Iron deficiency in whole blood donors in a resource-poor setting: a cross-sectional study in Uganda

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Abstract

Background and Objectives: Blood donation is known to result in iron deficiency (ID) in some individuals, with a higher prevalence in females. There is little published data on the frequency of ID among blood donors in resource-poor settings. We determined the prevalence of ID in blood donors in Uganda.

Materials and Methods: We conducted a descriptive cross-sectional study at the Uganda Blood Transfusion Service, Kampala from December 2021 to February 2022. A sample of 500 whole blood donors was enrolled. The evaluation included demographic characteristics, donation history, complete blood count, and serum ferritin. The primary outcome was the proportion of donors with serum ferritin <15µg/L.

Results: The median (IQR) serum ferritin was 25(12– 47) µg/L and 89(52–133)µg/L among female and male donors respectively. Overall, 20.6% (103/500) of blood donors (95% CI, 17.3– 24.4) had iron deficiency (serum ferritin <15µg/L). The prevalence among donating individuals was 11.5% (8.7–14.9), while among low hemoglobin deferrals, 61.5% (50.9–71.1). The prevalence of ID was high among females [33.0% (27.9–38.6)] compared with males [2.5% (1.0–5.8)], but even higher among females younger than 24 years [35.4% (29.2–42.1)]. Factors associated with ID (adjusted odds ratio, 95% CI, and significance) were; female donors (15.81, 5.17,48.28, p <0.001) and a high RDW (6.89, 2.99,15.90, p<0.001).

Conclusion: Iron deficiency is common among blood donors in Uganda, affecting mostly young female donors. Considerations to adopt evidence-based strategies to prevent and manage ID among blood donors–such as serum ferritin monitoring and iron supplementation are highly recommended.

Key words: Iron deficiency, blood donors, serum ferritin

Highlights

Iron deficiency is common among blood donors in Uganda (29.6% in donating individuals, while 80.2% among low hemoglobin deferrals)

Being a female donor, and a diet not considered to be 'iron-rich' were associated with iron deficiency in Uganda.

Uganda should adapt evidence-based strategies to prevent and manage iron deficiency among blood donors–such as serum ferritin monitoring and iron supplementation.

Introduction

Increasing blood supply remains a global priority for improving the efficiency of the healthcare system, whose transfusion services are reliant on the goodwill of blood donors. In low-income nations, maintaining an adequate blood supply still remains a challenge, largely due to low donor rates which have stagnated below the WHO recommended rate of 10 donations per 1000 population [1]. As such, more donations are needed to increase blood supply in those settings. However, regular blood donors are at risk of iron deficiency (ID) –defined by low serum ferritin levels [2], from repeated donations. Untreated, iron deficiency leads to iron deficiency anemia (IDA), which in turn makes the donor ineligible to donate. Beyond IDA, other complications include fatigue, low energy, and depression [2]. There is therefore a need to protect blood donors from such risks. Recent evidence has shown that using iron status to guide donor deferral policies has merit, and protects donors from ID [3,4].

The burden of ID tends to double among females compared with males. In other countries, ID affects about 40% and 18% of females and males respectively [5]. Factors associated with ID in blood donors include among others; age, gender, body weight, number of previous donations, inter-donation interval, and menopausal status [5-8].

There is, however, limited data on the burden of ID in blood donors in resource-poor settings. Moreover, the literature suggests that the profile of blood donors in those settings varies widely from what is seen in high-income countries, with the former being younger [1]. These differences may be explained by the strategy of their blood establishments which tend to target secondary school students for blood collection [9]. It remains unclear, how such a young donor population is affected by ID. However, we know that in Uganda for example, low hemoglobin deferral is the leading cause of donor deferrals (25% of all deferrals) [Unpublished data – *UBTS 2020*]. In the present study, we evaluated the burden of ID among donors in Uganda.

Materials and Methods

Study design and Setting: This was a descriptive cross-sectional study of Ugandan blood donors, conducted within the central region collection sites of the Uganda Blood Transfusion Service (UBTS), from December 2021 through February 2022.

UBTS is a national transfusion service that collects, tests, processes, and distributes blood and blood components throughout Uganda. UBTS operates eight regional blood banks at Nakasero–Kampala city (serving the Central region, including Kampala and the surrounding districts), Gulu, Lira and Arua (Northern region), Mbale and Soroti (Eastern region), Mbarara (Western region), Masaka/Kitovu (greater Masaka region), and Fortportal (South-western region). The Nakasero regional blood bank, based at the UBTS headquarters is also the biggest among the eight, collecting over 1/3 of the total annual national blood collection (about 300,000).

Study participants and eligibility criteria: Voluntary non-remunerated adult blood donors, who came to donate whole blood, at UBTS's collection sites/mobile clinics attached to the Central regional blood bank were recruited. UBTS's hemoglobin thresholds for donation are: ≥12.5 g/dL and ≥13.5 g/dL for women and men respectively. Consenting individuals, aged 18 to 65 years, who met the UBTS's eligibility criteria to donate whole blood were included. We aimed to exclude donors on iron supplementation at the time of donation, but we did not encounter anyone.

Sampling procedure and considerations: Based on the evidence on how disproportionately iron deficiency affects different categories of donors [5], a proportionate sample of donors was used (pre-determined in advance). Sampling was performed with respect to repeat status (repeat to first-time donors ratio of about 3:2), gender (male to female ratio of about 2:3), and included a minimum of 10% of participants with low hemoglobin deferrals. Upon completing the routine UBTS donor screening interview and donor health questionnaire, eligible donors were approached to participate in this study, consented, and enrolled consecutively. For hemoglobin estimation for eligibility to donate, UBTS used a point-of-care device (Hemochromax®, Angelholm, Sweden).

Sample size: The sample size of 500 was estimated based on: level estimates for the proportions of iron deficiency, adjusted for a 5% non-response rate, a 20% risk difference lower in first-time donors when compared to frequent/regular donors (3 times or more). We assumed a 5% level of significance and 90% power to detect the differences between first-time and frequent/regular donors. In total, 496 participants were needed; allocated in the ratios mentioned above.

Study variables and data collection: The following data were documented, using a structured case-report form: donor demographic characteristics (gender, age, occupation, marital status), body weight, donation history (including, whether first-time or repeat, number of lifetime donations, interval since the last donation), medical history, menstrual history, dietary history (vegetarian, and whether they considered their diet to be ‘iron-rich’, based on specific examples we provided such as liver, beef, green-leafy vegetables), etc. We defined the first-time donor as one who never donated before; a regular donor as one who donates frequently –at least twice every year; while ‘repeat but not regular’ donor as one who had ever donated, but not frequently. The inter-donation interval was the time between the current and the most recent donation.

Laboratory measurements: 2mL of blood was collected in an EDTA (purple-top) tube for a complete blood count (CBC), and 2-3mL of blood in a serum separating (yellow-top) tube for serum ferritin. For successful donations, the blood samples were obtained from the diversion pouch, while for low hemoglobin deferrals, a research assistant bled them. Blood specimens from the collection sites were transported daily, in cooler boxes (with ice packs) to Kampala, for testing (performed the same day) at an ISO [South African National Accreditation System (SANAS)] accredited laboratory. Serum ferritin was performed on the Abbott Architect *ci8200* machine using the chemiluminescent microparticle immunoassay method. The CBC tests were performed using the Sysmex automated hematology analyzer (XN-550, Sysmex Corporation, Kobe, Japan); which provided the following parameter; total white cell counts (WBC), hemoglobin (Hb), platelet count (PLT) and red cell indices that denotes iron deficiency (MCV, MCH, and RDW).

Data management and statistical analysis: Data were entered into EPI-DATA version 3.1 software package (The EpiData Association, Odense, Denmark) and analyzed using STATA v14.0 (Stata, College Station, TX, USA). For descriptive statistics, categorical variables are summarised into frequencies while continuous variables into medians (interquartile range) or means (standard deviations). The primary outcome was the proportion of donors with serum ferritin of <15µg/L. We present proportions and their 95% confidence intervals (CI) for each category of donor. Using logistic regression, we examined categorical variables associated with iron deficiency and assessed odds ratios (OR) and statistical significance. 95% test-based CI for odds ratios and p-values are presented. A p-value <0.05 was considered statistically significant.

Ethical Approval: We obtained ethical review from the Research and Ethics Committee of Makerere University School of Medicine (*Ref # 2020-221*), and clearance by the Uganda National Council for Science and Technology (*HS-2160ES*). Written informed consent was obtained from all study participants.

Results

A total of 500 donors were enrolled. **Table 1** shows the baseline characteristics of blood donors. 297 (59.4%) were females. 54.0% of the donors were students, while regular donors constituted only 19.2%. The median (IQR) age was 23 (19–29) years.

The mean (SD) hemoglobin performed at eligibility screening to donate (using the point-of-care device) was 14.3(2.0) g/dL. The median (IQR) serum ferritin in this study popolation was 43(19–86) µg/L, being much lower among female compared with males donors; 25(12– 47) µg/L and 89(52–133)µg/L respectively. Similarly, the median serum ferritin among 'low hemoglobin deferrals' was very low, at 12(8–27) µg/L compared with 51(27–94) µg/L among donors acceptable to donate (**Table 2**).

Primary outcome: Overall, 20.6% (103/500) of blood donors (95% CI, 17.3–24.4) had serum ferritin <15µg/L, and were considered to be iron deficient. The prevalence of iron deficiency among donors with hemoglobin levels acceptable to donate was 11.5% (8.7–14.9), while among 'low hemoglobin deferrals' was 61.5% (50.9–71.1). The prevalence of iron deficiency was higher among females [33.0% (27.9–38.6)] compared to males [2.5% (1.0–5.8)]. The prevalence is even higher among younger females less than 24 years [35.4% (29.2–42.1)]. On the basis of repeat status, the prevalence of iron deficiency was least among regular donors [11.5% (6.4–19.7)], compared with first-time or 'repeat but not regular' donors (**Table 3**).

The iron status of donors categorized by the screening hemoglobin for eligibility to donate is summarised in **Figure 1;** shows that up to 11.5% donating individuals were iron deficient.

Bivariable analysis: The factors that were independently associated with iron deficiency are summarised in **Table 4**. Female donors, younger donors aged 18–24 years, occupation, marital status, not eating an 'iron-rich diet', and the red cell indices that denote iron deficiency (low MCV, low MCH, and a high RDW) were significantly associated with iron deficiency.

Multivariable analysis: All covariates with a p<0.2 at bivariable analysis (gender, age, occupation, marital status, repeat (donation) status, iron-rich diet, MCV, MCH, and RDW) were entered into a logistic regression model. We found that the odds of iron deficiency among females were 15.81 times [95% CI (5.17,48.28)] p<0.001, compared with male donors; while the odds of iron deficiency among donors who regarded their diet to be 'iron-rich' were 1.91 times [95% CI (0.98,3.70), p = 0.056], compared with those whose diet was not 'iron-rich' – although the p-value was at the borderline of statistical significance (**Table 5**).

In addition, having an MCH ≤26pg, and an RDW ≥16% were also significantly associated with iron deficiency.

Discussion

The aim of the current study was to determine the prevalence and factors associated with iron deficiency in blood donors in Uganda. We found that the prevalence of iron deficiency (ID) among individuals with hemoglobin levels acceptable to donate was 11.5%, while 61.5% among individuals deferred for low hemoglobin. ID affected the following donor categories; females (33%) – in particular, young females (35.4%), students (27.4%), young donors (26.1%), as well as first-time donors (25%). Overall, being a female donor and having a high RDW were significantly associated with iron deficiency.

We have found the proportion of Ugandan female donors with ID (33.0%), to be much higher compared with 12.0% among female donors in Australia [10], fairly similar to what has been seen among female donors in France (40%) [5], but lower than findings reported among American female donors (66.1%) [11]. However, it is worthy noting that the thresholds for serum ferritin that investigotors apply to denote iron deficiency vary across studies. For example, whereas we defined ID as serum ferritin <15µg/L– as recommended by the World Health Organization [12], and indeed like the study in Australia [10], the RISE study used <24µg/L [11], while the study among France donors <26µg/L [5]. Under these circumstances, direct comparisions and contrasts become rather complex. Nevertheless, the explanation for these differences remains uncertain, but possibly may be due to differences in iron content in the diet [13]. Another potential explanation may be that our study included sizeable numbers (42%) of first-time donors. However, generally speaking, first-time donors were even more affected (25%) by ID. Indeed, at regression analysis, it was a diet poor in iron, rather than repeat status that we found to be associated with ID, although in the multivariable model, this association was not statistically significant.

Besides gender, the number of donations in any given interval is another factor that has been shown to predict ID in blood donors [14]. However, the current study did not find a significant association with the frequency of donation. Contrary to what other studies have shown [5,7,11], only 11.5% of regular donors were iron deficient. This may partly be due to the small number (19.2%) of regular donors evaluated, or other factors.

In the current study, 54% of donors were students, 27.4% of whom had ID. Over the years, blood establishments in sub-Saharan Africa have struggled to turn students into regular donors to ensure adequate blood supply. The current study has shown that students are at risk of ID. Practical strategies on how we can prevent both ID and IDA in this population of donors in these settings need to be explored.

Globally, hemoglobin-guided donations and gender-specific inter-donation intervals (IDI) are the commonest strategies employed by blood establishments to protect blood donors from ID, and iron deficiency anemia [15]. However, applying hemoglobin thresholds alone is not sufficient to prevent ID, because hemoglobin level does not accurately predict iron status, as shown in the current study where 11.5% of donating individuals were actually iron deficient. Recent evidence has shown that performing ferritin testing and extending the IDI when ferritin is low, and or targeted iron supplementation (for iron-depleted donors) protects donors from ID, improves donor health, and allows donors who were deferred for low hemoglobin levels to return and donate again [3,4, 16,17].

One major strength of our study was the proportionate sampling of donors (stratified by gender, repeat status, and low hemoglobin deferral) since iron deficiency tends to affect different categories of donors disproportionately.

Limitations: The current study was conducted during the post-COVID lockdown period. The preceding interval period of two years was characterized by frequent prolonged lockdowns and travel restrictions that affected donor collections. The effects of these social restrictions can be evidenced by the longer inter-donation intervals (44% >one year, while 46.5% >5months to one year). As a result, the current study may not be able to evaluate the effect of regular donations on ID, in Uganda.

Conclusion: Iron deficiency is common among blood donors in Uganda. The most affected category of blood donors were young females – a finding similar to what has been observed in high-income countries. ID was associated with poor Iron-intake.

Recommendation: The role of serum ferritin measurement in screening ID in blood donors in SSA need to be studied further. Data are needed to identify the best strategies to prevent and manage Iron deficiency among blood donors–such as Iron supplementation.

Conflict of interest: The authors have no competing interests.

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Tables and figures

Table 1. Baseline characteristics of whole blood donors in Uganda (n=500)

Characteristic	**Frequency (%)**
Gender, n=500	
Females	297 (59.4)
Males	203 (40.6)
Age in years, n=500	
18–24	317 (63.4)
25– 51	183 (36.6)
Home district, n=500	
Kampala metropolitan (Kampala, Wakiso,	198 (39.6)
Mukono)	302 (60.4)
Outside of Kampala area	
Age; median (IQR), n=500	23 (19 – 29)
Weight; median (IQR[‡]), n=500	65 (59 – 71)

Hemoglobin, at screening (g/dL); mean (SD*), n=500	14.3 (2.0)
Hemoglobin by CBC (g/dL); mean (SD), n=469	13.7 (2.3)
Total WBC (x10^{12}/L); mean (SD), n=469	5.4 (1.4)
Platelet count (x10^{9}/L); mean (SD), n=469	263.3 (81.3)
Repeat status (n=500)	
First-time donors	212 (42.4)
Repeat donors, but not regular	192 (38.4)
Regular/Frequent donors	96 (19.2)
Inter-donation interval (*repeat & regular donors,*	
n=288)	27 (9.4)
3–4 months	134 (46.5)
5–12 months	127 (44.1)
>12 months	
History of previous deferral (excludes first-time	
donors)	239 (47.8)
No	49 (9.8)
Yes	
Marital status, n=500	
Single	321 (64.2)
Married	163 (32.6)
Separated/Window	16 (3.2)
Highest level of education, n=500	
Primary and lower	47 (9.4)
Secondary	315 (63.0)
University and tertiary	138 (27.6)
Occupation	
Un-employed	11 (2.2)
Employed	219 (43.8)
Student	270 (54.0)
Red cell indices that denote Iron Deficiency	
MCV <80fL (n=471)	114 (24.2)
MCH <26 pg (n=471)	129 (27.4)
RDW >16 % (n=471)	54 (11.5)

‡IQR: interquartile range, *SD: standard deviation

Table 2. Serum ferritin among blood donors in Uganda (n=500)

Category	Median (IQR) Serum ferritin (µg/L)
Overall, (n=500)	43 (19 – 86)
By gender,	
Females (n=297)	25 (12 – 47)
Males (n=203)	89 (52 – 133)
By age	
18 –24 (n=303)	33 (14 – 67)
25– 51(n=197)	67 (29 –110)
By gender, and age combined for females	
Females, aged 18–24 (n=212)	22 (12 – 44.5)
Females, aged 25–51 (n=85)	33 (15 – 61)
By gender, and age combined for males	
Males, aged 18–24 (n=91)	70 (46 –104)
Males, aged 25–51 (n=112)	98 (55.5 –143)
Repeat status	
First-time donors (n=212)	41 (15.5 – 76.5)
Repeat donors, but not regular n=192)	46 (20 – 96.5)
Regular/Frequent donors (n=96)	47 (26.6 – 83)
Low hemoglobin deferral, on current donation	
No (n=409)	51 (27 – 94)
Yes (n=91)	12 (8 – 27)
Occupation	
Un-employed (11)	71 (36 – 86)
Employed (219)	67 (29 – 118)
Student (270)	31.5 (14 – 59)

Table 3. Proportion of blood donors in Uganda with serum ferritin <15µg/L

Category	**N[%] (95% CI) with serum ferritin (<15µg/L)**
Overall, (n=500)	103 [20.6] (17.3– 24.4)
By gender,	
Female (n=297)	98 [33.0] (27.9–38.6)
Male (n=203)	5 [2.5] (1.0–5.8)
By age	
18 –24 (n=303)	79 [26.1] (21.4–31.3)
25– 51(n=197)	24 [12.2] (8.3–17.6)
By gender, and age combined for females	
Female, aged 18–24 (n=212)	75 [35.4] (29.2–42.1)
Female, aged 25–51 (n=85)	23 [27.0] (18.5–37.7)
By gender, and age combined for males	
Male, aged 18–24 (n=91)	4 [4.4] (1.6–11.3)
Male, aged 25–51 (n=112)	1 [0.9] (0.1–6.2)
Repeat status	
First-time donors (n=212)	53 [25] (19.6–31.3)
Repeat donors, but not regular (n=192)	39 [20.3] (15.2–26.7)
Regular/Frequent donors (n=96)	11 [11.5] (6.4–19.7)
Low hemoglobin deferral, on current donation	
No (n=409)	47 [11.5] (8.7–14.9)
Yes (n=91)	56 [61.5] (50.9–71.1)
Occupation	
Un-employed (11)	1 [9.1] (0.9– 53.7)
Employed (219)	28 [12.7] (9.8– 23.8)
Student (270)	74 [27.4] (22.4– 33.1)
Red cell indices	
MCV <80fL (n=114)	51 (44.2)
MCH <26 pg (n=129)	58 (44.9)
RDW >16 % (n=54)	38 (70.4)

Table 4. Bivariable associations with iron deficiency among blood donors in Uganda

Variable	Observation N (%)	*Crude odds ratio (95% CI)	p-value
Gender, n (%)			
Male	5 (2.5)	1.00	
Female	98 (33.0)	19.6 (7.8–48.9)	< 0.001
Occupation, n (%)			
Student	74 (27.4)	1.00	
Un-employed	1 (9.1)	0.26 (0.33–2.10)	0.209
Employed	28 (12.7)	0.39 (0.24–0.61)	< 0.001
Highest education level, n (%)			
Primary and lower	11 (23.4)	1.00	
Secondary	70 (22.2)	0.94 (0.45– 1.93)	0.86
University and Tertiary	22 (15.9)	0.62 (0.27–1.40)	0.25
Donor's age, n (%)			
25– 51 years	24 (12.2)	1.00	
18 –24 years	79 (26.1)	2.54 (1.54–4.18)	< 0.001
Marital status, n (%)			
Single	83 (25.9)	1.00	
Married	14 (8.6)	0.27 (0.15–0.49)	< 0.001
Separated/Window	6 (37.5)	1.72 (0.61–4.87)	0.308
Repeat status, n (%)			
Repeat donors, but not regular	39 (20.3)	1.00	
First-time donors	53 (25)	1.31 (0.82–2.09)	0.263
Regular/Frequent donors	11 (11.5)	0.51 (0.25–1.04)	0.065
Vegetarian diet, n (%)			
No	98 (20.9)	1.00	
Yes	5 (16.1)	0.73 (0.27–1.94)	0.527
Iron-rich diet, n (%)			
Yes	70 (18.1)	1.00	
No	33 (29.2)	1.87 (1.15–3.02)	0.011
MCV, n (%)			
>80fl	45 (12.6)	1.00	

≤80fl	51 (44.7)	5.61 (3.46–9.10)	<0.001
MCH, n (%)			
>26 pg	38 (11.1)	1.00	
≤26 pg	58 (44.9)	6.53 (4.03–10.60)	<0.001
RDW, n (%)			
<16%	57 (13.7)	1.00	
≥16%	38 (70.4)	14.9 (7.83–28.58)	<0.001

Table 5. Multivariable results for factors associated with iron deficiency among blood donors in Uganda.

Variable	**Crude odds ratio (95% CI)**	**p-value**	**Adjusted odds ratio (95% CI)**	**p-value**
Gender, n (%)				
Male	1.00			
Female	19.6 (7.8,48.9)	< 0.001	15.81 (5.17,48.28)	**< 0.001**
Donor's age, n (%)				
25– 51 years	1.00			
18 –24 years	2.54 (1.54,4.18)	< 0.001	1.70 (0.71,4.13)	0.240
Marital status, n (%)				
Single	1.00			
Married	0.27 (0.15,0.49)	< 0.001	0.57 (0.22,1.46)	0.242
Separated/Window	1.72 (0.61,4.87)	0.308	0.91 (0.81,4.57)	0.907
Repeat status, n (%)				
Repeat donors, but not regular	1.00			
First-time donors	1.31 (0.82–2.09)	0.263	0.73 (0.39, 1.36)	0.321
Regular/Frequent donors	0.51 (0.25–1.04)	0.065	0.39 (0.13, 1.17)	0.093
Occupation, n (%)				
Student	1.00			

Un-employed	0.26 (0.33,2.10)	0.209	0.43 (0.39,4.58)	0.482
Employed	0.39 (0.24,0.61)	< 0.001	1.37 (0.57,3.24)	0.479
Iron-rich diet**,** n (%)				
Yes	1.00			
No	1.87 (1.15,3.02)	0.011	1.91 (0.98,3.70)	0.056
MCV, n (%)				
>80fl	1.00			
≤80fl	5.61 (3.46,9.10)	<0.001	1.53 (0.69,3.34)	0.293
MCH, n (%)				
>26 pg	1.00			
≤26 pg	6.53 (4.03,10.60)	<0.001	2.32 (1.07,5.02)	**0.032**
RDW, n (%)				
<16%	1.00			
≥16%	14.9 (7.83,28.58)	<0.001	6.89 (2.99,15.90)	**<0.001**

Figure 1: Graph showing iron status of blood donors categorized by the screening hemoglobin for eligibility to donate.