss from each donated blood unit is not compensated by iron absorption from the diet, and contributes to the development of anemia. MOZAHEB et al. (2011) have shown a significantly lower ferritin concentration in male donors in comparison

with male non-donors ($108 \mu\text{g l}^{-1}$ vs $42 \mu\text{g l}^{-1}$, $p < 0.001$). Higher TIBC and UIBC as well as lower ferritin concentration in male donors compared with male non-donors was also observed by WAHEED et al. (2017). One study of Polish honorary donors, published in 2003, also revealed a lower ferritin concentration and higher TIBC in male donors than in male non-donors (SZYMCZYK-NUŻKA, WOŁOWIEC 2003).

The results from the present study indicate that female donors have deep depletion of storage iron, reflected by a low ferritin concentration, compared with male donors and with female non-donors. It seems that repeated blood donations by young women may aggravate iron deficiency, which is already a common clinical problem among women in the general healthy population. Women in the reproductive age group, due to menstrual bleeding, pregnancies and poor nutritional habits caused by the current lifestyle are particularly vulnerable to iron deficiency. According to the World Health Organization data and many epidemiological studies, 16-30% of women in childbearing age suffer from iron deficiency or iron deficiency anemia (CHEŁCHOWSKA et al. 2007, FRIEDMAN et al. 2015). Studies by CHEŁCHOWSKA et al. (2007) indicate that about 20% of young Polish women have subclinical iron deficiency.

However, probably a more important issue that drew our attention is iron status of male donors. According to the study results, male donors have not only exclusive iron depletion in the storage pool (lower ferritin concentration than male non-donors) but also exhibit a very early onset of functional iron deficiency, expressed by increased TIBC and UIBC concentrations. A possible explanation of this condition can be related to the fact that male donors in Poland can give blood even 6 times per year and women up to 4 (VUK et al. 2017).

The influence of whole blood donation frequency per year on the iron status has been also investigated in gender separated subgroups. We observed physiological differences in the peripheral blood count between males and females, regardless of a donation frequency. However, the ferritin concentration in males donating blood once a year was significantly higher than observed in females donating 1 blood unit per year. Unsaturated iron binding capacity was significantly increased in female compared with male donors ($1 \text{ blood unit year}^{-1}$).

To our surprise, no statistical differences in iron metabolism parameters were found between male and female blood donors who gave blood 2-3 times in the last year. Serum ferritin in these males was only 8.850 ng ml^{-1} , being similar to the ferritin concentration observed in females (7.650 ng ml^{-1} , $p = \text{NS}$). Moreover, the percentage of iron-depleted males (defined as having ferritin levels below 12 ng ml^{-1}) strongly depended on a blood donation frequency and varied from 30% ($1 \text{ donation year}^{-1}$) to 69.60% (2-3 donations year^{-1}). On the other hand, iron depletion was observed in 72% and 95.5% women donating blood once or 2-3 times a year, respectively. The results

of our research correspond with the results of other studies conducted in this area. WAHEED et al. (2018) observed the lowest ferritin concentration in men donating blood 3 times a year compared with non-donors. MITTAL et al. (2006) found that an increase in the donation frequency (from 1 to 3 times/year) caused a significant decrease in serum ferritin, despite a normal hemoglobin concentration. BADAMI et al. (2008) noted that 25% of donors with an intense donation history (3-4 whole blood units during the previous 12 months) develop iron deficiency in the storage pool (ferritin levels lower than $12 \mu\text{g l}^{-1}$).

Summing up, the present study has shown that regular blood donations result in gradual iron depletion in both male and female blood donors, although hemoglobin levels remain within normal range. Serum ferritin concentrations in males donating blood 2-3 times a year were similar to the levels found in women. The percentage of iron-depleted males and females was strongly dependent on donation frequency. Our findings are consistent with the results of other studies, in which serum ferritin levels were significantly lower in regular, more-frequent blood donors (CANÇADO et al. 2001, DJALALI et al. 2006, RØSVIK et al. 2009, BRITTENHAM 2011). The main reason for iron deficiency in these donors is that repeated iron loss cannot be fully compensated by iron absorption from the diet (although it becomes alleviated) (KISS 2015). Moreover, according to the recently published data, in most European countries iron supplementation is used to manage iron deficiency, not to prevent it (VUK et al. 2017). Intervals between donations also have a great impact on the regulation of iron balance. A recently published randomised trial by DI ANGELANTONIO et al. (2017) has demonstrated that reduction of inter-donation intervals from 12 weeks (the United Kingdom) to 8 weeks (western European countries, and also Poland) did not have a major adverse effect on the quality of life, although it resulted in iron depletion of donors within 2 years of regular donations and as a consequence led to their deferral at least once in this time period.

Over the last couple years, many clinical studies have strongly underlined the need for better assessment of the iron status of regular blood donors (CANÇADO, LANGHI 2012, MAST 2014, DI ANGELANTONIO et al. 2017, PASRICHA et al. 2017). Considering the fact that honorary blood donors in Poland play a crucial role in the blood supply process, extensive studies should be conducted to develop strategies to prevent iron deficiency in blood donors and improve donor safety.

CONCLUSIONS

In conclusion, high-frequency blood donors, both males and females, are particularly exposed to iron deficiency. The serum ferritin concentration in males donating blood 2-3 times a year is similar to ferritin levels observed

in females. As hematologic parameters in whole blood donors and non-donors where comparable despite the deep iron deficiency in the storage pool, we suggest that inclusion of ferritin testing in pre-donation qualification of regular donors should be considered to detect subclinical iron deficiency and to prevent donor deferral.

Conflict of interest

The authors declare no conflict of interest.

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