

Original article

Prevalence of iron depletion in blood donors

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Abstract:

Introduction: Frequent whole blood (WB) donations can increase iron depletion (ID) risk. Although the donors' hemoglobin (Hb) levels met the minimum acceptable levels, they may have ID, and further donations can cause iron deficiency anemia (IDA). **Objectives:** The aims are to determine the ID prevalence in eligible donors and to implement serum ferritin (SF) testing for adjusting the interdonation intervals to prevent IDA in donors.

Materials and Methods: Four hundred thirty-three WB donors (251 males, 135 premenopausal and 47 menopausal females) from the Blood Bank of Ramathibodi Hospital were included in the cross-sectional study. They were classified into 2 groups. Group I consisted of first-time donors (FT) and reactivated donors (RA) who did not give blood in the past 2 years. Group II included repeat donors (RP) who donated WB at least 3 times during the past 12 months. Their Hb and SF were measured. The prevalence of ID (SF < 15 ng/mL) was determined.

Results: The prevalence of ID was 8.31%. RP had statistically significantly higher ID than FT/RA in males ($p = 0.002$) and premenopausal females ($p = 0.041$), but was not statistically significant in menopausal females ($p = 0.234$). RP females who took iron tablets had a lower prevalence of ID than non-iron-supplemented donors (9.3% vs 38.1% in premenopausal females, 5.26% vs 40% in menopausal females). However, ID in RP males was not statistically different. **Conclusion:** The prevalence of ID in eligible donors was significantly higher in RP donors. Moreover, RP females who received iron supplementation had a lower prevalence of ID than those who did not. Serum ferritin testing should be undertaken in RP donors who donate WB at least 3 times annually, especially in premenopausal females, to guide future interdonation intervals for donors at risk.

Keywords : ● Blood donation ● Iron depletion ● Serum ferritin

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นิพนธ์ต้นฉบับ

ความชุกของภาวะพร่องธาตุเหล็กในผู้ป่วยโรคโลหิต

วาสวรรณ เขียนดวงจันทร์ ศราวัลย์ จันทรเทศ วิมล เขียวโพธิ์ภักษ์ สุกัลยาณี อ่อนสีแดง และ พิมพ์พรณ กิจพอคำ
ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล

บทคัดย่อ

บทนำ การบริจาคโลหิตเป็นปัจจัยหนึ่งของการสูญเสียธาตุเหล็กของผู้บริจาคโลหิต การคัดกรองด้วยระดับของฮีโมโกลบิน (Hb) ไม่เพียงพอต่อการเฝ้าระวังภาวะขาดธาตุเหล็ก (iron depletion) ของผู้บริจาค และการบริจาคโลหิตอย่างต่อเนื่องอาจทำให้ผู้บริจาคโลหิตมีภาวะโลหิตจางจากการขาดธาตุเหล็ก (iron deficiency anemia) ได้ในอนาคต **วัตถุประสงค์** เพื่อศึกษาหาความชุกของภาวะขาดธาตุเหล็ก (iron depletion) ในผู้บริจาคโลหิตที่ผ่านเกณฑ์การคัดกรองของคลังเลือด และเพื่อนำการตรวจระดับเฟอร์ริตินในเลือด (serum ferritin) มาพิจารณาความถี่ในการบริจาคโลหิตของผู้ที่มีความเสี่ยงต่อ iron deficiency anemia **วัสดุและวิธีการ** ผู้บริจาคโลหิตที่ผ่านเกณฑ์คัดกรองของคลังเลือดโรงพยาบาลรามาธิบดีทั้งหมด 433 ราย ประกอบด้วย เพศชาย 251 ราย เพศหญิงวัยเจริญพันธุ์ 135 ราย และเพศหญิงวัยหมดประจำเดือน 47 ราย ถูกแบ่งเป็น 2 กลุ่ม คือ 1) ผู้บริจาคโลหิตครั้งแรก และผู้บริจาคโลหิตซึ่งเคยบริจาคครั้งล่าสุดนานกว่า 2 ปี (FT/RA) และ 2) ผู้บริจาคโลหิตประจำ ซึ่งบริจาคโลหิตตั้งแต่ 3 ครั้งขึ้นไปใน 12 เดือนที่ผ่านมา (RP) เก็บข้อมูลผลการตรวจ Hb และ serum ferritin โดยนิยาม serum ferritin ต่ำกว่า 15 ng/mL เป็น iron depletion (ID) คำนวณความชุกของการเกิด ID ในแต่ละกลุ่มตัวอย่าง แล้วเปรียบเทียบระหว่างกลุ่ม FT/RA และ RP ในเพศเดียวกัน **ผลการศึกษา** ความชุกของ ID ในผู้บริจาคโลหิตทั้งหมดคิดเป็นร้อยละ 8.31 เมื่อเปรียบเทียบในผู้บริจาคโลหิตเพศชาย กลุ่ม RP มี ID สูงกว่า FT/RA ($p = 0.002$) ในกลุ่มผู้บริจาคโลหิตเพศหญิงวัยเจริญพันธุ์ ($p = 0.041$) และในกลุ่มผู้บริจาคโลหิตเพศหญิงวัยหมดประจำเดือน ($p = 0.234$) นอกจากนี้ RP กลุ่มที่รับประทานธาตุเหล็กเสริมมีความชุกของ ID น้อยกว่ากลุ่มที่ไม่ได้รับประทาน ทั้งในเพศหญิงวัยเจริญพันธุ์ (ร้อยละ 9.3 vs 38.1) และในเพศหญิงวัยหมดประจำเดือน (ร้อยละ 5.26 vs 40) แต่ในเพศชายพบว่าไม่แตกต่างกัน **สรุป** ผู้บริจาคโลหิตประจำที่ผ่านเกณฑ์คัดกรองของคลังเลือด มีความชุกของภาวะขาดธาตุเหล็กสูงกว่าเมื่อเทียบกับกลุ่มผู้บริจาคโลหิตครั้งแรกและผู้บริจาคโลหิตล่าสุดนานกว่า 2 ปี นอกจากนี้พบว่าผู้บริจาคโลหิตประจำเพศหญิงที่รับประทานธาตุเหล็กมีภาวะขาดธาตุเหล็กน้อยกว่าผู้ที่ไม่ได้รับประทาน ดังนั้น ควรมีการตรวจระดับเฟอร์ริตินในเลือดในผู้บริจาคโลหิตทุกรายที่บริจาคโลหิตตั้งแต่ 3 ครั้งขึ้นไปใน 12 เดือน โดยเฉพาะในผู้บริจาคโลหิตเพศหญิงวัยเจริญพันธุ์ เพื่อใช้พิจารณาความถี่ในการบริจาคโลหิตเพิ่มเติม

คำสำคัญ : ● การบริจาคโลหิต ● ภาวะขาดธาตุเหล็ก ● ระดับเฟอร์ริตินในเลือด

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2569;36:105-12.

Introduction

Blood donation is known to cause iron depletion in healthy blood donors. Around 25 to 35% of blood donors are affected by iron depletion worldwide.^{1,9,11} One unit of whole blood donation reduces about 250 mg of iron from blood donors, which is approximately 30% of iron stores in males and as much as 60% of iron stores in females under the age of 50.¹ Depletion of body iron stores can progress to iron deficiency anemia (IDA), which causes affected people to experience the symptoms of IDA.² Although hemoglobin screening is used to detect anemia, it cannot estimate the iron status of blood donors in the early stage of iron depletion. Blood donors who meet the acceptable hemoglobin levels may already have iron depletion, and further blood donation can progress them to the stage of IDA.

The Association for the Advancement of Blood & Biotherapies (AABB) has updated strategies to take care of donors at risk of iron depletion, which are young donors, premenopausal females, donors with hemoglobin levels near the minimum acceptable level, and frequent donors who have given blood at least three times annually for males or at least two times annually for females. These strategies are lengthening interdonation intervals and/or decreasing the number of donations per year, iron supplementation, and ferritin testing as an additional test for advising donors.³ Many different cut-off values of serum ferritin were used for the diagnosis of iron deficiency or iron depletion.⁶ Therefore, the prevalence of iron depletion in blood donors varied across transfusion services.^{4,5}

The Blood Bank of Ramathibodi Hospital also implemented strategies to prevent iron deficiency in blood donors by following the Thai national guideline for transfusion services. Blood donors were deferred for three months between each whole blood donation, and iron tablets were offered to all of them. However, more than half of the females who visited the blood bank were deferred because their hemoglobin levels were lower than the acceptable level. Serum ferritin testing in blood donors, which had not been used at Ramathibodi Hospital, may be applied to decrease the deferral rate.

The aims of this study are to find the prevalence of iron depletion in eligible blood donors of the Blood Bank of Ramathibodi Hospital and to compare the iron status between first-time donors and repeat donors who donated whole blood at least three times in the past twelve months. The results of the study are expected to determine that serum ferritin testing could be used to adjust the interdonation interval of iron depleted donors to prevent iron deficiency anemia.

Materials and Methods

Sample population

This cross-sectional study was conducted at the Blood Bank of Ramathibodi Hospital. The study was approved by the Human Research Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University (COA. MURA2022/348). Whole blood donors who were at least 18 years old and eligible to donate blood were included in the study by stratified random sampling. Whole blood donors who had a plateletpheresis or double red cell donation in the past twelve months were excluded from the study because the interdonation interval and red cell loss from these procedures were not equal to those of whole blood donations.⁷

The demographic data of participants, including sex, menstrual status, number of whole blood donations in the past twelve months, and iron supplementation, were reviewed from computer records and self-questionnaires. Participants were classified into two groups. Group I consisted of first-time donors (FT) who never donated blood and reactivated donors (RA) who had not donated blood for at least two years. Group II included repeat donors (RP) who donated whole blood at least three times in the past twelve months.

Laboratory testing

The hemoglobin levels of whole blood donors who passed the self-questionnaires were measured by point-of-care testing using HemoCue® Hb 201 Microcuvettes (HemoCue AB, Angelholm, Sweden). The cut-off values for hemoglobin levels were 12.5 g/dL for females and 13.0 g/dL for males.

The leftover serum from each donor's clotted blood tube was aliquoted into a small test tube and stored at -40°C for the serum ferritin testing. On the day of serum ferritin testing, frozen sera were thawed at room temperature and centrifuged again. Serum ferritin testing was performed between June 2022 and September 2022 using the Alinity i Ferritin Reagent Kit (Abbott Ireland Diagnostics Division, Longford, Ireland) by using the Alinity i analyzer (Sanmina - SCI Systems Singapore Pte. Ltd, Singapore) which is a chemiluminescent microparticle immunoassay (CMIA) technology. The three levels of quality control materials were tested before each run. According to the World Health Organization (WHO) guidelines, a serum ferritin concentration below 15 ng/mL was defined as iron depletion in the study.⁸

Statistical analysis

The sample size was calculated using the computer software (MedCalc® Version 20.111). The prevalence of iron depletion of 15% in a previous study was used as the null hypothesis value.⁹ The calculated sample size was 430.

The statistical analysis was performed by the computer software (PASW Statistics Release 18.0.0). The data were described by the mean for normally distributed data and the median for non-normally distributed data. The prevalence of iron depletion was calculated for all blood donors and for each subgroup. The prevalence of

iron depletion between groups of donors was compared using Pearson's Chi-squared and Fisher's exact test. The *p*-value below 0.05 was considered statistically significant.

Results

A total of 433 whole blood donors were included in the study; 220 were FT/RA, and 213 were RP. The prevalence of iron depletion in all blood donors was 8.31% (36/433).

Table 1 shows the prevalence of iron depletion in eligible whole blood donors. In FT/RA, the prevalence of iron depletion was highest in premenopausal females, which was 7.04%. While 1.59% was found in FT/RA males, and none was found in FT/RA menopausal females. The prevalence of iron depletion was compared between FT/RA and RP males, premenopausal females, and menopausal females. The prevalence of iron depletion in RP males was statistically significantly higher than that of FT/RA males (11.20% vs 1.59%, *p* = 0.002), and the prevalence of iron depletion in RP premenopausal females was statistically significantly higher than in FT/RA premenopausal females (18.75% vs 7.04%, *p* = 0.041). The prevalence of iron depletion was also higher in RP menopausal females than the FT/RA group (12.50% vs. 0%), but it was not statistically significant (*p* = 0.234) due to small number of participants.

Table 1 The prevalence of iron depletion in eligible FT, RA and RP whole blood donors

Blood donors		Number	Iron depletion	No iron depletion	<i>p</i> -value
Males	FT/RA	126	2 1.59%	124 98.41%	0.002
	RP	125	14 11.20%	111 88.80%	
Premenopausal females	FT/RA	71	5 7.04%	66 92.96%	0.041
	RP	64	12 18.75%	52 81.25%	
Menopausal females	FT/RA	23	0 0.00%	23 100.00%	0.234
	RP	24	3 12.50%	21 87.50%	

Table 2 The prevalence of iron depletion in FT, RA and RP whole blood donors stratified by the number of donations in the past twelve months

Blood donors		Number of donations in 12 months	N	Iron depletion	No iron depletion	p-value
Males	FT	0	106	2 1.89%	104 98.11%	0.005
	RA	0	20	0 0.00%	20 100.00%	
	RP	3	108	14 12.96%	94 87.04%	
	RP	4	17	0 0.00%	17 100.00%	
Premenopausal females	FT	0	54	4 7.41%	50 92.59%	0.073
	RA	0	17	1 5.88%	16 94.12%	
	RP	3	56	9 16.07%	47 83.93%	
	RP	4	8	3 37.50%	5 62.50%	
Menopausal females	FT	0	8	0 0.00%	8 100.00%	0.322
	RA	0	15	0 0.00%	15 100.00%	
	RP	3	23	3 13.04%	20 86.96%	
	RP	4	1	0 0.00%	1 100.00%	

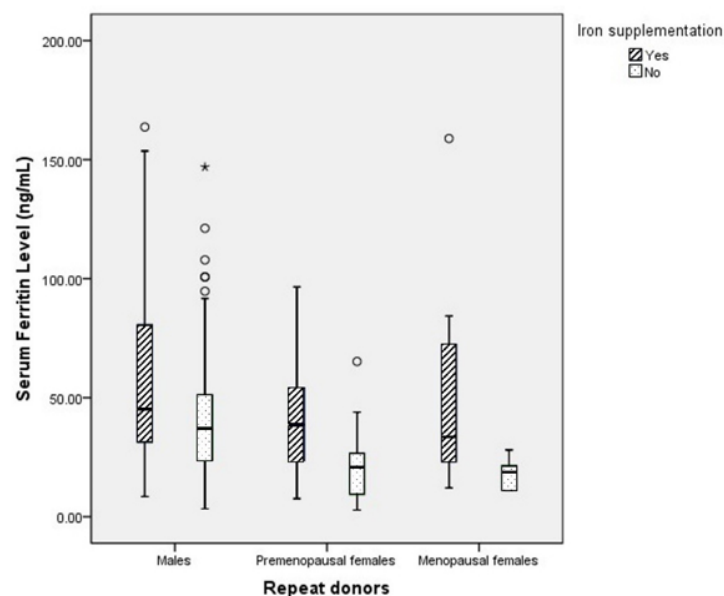
Table 2 shows the prevalence of iron depletion in FT/RA and RP whole blood donors stratified by the number of donations in the past twelve months. Donors who donated whole blood three times in twelve months had the highest prevalence of iron depletion in males and menopausal females, 12.96% and 13.04% respectively. On the other hand, the highest prevalence of iron depletion in premenopausal females was found in donors who donated whole blood four times in twelve months, which was 37.50%.

The data in Table 3 shows that 51.20% of RP males, 67.19% of RP premenopausal females, and 79.17% of RP menopausal females took iron supplementation. The

prevalence of iron depletion in donors who took iron tablets was lower than in donors who did not take any iron supplementation, especially in females, regardless of menstrual status. The prevalence of iron depletion in RP who took and did not take iron tablets was 9.30% vs 38.10% in premenopausal females, and 5.26% vs 40.00% in menopausal females. The prevalence of iron depletion was not different in males, 10.94% vs 11.48%. Besides, RP who took iron tablets had higher median serum ferritin levels than donors who did not take any iron supplementation in any sex and menstrual status as shown in Figure 1.

Table 3 The prevalence of iron depletion and serum ferritin level in repeat donors related to iron supplementation

Repeat donors	Iron supplementation	Donors		Serum ferritin level [median, (Q1, Q3)]	Iron depletion	
		Number	%		Number	%
Males	Yes	64	51.20	45.25 (31.00, 80.79)	7	10.94
	No	61	48.80	36.81 (23.61, 52.63)	7	11.48
Premenopausal females	Yes	43	67.19	38.70 (23.23, 54.98)	4	9.30
	No	21	32.81	20.97 (7.76, 30.47)	8	38.10
Menopausal females	Yes	19	79.17	33.41 (22.76, 74.59)	1	5.26
	No	5	20.83	18.72 (11.10, 24.80)	2	40.00

**Figure 1** Distribution of serum ferritin level of repeat donors who took iron supplementation (striped box) and did not take iron supplementation (dotted box)

Discussion

Frequent whole blood donation increases the risk of iron depletion in donors. The overall prevalence of iron depletion in the study was 8.31%. This was lower than in the previous studies in the United States (US) and Thai populations.^{9,10} In the US, donors can donate whole blood every 8 weeks. The shorter time for iron recovery resulted in greater iron depletion than in this study. Moreover, the previous study used a different cut-off value for serum ferritin to define absent iron stores, namely below 12 ng/mL.⁹ In the study of the Thai population in 2000, the serum ferritin cut-off value below 15 ng/mL and the interdonation interval were the same as those in this study. However, the number of repeat donors was more than that of first-time donors.¹⁰

Therefore, the prevalence of iron depletion was higher than in this study. First-time donors were included to reflect the iron status of the general population, without the effect of whole blood donations in this study, and it was found that premenopausal females were more iron-depleted than males and menopausal females. This is due to menstrual blood loss, which is one of the important factors of depleted iron stores in reproductive females.

Repeat donors had a higher prevalence of iron depletion than first-time and reactivated donors, regardless of sex and menstrual status. This is in accordance with previous studies.^{5,9-12} The donation frequency is an important factor of depleted iron stores. However, in this study, the prevalence of iron depletion among donors

who donated four times in the past twelve months was lower than that of donors who donated three times in both males and menopausal females. The most plausible explanation is that the number of donors who donated four times in the past twelve months was too small to provide a reliable result of prevalence of iron depletion in the study, as shown in Table 2. Furthermore, the prevalence of iron depletion in first-time and reactivated donors was not different in both sexes in this study. This is in accordance with the US study that showed no difference in serum ferritin levels between these two groups.⁹

According to the HEIRS study, blood donors with low serum ferritin levels take more than 24 weeks for iron recovery without oral iron supplementation.¹³ In this study, repeat donors who took iron tablets had higher median serum ferritin levels than donors who did not take any iron supplementation. Moreover, the prevalence of iron depletion in iron-supplemented females was lower than in non-iron-supplemented females. Nevertheless, the prevalence of iron depletion in repeat men was not statistically different. This assumes that iron supplementation shows less benefit in repeat men.

There are some limitations in the study. First, the confounding factors that affect iron stores other than blood donation, such as diet, pregnancy, or history of blood loss, were not identified in the study. Second, infection or inflammation can elevate serum ferritin levels¹⁴, but inflammatory markers were not tested in any participants. This provides a potential explanation for the low prevalence of iron depletion observed in our study. Third, the prospective study may better interpret the association between the number of whole blood donations per year and iron depletion, because baseline serum ferritin levels differ across donors. Finally, the cut-off value for serum ferritin level to define donors at risk should be determined. Prospective studies are required to determine the specific serum ferritin threshold that predicts donor deferral due to low hemoglobin at subsequent visits.

Conclusion

The prevalence of iron depletion in eligible whole blood donors was significantly higher in repeat donors than in first-time and reactivated donors, regardless of sex and menstrual status. Moreover, repeat donors who received iron supplementation had a lower prevalence of iron depletion than those who did not. Therefore, serum ferritin should be measured in repeat donors who donate whole blood at least three times annually, especially in premenopausal females, to guide the future interdonation intervals and prevent iron deficiency anemia in high-risk donors. Donors with low serum ferritin levels should be advised to defer for at least six months before the next donation.

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