Significantly Lower Serum Ferritin in Apheresis Platelet Donors Compared to Whole Blood Donors

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ABSTRACT

BACKGROUND: Iron deficiency is a recognized risk for frequent blood donors, particularly for platelet apheresis donors due to their increased donation frequency. This retrospective study examines ferritin levels in 31,661 blood donors, encompassing whole blood (n=26,129) and platelet apheresis (n=5,532) donors from 2018 to 2021. It aims to understand the impact of donation type, age, and sex on iron depletion, emphasizing the unique needs of platelet donors.

STUDY DESIGN AND METHODS: We analyzed data from a centralized blood donation database, stratifying donors by age, sex, and donation type. Ferritin levels, measured using a chemiluminescent immunoassay, served as a marker of iron stores. Statistical analyses included t-tests and ANOVA to compare ferritin levels across donation types and demographics, with a significance threshold of $p < 0.05$.

RESULTS: Platelet donors showed consistently lower mean ferritin levels than whole blood donors, with significant differences observed in males and older female donors across most age groups. This trend suggests cumulative iron depletion in platelet donors due to frequent donation, with marked sex and age-based variations in iron reserves.

DISCUSSION: This study highlights that platelet donors are at a considerable risk of iron depletion, with lower ferritin levels observed across most age and sex categories compared to whole blood donors. Despite the known risks associated with frequent apheresis, interventions have primarily focused on whole blood donors, leaving platelet donors without targeted strategies to mitigate iron deficiency. Our findings underscore the need for targeted interventions for platelet donors.

KEYWORDS: Blood donation; apheresis platelets; ferritin; iron deficiency; donor health

INTRODUCTION

Iron is an essential mineral that plays a critical role in numerous physiological processes, including oxygen transport, energy production, and the maintenance of immune function.[1] It is a key component of hemoglobin, the protein in red blood cells responsible for carrying oxygen from the lungs to the rest of the body.[2] Given its pivotal role in maintaining health, adequate iron levels are crucial for overall well-being. However, iron deficiency remains a prevalent concern, particularly among individuals who donate blood regularly.[3] The process of blood donation, whether through whole blood or apheresis, can exacerbate the risk of iron deficiency, leading to a range of health issues that can affect both the donor and the quality of blood products collected.[4,5]

Iron deficiency is a common nutritional disorder worldwide, with significant implications for public health.[6] The loss of iron during blood donation is an important factor contributing to this deficiency. Each time a donor gives blood, a substantial amount of iron is removed from the body. In whole blood donation, approximately 200–250 mg of iron is lost, primarily due to the removal of red blood cells, which contain hemoglobin.[7] Given that the body's iron stores are limited, frequent donations can lead to a gradual depletion of these stores, increasing the risk of iron deficiency.[8]

The consequences of iron deficiency extend beyond simple fatigue or weakness. Insufficient iron levels can impair cognitive function, leading to memory loss and difficulty concentrating. Iron deficiency is also associated with disrupted hair growth, restless leg syndrome, unusual cravings for non-nutritive substances (a condition known as pica), and immune system dysfunction, which can make individuals more susceptible to infections.[9,10] In the context of blood donation, these effects can be particularly concerning, as they may not only compromise the donor's health but also reduce the quality of the blood products collected.[11,12]

Apheresis donation, a process in which specific blood components such as platelets or plasma are collected while the remaining components are returned to the donor, also poses a risk of iron deficiency.[13] While the immediate loss of iron during apheresis is generally lower than in whole blood donation, frequent apheresis can still lead to significant iron depletion over time.[14] This is because apheresis donors often donate more frequently than whole blood donors, sometimes as often as twice a week. Over time, this can result in a gradual decline in iron stores, particularly if the donor's diet does not adequately compensate for the loss.[15]

Moreover, iron deficiency can have specific implications for the quality of blood products collected through

apheresis.[12,16] Platelets, one of the primary components collected during apheresis, play a crucial role in blood clotting and wound healing. Iron deficiency can impair platelet production and function, potentially reducing the therapeutic efficacy of the platelet products collected.[17] This is particularly concerning in apheresis, where the goal is to collect high-quality platelets for transfusion into patients with conditions such as thrombocytopenia or during chemotherapy.

The impact of iron deficiency in blood donors has led to increased awareness and efforts to mitigate its effects.[18] Monitoring ferritin levels, a marker of iron stores, is one approach used to assess the risk of iron deficiency in donors. Studies comparing ferritin levels among different types of blood donors have shown that frequent whole blood donors and apheresis donors are at the highest risk of developing iron deficiency.[15] To address this, some blood donation organizations have implemented measures such as iron supplementation programs and extended donation intervals to help maintain healthy iron levels in donors.[19,20]

MATERIALS AND METHODS

Study Design and Population

This retrospective cross-sectional study was conducted using data from 31,661 blood donors who donated between 2018 and 2021. Donors included in the study had donated whole blood (n=26,129) or platelets via apheresis (n=5,532), at least once during the study period. Donors who had incomplete records or pre-existing health conditions that could affect iron metabolism (hemochromatosis) were excluded from the analysis.

Sample Collection and Preparation

Blood samples were collected prior to donation using standard venipuncture procedures. The whole blood or platelet collection kit is used and there is a sample pouch that the blood is diverted into, and the samples are collected from there. These samples were processed and tested within 48 hours to ensure sample integrity. All samples were handled under strict quality control protocols, with regular participation in external proficiency testing programs to maintain assay accuracy.

Data Collection

Data were collected from a centralized blood donation database, including donor demographic information (age, sex, and ethnicity), donation type and laboratory results. Donors were divided into four age groups: 16–21 years (n=1600), 22–30 years (n=6387), 31–45 years (n=12015), and 46+ years (n=11659). This stratification allowed for analysis of ferritin levels across different life stages and helped identify age-related trends in iron depletion.

Ferritin levels in blood donors were measured using the Beckman Coulter AU Analyzer platform, a high-throughput clinical chemistry system. This assay was performed at one of Creative Testing Solutions' (CTS) accredited laboratories. The ferritin assay employed is a chemiluminescent immunoassay (CLIA), which quantitatively measures serum ferritin concentrations as an indicator of iron stores. The measurable ferritin range in this assay was between 1 and 451 ng/mL, which provides a broad reportable range to capture both severely depleted and high ferritin levels.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics (Version 27) to assess differences in ferritin levels between the donor groups. The primary variable of interest was ferritin concentration, while demographic factors were considered secondary variables. The normality of the data was evaluated using the Shapiro-Wilk test, and ferritin levels were found to follow a non-normal distribution. Therefore, non-parametric tests were used where applicable.

Descriptive Analysis: Descriptive statistics (mean, standard deviation, and median) were computed for ferritin levels, stratified by donation type, sex, and age group.

T-Tests and ANOVA: Independent sample t-tests were employed to compare ferritin levels between two donor groups, while one-way ANOVA was used for multi-group comparisons (e.g., donation type, age group, sex). Welch's t-test was conducted for multiple pairwise comparisons.

Significance Thresholds: A p-value of less than 0.05 was considered statistically significant for all comparisons.

RESULTS

Approximately 51% of the donors were male and 49% were female with mean ferritin values of 111.62 ng/mL and 53.78 ng/mL [**Table 1** and **Table 2**]. The donation frequency differed between the two groups: whole blood donors averaged 1.36 donations per year, whereas platelet donors donated more frequently, with an average of 3.33 times per year. Whole blood donors were overwhelmingly single-time donors (73.9%), whereas platelet donors demonstrated a higher donation frequency – with only 44.9% donating once and 25.5% donating two to three times over the same period as summarized in **Table 3**. The average serum ferritin concentrations for whole blood and Platelet donors, stratified by annual donation frequency, are summarized in **Table 4**. Among one-time donors, mean ferritin levels were virtually identical between whole blood and platelet donors (102.13 ng/mL vs. 103.58 ng/mL, respectively). As donation frequency increased to 2–3 donations per year, whole blood donors exhibited a marked decline in ferritin (66.44 ng/mL), whereas platelet donors showed a more moderate decrease (83.03 ng/mL). In the 4–6 donations category, whole blood donor ferritin fell further to 53.64 ng/mL, while platelet donor ferritin remained comparatively elevated at 83.19 ng/mL. For higher frequency brackets, however, platelet donor ferritin continued to decline, averaging 63.57 ng/mL in the 7–12 group and 53.96 ng/mL in the 12–24 group.

Table 1. Distribution of the Donor Population by Age, Sex, and Donation Type

Age Group	Female (%)	Male (%)	Male and Female (%)
Whole Blood (WB)			
16–21	2.6	2.0	4.6
22–30	13.2	8.1	21.4
31–45	21.6	18.1	39.6
46+	17.0	17.4	34.3
All Ages	54.4	45.6	100.0
Platelets (PLT)			
16–21	0.3	0.3	0.6
22–30	4.8	7.5	12.2
31–45	8.9	21.5	30.4
46+	10.3	46.4	56.8
All Ages	24.3	75.7	100.0
All Donors (WB & PLT)			
16–21	2.2	1.7	3.9
22–30	11.7	8.0	19.7
31–45	19.3	18.7	38.0
46+	15.8	22.5	38.3
All Ages	49.1	50.9	100.0

Table 2. Mean Ferritin (ng/mL) Values Across Age and Sex

Age and Sex	Whole Blood Donation	Platelet Donation	All Donors (WB & PLT)
Male			
16–21	93.82	120.74	94.50
22–30	124.18	63.97	114.48
31–45	133.63	89.17	124.54
46+	117.63	73.89	101.64
All Ages	123.66	77.55	111.78
Female			
16-21	37.84	51.16	38.23
22-30	46.83	43.35	46.57
31-45	48.78	45.88	48.53
46+	70.22	58.54	68.84
All Ages	54.09	50.67	53.78
Male and Female, All Ages	85.87	70.80	83.24

Table 3. Annual Donation Frequency by Donation Type

Donation Count Range	Whole Blood (%)	Platelet (%)
1	73.93	44.90
2–3	20.35	25.49
4–6	4.97	13.14
7–12	0.00	9.02
12–24	0.00	7.45

Table 4. Average Ferritin by Donation Frequency

Frequency Category	Whole Blood (WB) Avg Ferritin (ng/mL)	Platelet Avg Ferritin (ng/mL)
1	102.13	103.58
2–3	66.44	83.03
4–6	53.64	83.19
7–12	N/A	63.57
12–24	N/A	53.96

Comparison of Ferritin Levels Between Whole Blood and Platelet Apheresis Donors

The comparative analysis of ferritin levels between whole blood and platelet apheresis donors demonstrated significant disparities, with platelet donors showing notably lower mean ferritin concentrations across most age and sex categories. Donors were categorized into four age groups: 16–21, 22–30, 31–45, and 46+ years. Platelet donors exhibited consistent patterns of iron depletion across these groups, with significantly lower mean ferritin levels than whole blood donors in all age groups except 16–21 years ($p = 0.11$). In this age group, although mean ferritin concentrations in platelet donors were higher than those in whole blood donors, the difference was not statistically significant [**Figure1**].

Figure 1. Comparison of mean ferritin levels between whole blood donors and platelet apheresis donors across different age groups. Platelet donors exhibited significantly lower ferritin levels in all age groups except for the 16–21-year-old category.

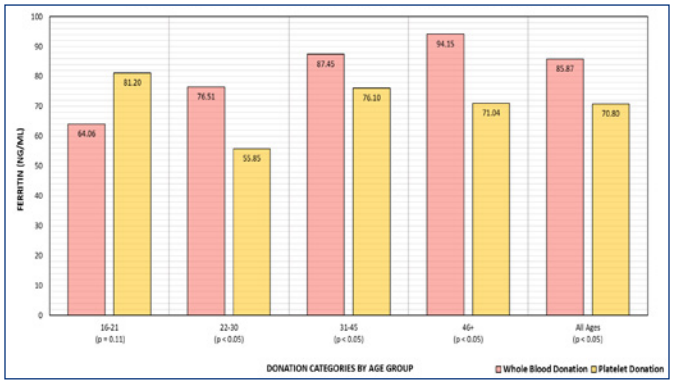
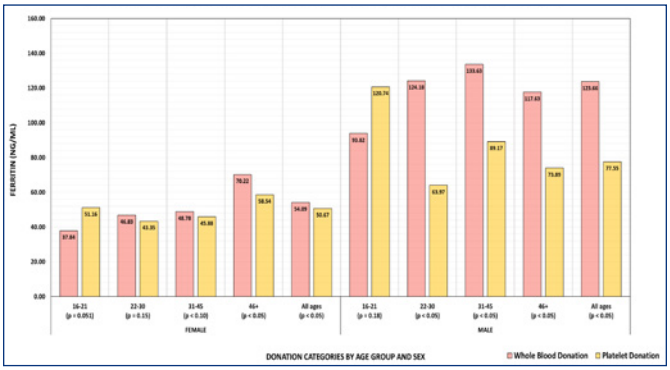


Figure 2. Age- and sex-stratified analysis of ferritin levels in male and female donors. Male platelet donors demonstrated significantly lower ferritin levels than male whole blood donors, while the effect in female donors was more pronounced in older age groups.



Age and Sex-Based Ferritin Level Comparisons in Male Donors

Male platelet donors consistently exhibited lower ferritin levels compared to their whole blood counterparts across most age groups. Specifically, in the 22–30, 31–45, and 46+ age groups, the differences were statistically significant ($p < 0.05$), with mean ferritin concentrations of 63.94, 89.17, and 73.89 ng/mL for platelet donors compared to 124.18, 133.63, and 117.63 ng/mL for whole blood donors, respectively. For the youngest age group (16–21), mean ferritin levels for platelet donors were higher than for whole blood donors (120.74 ng/mL vs 93.82, $p = 0.18$), though not significant. The mean ferritin concentration for male platelet donors across all ages was significantly lower than that for male whole blood donors (77.55 vs. 123.66 ng/mL, $p < 0.05$) [**Figure 2**].

Age and Sex-Based Ferritin Level Comparisons in Female Donors

Female platelet donors generally exhibited lower ferritin levels than female whole blood donors, though most age group comparisons were not statistically significant. Across all age groups, the mean ferritin level for female platelet donors was 50.67 ng/mL, significantly lower than the 54.09 ng/mL observed in female whole blood donors ($p < 0.05$). In the youngest group (16–21 years), female platelet donors had a higher mean ferritin level (51.16 ng/mL) than whole blood donors (37.84 ng/mL), though this difference was not statistically significant ($p = 0.051$). For the 22–30 age group, female platelet donors showed lower mean ferritin levels (43.35 ng/mL) compared to whole blood donors (46.83 ng/mL), but this difference was also not statistically significant ($p = 0.15$). In the 31–45 age group, mean ferritin levels were 45.88 ng/mL for platelet donors versus 48.78 ng/mL for whole blood donors, with the difference remaining statistically insignificant ($p = 0.10$). Only in the 46+ age group, female platelet donors showed significantly lower ferritin levels (58.54 ng/mL) compared to their whole blood counterparts (70.22 ng/mL, $p < 0.05$) [**Figure 2**].

Overall Comparison Across All Ages and Sex

In summary, across all age groups and sexes, mean ferritin levels in platelet donors were significantly lower than in whole blood donors ($p < 0.05$), indicating a higher prevalence of iron depletion among platelet apheresis donors.

DISCUSSION

Iron deficiency remains a critical issue in blood donation, particularly for frequent donors, due to the gradual depletion of iron stores, which can lead to adverse health effects.[21] The present study evaluates ferritin levels in 31,773 donors, encompassing whole blood and platelet apheresis, with the aim of identifying which groups are at highest risk for iron deficiency. Ferritin is a key biomarker used to assess iron stores in the body, and its levels are vital in maintaining donor health and ensuring the quality of blood products.[22] The findings of this study indicate a significantly lower ferritin concentration in platelet apheresis donors compared to whole blood donors, with marked differences seen across age and sex categories. This difference highlights the unique impact of apheresis on iron stores and raises questions about the long-term health implications for these donors. The discussion explores these disparities in relation to previous studies, evaluates the physiological basis for iron depletion in platelet donors, considers the implications for donor health and blood product quality, and proposes possible interventions for mitigating iron deficiency risk among frequent platelet apheresis donors.

The current study's findings align with earlier research showing that apheresis donors are particularly susceptible to iron depletion despite the generally lower immediate iron loss compared to whole blood donation.[23] The mechanism behind this phenomenon, although multifactorial, appears to be related to the frequency of donations rather than the volume of iron lost per session. In apheresis donation, only desired components are removed, and red blood cells (RBCs) are returned to the donor. While this process theoretically preserves hemoglobin and iron levels in the short term, the more frequent donation intervals allowed for apheresis donors (up to twice a week) lead to cumulative iron loss over time. Frequent platelet donations, potentially compounded by lower dietary compensation, can progressively reduce ferritin levels, resulting in chronic iron depletion.

In addition to cumulative iron loss from frequent donations, other mechanisms may contribute to the observed ferritin depletion among blood donors. Gene regulation may play a role, with possible differences in genetic control mechanisms influencing iron absorption rates, particularly when whole blood donors lose iron more quickly than platelet donors.[24] Additionally, the direct removal of ferritin

from the bloodstream during apheresis could contribute to lower ferritin levels in platelet donors, as this process may inadvertently deplete iron stores despite the return of red blood cells. The findings underscore this cumulative effect, with apheresis donors displaying consistently lower ferritin across most age groups and sex, particularly evident in males and older female donors.

While both whole blood and platelet donors experience progressively lower ferritin levels with increasing donation frequency [**Table 4**], the impact is especially marked among platelet donors because a substantial number of these donors give seven or more times per year. Their high-frequency donations disproportionately draw down platelet donor's average ferritin. Thus, although each apheresis session removes less iron than a whole blood donation, the sheer volume of repeated platelet donations drives a significant cumulative decline in iron stores, pulling the overall mean ferritin for platelet donors lower.

The analysis of sex-based differences reveals that male platelet donors show more pronounced iron depletion than their female counterparts, as evidenced by the significantly lower mean ferritin concentrations across most age groups. This discrepancy may relate to the generally higher baseline iron requirements in males due to muscle mass and higher circulating blood volume, factors that increase iron demands.

Age-related trends further emphasize the effect of donation frequency, as older age groups displayed more significant ferritin depletion in both male and female platelet donors. This trend may reflect the cumulative impact of repeated donations over time, compounded by the natural decline in ferritin levels with age. Older adults may also have dietary insufficiencies or reduced gastrointestinal absorption, potentially exacerbating iron deficiency risk.[25,26] These age-related effects are crucial to consider when developing interventions, as tailored strategies might be necessary to address the specific needs of older donors.

Iron deficiency in blood donors can lead to adverse health outcomes, which, as previous studies have shown, include fatigue, cognitive impairments, compromised immune function, and increased susceptibility to infections.[21] In donors, these symptoms could decrease the likelihood of continued donation, thereby impacting the overall blood supply. Given that platelet donors are often among the most frequent donors, managing their health is essential to sustaining the platelet supply chain. Furthermore, suboptimal iron levels in donors may have implications for the quality of the platelet products collected. Iron deficiency can impair thrombopoiesis, leading to potentially compromised platelet function and decreased therapeutic efficacy.[5] While this study did not directly assess platelet quality, the association between ferritin levels and platelet functionality warrants further investigation.

The results underscore the need for targeted measures to mitigate iron deficiency risk in apheresis donors especially for frequent donors. Routine ferritin level monitoring prior to donations could help identify donors at risk for iron depletion, enabling blood centers to proactively adjust donation frequency or defer donations as needed. Setting ferritin thresholds could act as a safeguard, ensuring donors do not dip below a level that risks health complications. Specifically, low-dose, over-the-counter iron supplements can effectively raise ferritin levels, though adherence and potential side effects must be managed. Adjusting the permissible frequency of platelet apheresis donations could help mitigate the cumulative iron loss observed in this study. While less frequent donations may temporarily impact blood product availability, the potential long-term health benefits for donors could support sustainable donation practices. Educating platelet donors on iron-rich diets and the importance of adequate iron intake could help improve dietary compensation for iron loss. Providing resources on iron-rich foods or dietary counseling services could encourage better dietary habits, particularly for high-frequency donors.

The heavy focus on iron loss in whole blood donation may also leave platelet donors overlooked regarding iron deficiency management, as interventions such as iron supplementation and donation interval adjustments are often implemented primarily for whole blood donors. This emphasis may inadvertently overlook the unique needs of frequent apheresis donors, who are also at substantial risk of iron deficiency and would benefit from similar protective measures.

Further research is needed to explore the direct impact of iron deficiency on the quality of platelet products and the physiological mechanisms underlying the observed differences between donor groups. Future studies could assess functional outcomes, such as donor fatigue levels, mental focus, and physical endurance, to capture the broader implications of iron depletion. Additionally, randomized controlled trials examining the efficacy of iron supplementation, interval extension, and dietary interventions for apheresis donors would provide valuable insights into practical solutions. Finally, exploring genetic factors or biomarkers that predispose certain donors to iron deficiency could enable personalized donor care.

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