Predonation Iron and Hematological Status of Whole Blood Donors in Lagos, Nigeria: Impact on Blood Supply

Olufemi A. Oyedeji, Obiefuna I Ajie[1], Sarah O. John-Olabode, Gbenga Olorunfemi[2]

Departments of Haematology and Blood Transfusion and [1]Chemical Pathology, College of Medicine, University of Lagos, Lagos, Nigeria, [2]Division of Epidemiology and Biostatistics, School of Public Health, University of Witwatersrand, Johannesburg, South Africa

Abstract

Context: Regular blood donations can engender iron depletion and its complications; reducing the prevalence of iron depletion among blood donors is a key strategy for optimizing donors' health. However, the factors impacting on iron deficiency among blood donors are not yet well characterized in our environment. **Aim:** The aim of this study is to determine predonation iron status and hematological profile among blood donors. **Settings and Design:** We conducted a comparative cross-sectional study of eligible blood donors at Lagos University Teaching Hospital. Consenting participants were consecutively recruited. **Materials and Methods:** Sociodemographic data were collected using an interviewer-administered questionnaire. Blood samples for estimation of ferritin, serum iron, total iron-binding capacity, and complete blood count were collected. **Statistical Analysis Used:** Statistical analysis was conducted using Stata version 14 software. **Results:** About three-fourths of the participants (n = 234, 74.8%) were first-time donors and one-fourth (n = 79, 25.2%) were frequent donors. Overall, 16 (5.1%) of the blood donors had depleted iron stores. There was a significant difference in the prevalence of iron depletion between first-time and regular donors ($P < 0.01$). Multivariable analysis showed that the odds of iron deficiency decreased by 58% for every g/dl increase in hemoglobin levels (odds ratio = 0.42, 95% confidence interval: 0.24–0.73, $P = 0.002$). Smokers had about 14-fold odds of having iron deficiency as compared to nonsmokers. **Conclusion:** Although current donation strategies to mitigate donation-related iron loss have resulted in a significant decline in the prevalence of iron deficiency in frequent blood donors, we are still a long way from keeping our iron-replete blood donors.

Keywords: Ferritin, iron depletion, predonation hemoglobin

Introduction

Reducing the prevalence of iron depletion among blood donors is integral to optimizing donors' health. This is instrumental to maintain the national blood supply, especially in Nigeria where the prevalence of iron deficiency among adults is 10%–40%.[1] The current status and factors impacting on iron deficiency and other hematological parameters among typical cohort of blood donors are not yet well characterized in our environment. Thus, this study aimed to determine predonor hemoglobin (HB) concentration and iron status among blood donors in a tertiary hospital, to provide evidence for assessing the effectiveness of current strategies mitigating iron depletion among blood donors.

Materials and Methods

We conducted a comparative cross-sectional study of 350 eligible blood donors (with HB concentration >12.5 g/dl by copper sulfate test) at the blood donor clinic of Lagos University Teaching Hospital (LUTH), between January and May 2018. Consenting participants were consecutively recruited immediately before donating a unit of whole blood. The study protocol was reviewed and approved by the Human and Ethics Committee of LUTH (NHREC: 19/12/2008a). All procedures followed were in accordance with the Helsinki Declaration of 1975.

Inclusion criteria

Voluntary blood donors and replacement donors of both sexes who have previously completed the national medical

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Address for correspondence: Dr. Sarah O. John-Olabode, Department of Haematology and Blood Transfusion, College of Medicine, University of Lagos, Lagos State, Nigeria.
E-mail: sarahajibola@yahoo.com

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questionnaire and have been found eligible according to the selection criteria for blood donation were included in the study.

Exclusion criteria

Commercial blood donors, regular blood donors, and first-time donors who do not meet the criteria for blood donation were excluded from the study population.

Two groups of participants were recruited. The first group was eligible first-time donors (n = 234), while the second group was eligible frequent or regular donors who have had two or more whole blood donations in the preceding 12 months, with an average donation interval of 12 weeks.[2]

Sociodemographic history, coupled with blood donation history, smoking habits, and use of iron supplements were elicited through a self-administered questionnaire. Serum sample for estimation of ferritin, serum iron, total iron-binding capacity (TIBC), and whole blood for estimation of complete blood count (CBC) was collected from the participants. CBC was done on CELL-DYN Emerald cell counter (Abbott Laboratories, Abbott Park, IL, USA). Serum ferritin was estimated by automated chemiluminescence immunoassay method, and serum iron and unsaturated iron-binding capacity (UIBC) were estimated by direct colorimetric determination (Abbott Laboratories, Abbott Park, IL, USA) all performed on the Abbott Architect ci4100 Architect ferritin (07K59-25), iron (6K95-30), transferrin (306746/R05), and UIBC (07056-21) reagents. The sum of serum iron and UIBC represents TIBC while transferrin saturation (Tf) was calculated from serum iron and TIBC values using the formula:

Tf = Serum iron (μmol/L)/TIBC (μmol/L) × 100

Statistical analysis

Statistical analysis was conducted using StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. Descriptive statistics were conducted, and categorical variables were expressed as frequencies and percentages while normally distributed continuous variables were presented as mean (standard deviation). Nonnormally distributed continuous variables were presented as median (interquartile range).

In this study, depletion of iron stores and anemia are defined as below:[3]

- Iron depletion – serum ferritin <20 ng/l with normal transferrin saturation and HB level[3]
- Anemia – HB <12.5 g/dl with normal serum ferritin and transferrin saturation.[3]

Pearson's Chi-square test was used to find an association between categorical sociodemographic variables and the stages of iron deficiency, on the one hand, and the relationship between categorical variables and frequency of blood donations.

Analysis of variance (and Bonferroni *post hoc* test) or Kruskal–Wallis test was used to check the differences in mean or median of continuous variables and the stages of iron-deficiency anemia. Student's independent t-test or Mann–Whitney U-test was used to evaluate the differences among first-time donors and multiple blood donors. Univariable and multivariable binary logistic regression analysis, using backward stepwise regression, was used to evaluate the association of the frequency of donation and iron deficiency (iron deficiency defined as ferritin <20 ng/ml). Two-tailed test of hypothesis was assumed, and $P < 0.05$ was considered statistically significant.

Results

Three hundred and fifty blood donors participated in the study, of these only 313 samples were analyzed as some samples could not be analyzed due to preanalytical deficiencies or incomplete questionnaire response.

Of the 313 blood donors, 285 (90.9%) were male and 28 (9.2%) were female. About three-quarters of the participants (n = 234, 74.8%) were first-time donors and one-quarter (n = 79, 25.2%) were frequent donors. There was no significant difference in the average age of first-time donors and frequent donors (32.3 ± 9.4 vs. 31.6 ± 9.1 years, $P = 0.54$) [Table 1].

The mean predonation hemoglobin (PDH) concentration was significantly lower in female donors compared to male donors (14.29 ± 1.05 vs. 12.74 ± 1.39 g/dl, $P < 0.001$). Similarly, the first-time donors had lower mean PDH levels (14.1 ± 1.2 g/dl) as compared to regular donors (14.5 ± 1.2 g/dl) ($P = 0.01$) [Table 2].

Some donors who were determined to be eligible to donate using copper sulfate for PDH measurement were subsequently found to have reduced PDH level (HB <12.5 g/dl) using the automated cell counter. Overall, 18 (5.8%) blood donors had PDH <12.5 g/dl [Table 3]. Of the 18 blood donors with PDH <12.5 g/dl using automated cell counter, 12 (66.7%) were female and 6 (33.3%) were male. Over two-third (n = 16/18, 83.3%) were first-time donors while 16.7% (3/18) were frequent donors; there was no significant difference between the mean ferritin level in these anemic first-time donors compared to regular donors (87.6 ± 23.9 vs. 46.4 ± 31.4 ng/l, $P = 0.4$). Nearly all (94.4%) of these blood donors found to be anemic using automated cell counter were not on any iron supplement.

Table 1 summarizes the characteristics of the participants. As presented in Table 2, all iron status indicators were significantly lower in regular donors in comparison with first-time donors.

Overall, 16 (5.1%) of the blood donors had depleted iron stores. There was a significant difference in the prevalence of iron depletion between first-time and regular donors ($P < 0.01$) [Table 3].

From the multivariable regression analysis, there was about 5-fold odds of iron deficiency (serum ferritin <20 ng/ml) among frequent donors as compared to first-time donors (odds ratio [OR] = 5.3, 95% confidence interval [CI]: 1.12–25.39, $P = 0.035$). Further multivariable analysis showed that the odds

Table 1: Comparison of sociodemographic characteristics in first-time and frequent donors

Characteristics	Donor type		Total	*P*
	First-time donors (*n*=234)	Frequent donors (*n*=79)		
Age (mean±SD)	32.3±9.4	31.6±9.1	32.1±9.3	0.5417
18-24	70 (29.9)	17 (21.5)	87 (27.8)	0.180
25-34	75 (32.1)	40 (50.6)	115 (36.7)	
35-44	52 (22.2)	16 (20.3)	68 (21.7)	
≥45	37 (15.8)	6 (7.6)	43 (13.7)	
Gender				
Male	208 (88.9)	77 (97.5)	285 (91.1)	
Female	26 (11.1)	2 (2.5)	28 (8.9)	
Marital status				
Single	102 (43.6)	26 (32.9)	128 (40.9)	
Married	132 (56.4)	53 (67.10)	185 (59.1)	
Use of iron supplements				
Yes	47 (20.1)	6 (7.6)	53 (16.9)	0.027
No	187 (79.9)	73 (92.4)	260 (83.1)	
Cigarette smoking				
Smoker	32 (13.7)	4 (5.1)	36 (11.5)	0.038
Nonsmoker	202 (86.3)	75 (94.9)	277 (88.5)	
Alcohol use				
Yes	120 (51.3)	18 (22.8)	138 (44.1)	<0.001
No	114 (48.7)	61 (77.2)	175 (55.9)	

Table 2: Comparison of hematologic and iron profile among first-time and frequent donors

	First-time donors	Frequent donors	Total	*P*
White cell count ($\times10^9$/L)	4.5±1.4	5.0±1.2	4.6±1.4	0.0071
Hb (g/dl)	14.1±1.2	14.5±1.2	14.2±1.2	0.0101
MCV (fl)	105.4±52.2	86.8±35.9	100.7±49.2	0.0037
RBC ($\times10^{12}$/L)	4.6±0.6	5.1±0.5	4.7±0.6	<0.0001
MCH (pg)	31.0±2.8	28.3±2.5	30.3±3.0	<0.0001
MCHC (g/l)	34.2±1.2	33.5±0.7	34.0±1.1	<0.0001
Platelet ($\times10^9$/L)	192.9±68.1	251.1±73.4	207.6±73.8	<0.0001
Iron (µmol/l)	14.6±5.3	13.1±4.7	14.2±5.2	0.0289
UIBC (µmol/l)	35.1±11.1	40.9±10.6	36.5±11.3	0.0001
TIBC (µmol/l)	49.7±10.4	54.0±9.3	50.7±10.3	0.0012
Transferrin (mg/dl)	197.8±41.3	210.6±44.0	201.0±42.3	0.0192
TS (%)	30.2±11.2	25.0±9.5	28.9±11.0	0.0002
Ferritin (ng/ml), median (IQR)	107.7 (65.6-195.1)	77.9 (46.7-41.5)	102.7 (62.4-82.0)	0.0176

TIBC: Total iron-binding capacity, Hb: Hemoglobin, RBC: Red blood cell, MCV: Mean cell volume, MCHC: Mean cell hemoglobin concentration, UIBC: Unsaturated iron-binding capacity, TS: Transferrin saturation. IQR: Interquartile range, MCH: Mean corpuscular hemoglobin

of iron deficiency decreased by 58% for every g/dl increase in HB levels (OR = 0.42, 95% CI: 0.24–0.73, *P* = 0.002). Smokers had about 14-fold odds of having iron deficiency as compared to nonsmokers [Table 4]. Furthermore, blood donors older than 30 years were 81% less likely to have iron deficiency as compared to blood donors younger than 30 years. Nonetheless, gender and educational qualification did not statistically impact the odds of having iron deficiency; postestimation test showed that the *P* value of the goodness-of-fit test was 1.00 and area under receiver operator characteristic curve = 0.8969.

Discussion

This study was conducted to add to evidence on the prevalence and pattern of iron store among a typical cohort of blood donors in Lagos, Nigeria. Consistent with previous studies, our study shows isolated iron depletion (serum ferritin <20 ng/ml) was more frequent among nondeferred regular blood donors compared with nondeferred first-time donors. As observed, 11.4% of regular donors and 2.9% of first-time donors had isolated iron store depletion despite meeting the HB criteria for donation. This finding is similar to other studies in blood donors done in various regions of the country. Jeremiah and Koate[4] obtained isolated iron deficiency in 20.6% of regular donors in their cohort of 348 whole blood donors in Port Harcourt, Southeast, Nigeria. Similarly, Okpokam *et al.*[5] reported the prevalence of

Table 3: Prevalence of iron depletion and anemia between first-time and regular donors

Iron-deficiency status	First-time donors (%)	Regular donors (%)	Total (%)	*P*
Iron depleted (ferritin <20 ng/l)	7 (2.99)	9 (11.4)	16 (5.1)	0.010
Noniron depleted (ferritin >20 ng/l)	227 (97)	70 (88.6)	297 (94.9)	
Anemia status				
Anemic (Hb <12.5 g/dl)	15 (6.4)	3 (3.8)	18 (5.8)	0.01
Nonanemic (Hb >12.5 g/dl)	219 (93.6)	76 (96.2)	295 (94.2)	

Hb: Hemoglobin

Table 4: Logistic regression of the relationship between iron depletion and donor type

Factor	Univariable			Multivariable[c]		
	OR	95% CI	*P*	Adjusted OR	95% CI	*P*
Donor type						
First-time donor	1.00	Reference	Reference	1.00	Reference	Reference
Regular donor	4.73	1.30-17.24	0.019	5.34	1.12-25.39	0.035
Age (years)						
<30	1.00	Reference	Reference	1.00	Reference	Reference
≥30	0.23	0.05-1.12	0.069	0.19	0.04-0.85	0.029
Gender						
Male	1.00	Reference	Reference	1.00	Reference	Reference
Female	1.11	0.13-9.10	0.925	0.32	0.02-5.13	0.424
Alcohol use						
No	1.00	Reference	Reference	1.00	Reference	Reference
Yes	0.13	0.02-1.07	0.058	0.05	0.01-0.21	<0.001
Hb	0.55	0.35-0.87	0.011	0.42	0.24-0.73	0.002

[c]Multivariable model was adjusted for Hb, smoking, alcohol intake, age, and gender. Hb: Hemoglobin, OR: Odd ratio, CI: Confidence interval

iron deficiency at 31.6% among regular donors in the same region. The lower prevalence in this study could be reflective of various reasons which include the lack of standardized iron-deficiency mitigation policy in the country. Currently, some blood donation centers practice iron supplementation while some do not. Another possible reason for the low prevalence observed is the use of self-administered iron supplements, especially in urban centers (where there is a high level of awareness of complications of iron-deficiency anemia) for nontransfusion-related reasons.

Similar to findings in developed countries,[6,7] this study show that markers of iron-related disorder such as serum iron, transferrin TIBC, transferrin saturation, and hematological parameters in repeat donors are significantly lower than in first-time donors. This difference between first-time and frequent donors became more pronounced in our study because only 7.6% of the regular donors in our cohort were on iron supplementation. This implies that without the effective implementation of iron supplementation program, these donors with iron-depleted stores will continue to donate till they develop iron-deficiency anemia. The high prevalence (18%) of iron supplementation seen among first-time donors is encouraging as it indicates that an effective iron replacement program can be acceptable to blood donors.

In agreement with the findings of Salvin *et al*. and Tan and Alcantara, a higher proportion of female donors compared to male donors donating for the first time had low HB concentration on automated count.[8,9] As observed from our data, more than two-thirds of donors with anemia (HB <12.5 g/dl) were female. These donors considered eligible using finger-stick capillary HB measurement were found to have HB concentration lower than the HB cutoff recommended for blood donation using automated count; this shows that for the particular group of donors known to be at a higher risk of developing iron deficiency, i.e., women and adolescents, automated HB measurement will be beneficial for early identification of anemia. Worthy of note in our study is the high mean HB concentration seen in regular donors compared to first-time donors. The reason for this is unknown; we postulate that this could be due to the stimulating effect of frequent donation on the bone marrow.

To the best of our knowledge, this study is the first study in Nigeria to look at independent predictors of developing iron deficiency in blood donors. Based on univariate and multivariate analysis, our data show that blood donors who smoke had about 14-fold higher odds of having iron depletion as compared to nonsmokers. This finding has been previously reported in 138 "super donors," by Mast *et al*. who reported a negative association between smoking and ferritin level in blood donors in a univariable analysis.[10] Milman and Kirchhoff reported a similar finding in their multivariable model in middle-aged Danes where smoking was associated with reduced ferritin values in male smokers.[11] In contrast, other studies done in

blood donors using multivariable models such as the Retrovirus Epidemiology Donor Study-II Donor Iron Status Evaluation study[4] reported a positive association between smoking and higher ferritin levels in blood donors. The potential association between smoking and ferritin levels in blood donors needs to be further investigated to determine if certain behavioral factors including alcohol consumption have a direct biological effect on iron status in Nigerian blood donors.

Conclusion

Our study demonstrates that although current donation strategies to mitigate donation-related iron loss such as prolonging interdonation interval, providing donors with information on risks of postdonation iron deficiency in menstruating women, and PDH estimation[2] have resulted in a significant decline in the prevalence of iron deficiency in frequent blood donors, we are still a long way from keeping our iron-replete blood donors.

Potential strategies to mitigate the impacts of donation-related iron loss which includes a coordinated implementation of iron supplementation program to standardize replacement of iron losses with supplemental iron nationwide, targeted automated PDH screening for women, and ferritin measurement in subsets of donors, mainly women and adolescents, are some of our recommendations to assist policy-makers in protecting these valuable blood donors.

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Conflicts of interest

There are no conflicts of interest.

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