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Analysis of Biochemical Indicators of Iron Metabolism in Primary Allogenic Blood Donors

Abstract: Currently, there is a significant shortage of donated blood and blood components worldwide. According to WHO recommendations, an adequate and reliable supply of safe and high-quality donated blood and blood components can only be achieved through regular voluntary unpaid donations. The study aims to examine the main biochemical indicators characterising iron metabolism in first-time allogeneic blood donors, in order to subsequently use them as reference values for comparative analysis in scientific research, as well as for developing practical recommendations concerning strategies for recruiting and retaining first-time voluntary unpaid blood donors. The methodological basis of this study was a systematic approach, which allowed for a comprehensive study and analysis of the biochemical indicators of iron metabolism in primary allogenic blood donors. The results obtained were used to develop practical recommendations for the Blood Centre of the Armed Forces of Ukraine regarding the strategy for attracting and retaining primary blood donors who make voluntary unpaid donations. Based on mathematical analysis, a positive correlation has been established between the indicators of secondary metabolic disorders in the examined donors and the main biochemical indicators of iron metabolism in first-time allogeneic blood donors, which may be used as reference values in conducting comparative analyses in future scientific studies.

Keywords: blood donors, donations, iron, biochemical parameters, primary allogeneic blood donors.

Андрій Володимирович Корж, старший викладач, кафедра анестезіології та реаніматології, факультет перепідготовки та підвищення кваліфікації, Українська військово-медична академія. Київ, Україна.

Аналіз біохімічних показників обміну заліза у первинних донорів алогенної крові

Анотація: Наразі в світі існує значний дефіцит донорської крові та компонентів крові. Згідно з рекомендаціями ВООЗ, адекватне і надійне забезпечення безпечною та якісною донорською кров'ю та компонентами крові може здійснюватися виключно на базі регулярних добровільних безоплатних донацій. Мета роботи – дослідити основні біохімічні показники, що характеризують біохімічні показники обміну заліза у первинних донорів алогенної крові для подальшого їх

використання як контрольних значень для порівняльного аналізу при проведенні наукових досліджень та використання для розробки практичних рекомендацій відносно стратегії із залучення та утримання первинних донорів крові, які здійснюють добровільні безоплатні донації. Методологічною основою даного дослідження був системний підхід, який дозволив різнобічно вивчити та проаналізувати біохімічні показники обміну заліза у первинних донорів алогенної крові. Отримані результати були використані для розробки практичних рекомендацій для Центру крові Збройних Сил України відносно стратегії з залучення і утримання первинних донорів крові, які здійснюють добровільні безоплатні донації.

Ключові слова: донори крові, донації, залізо, біохімічні показники, первинні донори алогенної крові.

Abbreviations:

Ft is ferritin,

GMP is Good Manufacturing Practice,

SI is serum iron (concentration),

Tf is transferrin,

$TIBC$ is total iron-binding capacity,

TS is transferrin saturation,

$UIBC$ is unsaturated (latent) iron-binding capacity.

Introduction

According to the Association Agreement between Ukraine and the European Union, the European Atomic Energy Community and their Member States, our country embarked on the path of integration into the European Community. This, in particular, imposed requirements to review and reform the existing blood service in Ukraine, and envisaged the mandatory establishment of production in line with the requirements of GMP and the European Pharmacopoeia (*Vidborets & Derpak, 2022*; *Perekrestenko et al., 2014*; *Haidukova et al., 2014*).

The main provisions and principles were adopted as the basis for reforming the blood system in Ukraine, a process that continues successfully. Taking into account the general approaches to reforming transfusion medicine in Ukraine, in recent years the country has achieved the maximum possible implementation of organisational, methodological and legal approaches in accordance with European and global standards (*On Infectious Safety…, 2005*; *On Approval of the Procedure…, 2013*; *Guide…, 2020*).

The reform of the blood system in Ukraine has strengthened the position of transfusiology as an integral part of the healthcare system, which holds strategic significance for the state as a whole. Over the course of the reform, Ukraine's blood system has become more structured, acquired a truly systemic character, and now represents a synthesis of scientific achievements and practical work in the organisation and technology of blood collection, the production and use of blood components, the organisation, methodology and techniques of transfusion, and the protection of donor health (*Guide…, 2020*; *AABB Standards…, 2016*; *Fung et al., 2014*).

The main task of the blood service is to ensure equal access for the population of Ukraine to high-quality and safe components of donor blood in the required quantity (*On Infectious Safety…, 2005*; *Activities…, 2021*). The quality and safety of blood components refer to the

compliance of donor blood, as the basis for the production of blood components, or components of blood directly collected from the donor (apheresis), which are supplied to consumers, with the legally established standards of quality and safety (*Fung et al., 2014*; *Blood Safety…, 2020*). Strict adherence to the established regulations and procedures for collection, testing, processing, storage, distribution, and transportation of donor blood and its components by the entities of the blood service serves as a guarantee of the quality and safety of blood components used for transfusion purposes, upon which the safety of recipients and the clinical effectiveness of transfusion directly depend (*Vidborets & Derpak, 2022*; *Perekrestenko et al., 2014*; *Haidukova et al., 2014*; *On Infectious Safety…, 2005*; *On Approval of the Procedure…, 2013*; *Guide…, 2020*; *Fung et al., 2014*; *Blood Safety…, 2020*).

Despite the obvious relevance of this issue for the blood service, few studies have been devoted to examining iron metabolism disorders in donors; the results presented are often contradictory, there is a lack of controlled studies and an insufficient evidence base, data regarding biochemical changes at different stages of participation in donation are not clearly defined, and the issues of post-transfusion reactions and complications, as well as the transmission of transfusion-transmitted infections, remain unresolved (*On Infectious Safety…, 2005*; *On Approval of the Procedure…, 2013*; *Activities …, 2021*; *Assessment…, 2020*; *Weiss et al., 2019*; *Vidborets et al., 2021*). This has prompted us to perform the present study.

The study aims to investigate the main biochemical parameters that characterise iron metabolism in first-time allogeneic blood donors, with a view to using them as reference values for comparative analysis in scientific research and for developing practical recommendations regarding strategies for recruiting and retaining first-time voluntary unpaid blood donors.

Methods and Materials

The methodological basis of this study was a systemic approach, which made it possible to comprehensively examine the biochemical indicators of iron metabolism in the blood of donors. We examined 135 first-time allogeneic blood donors from the Blood Centre of the Armed Forces of Ukraine.

According to the age classification (WHO, 2025), all the examined first-time donors were divided into three subgroups:

- young donors are 69 individuals (47 men and 22 women) aged 18 to 44 years;
- middle-aged donors are 47 individuals (35 men and 12 women) aged 45 to 59 years;
- older donors are 19 individuals (13 men and 6 women) aged 60 to 74 years (*Table 1*).

Thus, in the study group, the average age of the examined first-time donors was (37.87±1.33) years, with individual variations ranging from 20 to 59 years. The average age of male donors was (38.46±1.52) years, with individual variations from 20 to 59 years. The average age of female donors was (36.49±2.38) years, with individual variations from 22 to 56 years.

All 135 primary allogeneic blood donors were practically healthy and, based on the results of a questionnaire, specialist examination and determination of haemoglobin levels, were admitted to donate blood. The results of testing the donated blood for the presence of markers of transfusion-transmissible infections were negative. All donors were examined in accordance with the requirements of the "Procedure for Medical Examination of Blood Donors and/or Its

Components", approved by Order of the Ministry of Health of Ukraine No. 385 dated August 1, 2005 (*On the Infectious Safety…, 2025*), as donors whose blood is used for the preparation of components, as well as in line with other applicable regulatory legal acts.

Before donating blood, the donors completed a questionnaire and underwent a medical examination by qualified specialists according to the requirements of the current "Procedure for Medical Examination of Blood Donors and Blood Components". For each donor, the haemoglobin content was determined (normal is not less than 135 g/L for men, not less than 125 g/L for women). Based on the examination results, the volume of blood donation was determined for each donor (there is 450 ml of the maximum permissible dose, excluding up to 40 ml of blood taken for testing).

After donation, the main biochemical parameters were determined in the donors' plasma, and screening for markers of transfusion-transmissible infections (HIV-1/2, hepatitis B, hepatitis C, syphilis) was performed. For the research, devices and reagents registered and certified for use in Ukraine were used. The devices underwent metrological control in accordance with the established periodicity.

The haematological parameters of peripheral blood were determined on automatic haematology analysers "Micros 60" (ABX, France) and "PCE-210" (ERMA, Japan), and the main biochemical parameters were measured on a semi-automatic biochemical analyser "STARDAST-MC-15" (DiaSys Diagnostic Systems, Germany). The iron content in serum was determined using the bathophenanthroline method. The $TIBC$ of serum was determined by saturating transferrin with trivalent iron. The unsaturated (latent) iron-binding capacity of serum was calculated as the difference between the total iron-binding capacity of serum and the serum iron content. The transferrin saturation coefficient was calculated as the ratio of serum iron content to the total iron-binding capacity of serum. The Tf content in serum was determined according to the total iron-binding capacity of serum. The ferritin content in serum was determined by the radioimmunoassay method. The obtained study results were processed using methods of variational statistics.

Results

All 135 first-time allogeneic blood donors were practically healthy and, based on the results of questionnaires, examinations by specialists and determination of haemoglobin content, were deemed eligible to donate blood. The results of the donated blood screening for markers of transfusion-transmissible infections were negative.

A detailed peripheral blood analysis was performed for all examined first-time allogeneic blood donors at the laboratory of the Blood Centre of the Armed Forces of Ukraine; the results are presented in the appendix (*Table 2*).

As can be seen from the data in Table 2, the mean haemoglobin concentration among the group of first-time allogeneic blood donors was 133.50±1.99 g/l.

The mean haemoglobin concentration among the male donors was 138.13±2.49 g/l, with individual variations ranging from 133 g/l to 143 g/l, whereas among the female donors it was 129.09±1.51 g/l, with individual variations from 123 g/l to 135 g/l. The haemoglobin concentration in male donors was higher than that in female donors ($p<0.001$).

The mean red blood cell (erythrocyte) count among the group of first-time donors was (4.74±0.32)×10^{12}/l. Among the examined male donors, the mean count was (5.06±0.51)×10^{12}/l, while among female donors it was (4.43±0.13)×10^{12}/l, with individual variations in men from 4.3×10^{12}/l to 5.2×10^{12}/l, and in women from 4.0×10^{12}/l to 4.8×10^{12}/l. The erythrocyte count in male donors was higher than in female donors ($p<0.001$).

The mean leukocyte count in male donors was (6.54±0.29)×10^{9}/l, with individual variations from 4.5×10^{9}/l to 8.6×10^{9}/l, whereas in female donors it was (6.37±0.14)×10^{9}/l, with variations from 4.9×10^{9}/l to 8.0×10^{9}/l. Overall, in the group of first-time donors, the mean leukocyte count was (6.45±0.21)×10^{9}/l.

The mean platelet count among the group of first-time donors was (227.73±2.44)×10^{9}/l. Among male donors, the mean platelet count was (241.18±2.54)×10^{9}/l, while among female donors it was (213.55±2.35)×10^{9}/l, with individual variations in men from 202×10^{9}/l to 253×10^{9}/l, and in women from 190×10^{9}/l to 237×10^{9}/l.

As can be seen from Table 2, among the examined first-time allogeneic blood donors, we did not find a statistically significant difference in the mean leukocyte and platelet counts by sex ($p>0.05$).

Below is a definition of the main indicators characterising the state of iron metabolism in the bodies of first-time allogeneic blood donors.

The SI concentration and the $TIBC$ of serum were determined using the bathophenanthroline method. In determining $TIBC$, magnesium carbonate was used as the sorbent. The $UIBC$ was calculated as the difference between $TIBC$ and SI. TS with iron was determined as the ratio of SI to $TIBC$ multiplied by 100%. The Tf content was assessed based on $TIBC$. The determination of FN content in blood serum was carried out using the radioimmunoassay method. The data on the analysis of the main indicators of iron metabolism in the plasma and serum of the examined first-time allogeneic blood donors are presented in the appendix (*Table 3*).

As shown in Table 3, the mean level of SI in the group of first-time donors was (20.38 ± 2.10) μmol/l. Among the examined male donors, this indicator averaged (22.75 ± 1.33) μmol/l, with individual variations ranging from 17.25 to 24.40 μmol/l, whereas in female donors it averaged (18.02 ± 1.30) μmol/l, with individual variations from 16.27 to 21.24 μmol/l. The SH content in male donors was higher than in female donors ($p < 0.01$).

The $TIBC$ indicator in the group of first-time donors averaged (57.70±2.51) μmol/l. In the examined male donors, this indicator was (56.72±2.37) μmol/l, and (58.68±2.20) μmol/l in females, with individual variations in males ranging from 52.06 to 61.02 μmol/L, and from 54.83 to 62.03 μmol/l in females. $TIBC$ in female donors was higher than in male donors ($p<0.01$).

The $UIBC$ indicator in the examined male donors averaged (34.99±4.08) μmol/l, with individual variations from 28.03 to 43.34 μmol/l, and (39.98±3.54) μmol/L in females, with individual variations from 34.16 to 45.62 μmol/l. Overall, in the group of first-time donors, $UIBC$ amounted to (37.48±4.35) μmol/l. $UIBC$ in female donors was higher than in male donors ($p<0.01$).

The iron TS indicator in the group of first-time donors averaged (34.80±4.93)%. In the examined male donors, this indicator averaged (36.58±4.74)%, and (33.02±3.63)% in females, with individual variations in males ranging from 28.62 to 46.11%, and from 26.39 to 38.31% in females. TS in male donors was higher than in female donors ($p<0.01$).

The Tf content in the group of first-time donors averaged (2.24±0.12) g/l. In the examined male donors, this indicator averaged (2.22±0.11) g/l, and (2.25±0.13) g/l in females, with individual variations in males ranging from 2.02 to 2.38 g/l, and from 2.14 to 2.50 g/l in females. The Tf content in female donors was higher than in male donors ($p<0.01$).

The FN content in the examined male donors averaged (24.98±2.10) μg/l, with individual variations from 20.17 to 30.60 μg/l, and (21.78±1.17) μg/l in females, with individual variations from 17.27 to 22.10 μg/l. Overall, in the group of first-time donors, FN content was (23.38±2.19) μg/l. The FN content in male donors was higher than in female donors ($p<0.001$).

Thus, the current research results have covered a larger cohort of first-time allogeneic blood donors compared to previous studies and can be used as control values for comparative analysis in future scientific research.

Conclusion

Based on mathematical analysis, a positive correlation has been established between indicators of secondary metabolic disturbances in the examined donors and the main biochemical parameters of iron metabolism in primary allogeneic blood donors. These parameters can be used as reference values for comparative analysis in further scientific studies. The obtained results are recommended for use in developing practical guidelines regarding strategies for recruiting and retaining primary allogeneic blood donors who provide voluntary unpaid donations.

A promising direction is the search for new additional diagnostic criteria for iron metabolism disorders in primary allogeneic blood donors, as well as the study of secondary metabolic disturbances accompanying its deficiency.

It has been determined that when allowing subsequent donations, the levels of iron metabolism indicators in the plasma and serum of primary allogeneic blood donors—particularly ferritin—are worth considering. The results of the conducted studies allow for the formation of a risk group of blood donors based on informative biochemical characteristics of iron metabolism.

Conflict of interest

The author declares that there is no conflict of interest.

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Appendix

Table 1. Age structure of examined primary allogeneic blood donors depending on age (n=125)

Age group of donors	Men (n)	Women (n)	Total (n)
Youth, 18–44 років	47	22	69
Average, 45–59 років	35	12	47
Old, 60–74 років	13	6	19
Total:	95	40	135

Table 2. peripheral blood parameters in primary allogeneic blood donors (M+m)

Indicator, unit of measurement	All donors (n=135)	Men (n=95)	Women (n=40)	Достовірність різниці (p)
Hemoglobin concentration, g/l	133,50±1,99	138,13±2,49	129,09±1,51	p<0,001
Number of red blood cells, 10^{12}/l	4,74±0,32	5,06±0,51	4,43±0,13	p<0,001
Кількість лейкоцитів, 10^9/l	6,45±0,21	6,54±0,29	6,37±0,14	p>0,05
Кількість тромбоцитів, 10^9/l	227,73±2,44	241,18±2,54	213,55±2,35	p>0,05

Note: p is reliability of the difference between indicators depending on gender.

Table 3. indicators of iron metabolism in plasma and serum of primary allogeneic blood donors (M±m)

Indicator, unit of measurement	All donors (n=135)	Men (n=95)	Women (n=40)	Reliability of the difference (p)
SI, mmol/l	20,38±2,10	22,75±1,33	18,02±1,30	p<0,01
$TIBC$, mmol/l	57,70±2,51	56,72±2,37	58,68±2,20	p<0,01
$UIBC$, mmol/l	37,48±4,35	34,99±4,08	39,98±3,54	p<0,01
TS, %	34,80±4,93	36,58±4,74	33,02±3,63	p<0,01
Tf of serums, g/l	2,24±0,12	2,22±0,11	2,25±0,13	p<0,01
FN of serum, mcg/l	23,38±2,19	24,98±2,10	21,78±1,17	p<0,001

Note: p is reliability of the difference between indicators depending on gender.