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Depleted iron stores in voluntary blood donors: A three-center cross-sectional study in Ghana

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Abstract:

BACKGROUND: Blood donation is frequently associated with iron deficiency. Although iron deficiency is endemic in Ghana, there is a scarcity of data on iron stores in blood donors to inform donor recruitment policy. This study determined the prevalence and factors predictive of depleted iron stores in blood donors.

MATERIALS AND METHODS: This cross-sectional study recruited 287 blood donors from three regions in Ghana. Venous blood samples were collected for estimation of C-reactive protein, full blood count, and serum ferritin. Questionnaires were used to capture sociodemographic data. Data were analyzed using SPSS or GraphPad Prism. Multivariate logistic regression and receiver operator characteristics (ROC) analyses were, respectively, used to determine the factors associated with depleted iron stores or sensitivities of calculated red cell indices in predicting depleted iron stores in the participants.

RESULTS: Whereas 27.4% of the blood donors had depleted iron stores (ferritin <15 ng/dL), only 11% took iron supplementation. While ferritin levels significantly increased with age, 49.5% of the blood donors were aged 20–29 years. Whereas 39.5% of participants had never donated blood, 24.9% had donated ≥3 units of whole blood in the past 2 years. Female (adjusted odds ratio [aOR]: 7.407, $P = 0.005$), multiple previous donations (1–2 [aOR: 1.846, $P = 0.431$]; ≥3 [aOR: 6.297, $P = 0.016$]), no iron supplementation (aOR: 17.553, $P = 0.078$), or platelet count ≥150 × 10^9/L (aOR: 2.689, $P = 0.354$) significantly associated with iron depletion. ROC analyses showed that whereas mean cell hemoglobin (MCH) density (area under the curve [AUC]: 0.735, $P < 0.01$), MCH (AUC: 0.772, $P < 0.01$) or Shine and Lal (AUC: 0.736, $P < 0.01$) fairly predicted iron depletion, combined cell index (AUC: 0.660, $P < 0.01$) or Green and King (AUC: 0.603, $P < 0.01$) indices poorly predicted iron depletion.

CONCLUSIONS: More than quarter of voluntary blood donors suffers postdonation sideropenia. Calculated red cell indices should be investigated in different settings to validate usefulness in detecting iron depletion.

Keywords:

Blood donors, calculated red cell indices, depleted iron stores, serum ferritin

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Introduction

Improved life expectancy as a consequence of advances in medicine has led to a corresponding increased demand for blood transfusion. As the scientific quest for *in vitro* red cell blood production has not been optimized for large-scale production,[1,2] blood donor collection centers are under increased pressure to increase donor pool so as to meet the increasing demand for transfusion requirement. It has been suggested that blood donation at the rate of 1/100 persons[3] is sufficient to meet the transfusion needs of any population. However, sub-Saharan African countries

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struggle to meet this critical need with only 41.5% of annual transfusion needs being met.[3]

Donation of 1 mL of blood is however associated with a loss of 0.5 mg iron; thus, donation of one unit of whole blood leads to a loss of approximately 236 or 213 mg of iron in men and women, respectively.[4] In countries like Ghana where anemia is a severe public health problem,[5] blood donation may therefore be another risk factor that compounds the tendency to develop negative iron balance in those with borderline iron stores. It is an established fact that hemoglobin levels drop only in late stages of iron deficiency when iron stores have been depleted.[6-8] Therefore, in places like Ghana where iron deficiency is endemic in the general populace, relying on prospective donor hemoglobin levels alone for donor recruitment may be associated with increased risk of drawing blood from iron-depleted individuals and thereby compromise their general well-being in the postdonation period.

It is an established fact that the best way to estimate the iron stores of individuals is to undertake specific biochemical measurements.[9] However, this is not practicable for the screening of all prospective blood donors due to cost implications as well as time constraints. In the light of these constraints, scientists have been exploring the potential of specific indices calculated from variables on the completed blood count profile in connection with their ability to predict individuals with low or depleted iron stores.[10-12] In this study, we investigated the prevalence of depleted iron stores, factors associated with depleted iron stores in voluntary blood donors as well as calculated red cell indices that could be predictive of depleted iron stores in these participants. The aim was to identify prospective algorithms that could be included in the predonation screening protocols in resource-poor settings to assist in the decision to exclude prospective donors who may have depleted iron stores so as to protect these donors.

Materials and Methods

Study design/study site

The study was an institutional-based cross-sectional study that recruited 287 voluntary blood donors (17–60 years) between January 2017 and May 2017. Three study sites were selected to represent the three zones of Ghana: Tumu Government hospital in the Upper-West Region (Northern zone), Cape Coast Teaching Hospital, Central region (CR) (Central Zone), and Koforidua Regional Hospital, Eastern region (ER) (Southern zone). Although the study initially targeted recruiting 450 participants over the study period (150 participants per center), only a total of 287 agreed to be a part of the study.

Predonation screening

All blood donors filled the universal donor recruitment questionnaire and met the predonation selection criteria of weight ≥50 kg, hemoglobin concentration (≥12.5 g/dl), body temperature (37°C ± 0.5°C) and were nonreactive for transfusion-transmitted infections (HIV, hepatitis B and C, and syphilis). All prospective donors with acute liver diseases or any inflammatory conditions were deferred and were therefore excluded from the study. Furthermore, female participants who were in their menses, or nursing mothers, or pregnant were also excluded from the study.

Questionnaire

A well-structured closed-ended questionnaire was administered to each participant to help obtain information on sociodemographic variables such as age, region of residence, occupation, educational status, marital status, and iron supplementation.

Laboratory assays

A volume of 5 mL of blood was taken from the forearm of each participant (3 mL into ethylenediaminetetraacetic acid [EDTA] tube and 2 mL into serum separator tube [SST]) for the laboratory assays as explained below. All sampling was undertaken between 8:00 and 10:00 a.m. after an overnight fast. The EDTA anticoagulated samples were used for full blood count (FBC), and transfusion-transmissible infections screening. Samples in the SST were allowed to clot, spun at 5000 rpm for 5 min to obtain serum, transferred into Eppendorf tubes and stored at – 25°C until required (for serum ferritin and C-reactive protein [CRP] estimation).

Full blood count

FBC of the participants was estimated with the Sysmex (XS 500i) hematology analyzer (Sysmex Corporation, Kobe, Japan) in accordance with manufacturer's specifications. Based on the WHO guidelines,[13] anemia was defined as hemoglobin <12.5 g/dl. The hematology analyzer was used at the Tumu Government Hospital and Cape Coast Teaching Hospital as were the hospital's policy for screening prospective blood donors. However, at the Eastern regional hospital, the copper sulfate density method was employed in line with the existing hospital policy for donor hemoglobin screening.

C-reactive protein

Serum CRP was estimated using the ELISA method in accordance with manufacturer's specifications (R & D Systems China Co., Ltd., China). Plates were then read on the URIT-660 Microplate Reader (URIT Medical Electronic Co., Ltd., Guangxi, P. R China). As per the

WHO recommendation, CRP cutoff for no inflammation was taken as ≤5 mg/l.[14]

Serum ferritin

Serum ferritin was estimated using the ELISA method in accordance with manufacturer's specifications (Chemux Bioscience Inc., USA). All plates were read on the URIT-660 Microplate Reader (URIT Medical Electronic Co., Ltd., Guangxi, China). Low iron store was defined as ferritin levels <15 ng/dl[9,15] in the absence of inflammation.[14]

Statistical analysis

All analyses were performed using IBM Statistical Package for Social Science version 20.0 for Windows (IBM Inco., USA) or GraphPad Prism software, version 6.01 for Windows (GraphPad, San Diego, USA). Continuous variables were expressed as mean ± standard deviation. To analyze the differences between groups, the independent *t*-test was used for continuous variables, and Chi-square test was used for nominal variables. Factors associated with inadequate iron stores (ferritin levels ≤15 ng/mL)[9,15] were predicted using multivariate logistic regression analysis. In addition, receiver operating characteristics (ROC) was used to estimate area under curve (AUC) so as to predict the sensitivity of calculated red cell indices combined cell index (CCI), mean cell hemoglobin density (MCHD), Green and King (G and K), and Shine and Lal (S and L) to predict depleted iron stores in participants. In the ROC analyses, the test direction was chosen to reflect the direction of the correlation coefficient between ferritin and the variable in question. All statistical analyses were carried out as a two-tailed test at 95% confidence interval (CI) (95%) and on a 5% level of statistical significance ($P < 0.05$).

Results

The sociodemographic characteristics of the blood donors are presented in Table 1. Six participants with CRP >5 mg/l were considered to have some underlying inflammatory condition and were thus excluded from the analyses. Self-employed individuals constituted the highest proportion (29.9%) compared to professional athletes who comprised the least proportion of donors (1.4%). Whereas majority of the donors were in their 20s, fewer individuals donated as the age increased (13.9% [<20 years] vs. 49.5% [20–29 years] vs. 26.7% [30–39 years] vs. 9.3% [>39 years]). The donors were also predominantly males (89% males vs. 10.7% females). Majority of the participants who consented to participate in the study were from CR (44.1% CR vs. 22.8% Upper West vs. 33.1% ER).

Table 1: Sociodemographic details of blood donors

Variable	*n* (%)
Employment	
Self-employed	84 (29.9)
Health worker	13 (4.6)
Civil servant	33 (11.7)
Student	64 (22.8)
Unemployed	12 (4.3)
Sportsperson	4 (1.4)
Age (years)	
<20	39 (13.9)
20-29	139 (49.5)
30-39	75 (26.7)
>39	26 (9.3)
Gender	
Female	30 (10.7)
Male	250 (89.0)
Education	
Primary	11 (3.9)
Secondary	145 (51.6)
Tertiary	99 (35.2)
Uneducated	24 (8.5)
Marital status	
Single	181 (64.4)
Married	65 (23.1)
Divorced	27 (9.6)
Widowed	6 (2.1)
Region	
Central	124 (44.1)
Upper West	64 (22.8)
Eastern	93 (33.1)

Table 2: Donation history and serum ferritin levels in blood donors

Parameter	*n* (%)
Number of donations per past 2 years	
None	111 (39.5)
1-2	99 (35.2)
≥3	70 (24.9)
Ferritin concentration (ng/dL)	
Depleted iron stores (ferritin <15)	77 (27.4)
Iron-deficient erythropoiesis (ferritin 15-30)	57 (20.3)
Normal ferritin (>30-300)	147 (52.3)
Iron supplementation	
No	249 (88.6)
Yes	31 (11.0)
Alcohol intake	
Yes	65 (23.1)
No	215 (76.5)

The donation history, donor iron stores, and participant lifestyle choices are presented in Table 2. Although 60.1% were repeat donors, only 11.0% of the participants routinely took iron supplementation. The forms of iron supplementation were usually nonprescribed hematinic syrups bought over-the-counter and taken over variable periods depending on the individuals' financial means.

Overall, 47.7% of participants had negative iron balance; 27.4% depleted iron stores, and 20.3% iron-deficient erythropoiesis. In addition, 23.1% of the blood donors regularly took alcoholic beverages.

Table 3 stratifies blood donor characteristics as per their serum ferritin levels. Whereas 38.5% of adolescent participants were iron-depleted, only 3.3% of participants aged >39 years were iron depleted. Increasing number of donations were also associated with increased proportion of participants with depleted iron stores. A higher proportion of female donors were iron depleted (40% females vs. 25.7% males). Participants with secondary education comprised the majority of donors with uneducated participants being the least. Moreover, more participants from ER were iron depleted compared to the other regions.

This study also investigated the relationship between serum ferritin levels and FBC parameters [Table 4]. Whereas serum ferritin was significantly positively correlated with mean cell volume (MCV), mean cell hemoglobin (MCH), and hemoglobin level, it was inversely correlated with platelet count, white blood cell (WBC), and red cell distribution width (RDW). Furthermore, MCV was positively correlated with MCH and hemoglobin but inversely correlated with platelet count, WBC, and RDW. With the exception of WBC which positively correlated with RDW ($r = 0.181$, $P = 0.044$), all the other parameters inversely correlated with RDW. Furthermore, with the exception of platelet count ($r = -0.178$, $P = 0.014$), that inversely correlated with hemoglobin level, all the other parameters positively associated with hemoglobin levels.

Table 3: Stratification of blood donors based on serum ferritin levels

	Ferritin concentration (ng/dL)		*P*
	<15 (%)	≥15	
Age (years)			
<20	15 (38.5)	24	<0.001
20-29	48 (34.5)	91	
30-39	11 (14.7)	64	
>39	1 (3.3)	29	
Number of donations/past 2 years			
None	21 (18.9)	90	0.022
1-2	29 (29.6)	69	
≥3	26 (37.1)	44	
Gender			
Female	12 (40)	18	0.097
Male	64 (25.7)	185	
MCV			
<80	46 (36.2)	81	<0.001
≥80	17 (13.6)	108	
Iron supplementation			
No	61 (24.6)	187	0.005
Yes	15 (48.4)	16	
Education			
Primary	2 (18.2)	9	0.005
Secondary	52 (36.1)	92	
Tertiary	20 (20.2)	79	
Uneducated	2 (9.1)	22	
Region of residence			
ER	42 (45.16)	51	<0.001
CR	26 (20.96)	98	
UWR	9 (14.06)	55	

MCV=Mean cell volume, ER=Eastern region, CR=Central region, UWR=Upper West region

In order to understand what prospective donor characteristics could be predictive of depleted iron stores (ferritin <15 ng/dL), we explored the data using multinomial logistic regression analyses [Table 5]. This study found that female gender (adjusted odds ratio [aOR] 7.407; $P = 0.005$), or ≥3 previous donations were significantly associated with higher odds of having depleted ferritin stores. In addition, primary education (aOR: 3.437, $P = 0.644$), secondary education (aOR: 1.619; $P = 0.456$), having previously donated 1–2 times (aOR: 1.846; $P = 0.431$), not taking iron supplementation (aOR: 17.553, $P = 0.078$), MCV <80 (aOR: 1.868, $P = 0.364$), or platelet count >400 × 10^9/L (aOR: 2.689, $P = 0.354$) were all each associated with higher odds of having depleted iron stores. However, participant's weight >70 kg was statistically significantly associated with reduced odds of having depleted iron stores (aOR: 0.240, $P = 0.049$).

We also explored the relationship between serum ferritin levels and various calculated red blood cell indices [Table 6]. Whereas serum ferritin was inversely correlated with CCI ($r = -0.222$; $P < 0.001$), and G and K ($r = -0.085$; $P = 0.164$), it positively associated with MCHD, S and L, and MCH.

Receiver operator characteristics (ROCs) were used to estimate sensitivity and specificity of various red cell indices in predicting depleted iron stores by means of AUC [Figure 1]. MCHD, MCH, hemoglobin as well as S and L indices all had fair sensitivity and specificities in predicting depleted ferritin stores (AUC >0.7 but <0.8; $P < 0.01$ in each case). However, CCI was poor in predicting depleted ferritin levels (AUC = 0.660; $P < 0.01$).

Figure 2 stratifies serum ferritin based on number of previous donations, age, and region of residence. Ferritin levels were lower in participants who have had 3 or more donations in the past. Furthermore, participants from ER had significantly lower serum ferritin levels compared to participants from the other regions ($P < 0.001$ [ER vs.

Table 4: Spearman's Rho correlations analyses between serum ferritin and hematological parameters

	Ferritin	MCV	MCH	Platelet	WBC	Hgb	RDW
Ferritin							
r	1						
P							
MCV							
r	0.211**	1					
P	0.001						
MCH							
r	0.364**	0.706**	1				
P	0.000	0.000					
Platelet							
r	−0.113	−0.104	0.014	1			
P	0.124	0.155	0.850				
WBC							
r	−0.09	−0.132	−0.125	0.115	1		
P	0.220	0.072	0.088	0.117			
Hgb							
r	0.434**	0.287**	0.640**	−0.178*	0.073	1	
P	0.000	0.000	0.000	0.014	0.319		
RDW (%)							
r	−0.089	−0.515**	−0.415**	−0.052	0.181*	−0.170*	1
P	0.269	0.000	0.000	0.566	0.044	0.033	

**Correlation is significant at the 0.01 level (two-tailed); *Correlation is significant at the 0.05 level (two-tailed). MCV=Mean cell volume, WBC=White blood cell count, Hgb=Hemoglobin, RDW=Red cell distribution width, MCH=Mean cell hemoglobin

Table 5: Regression analysis for factors associated with ferritin levels <15 ng/dL

	aOR	*P*	95% CI
Gender			
Female	7.407	0.005	1.815-30.229
Male*			
Education			
Primary	3.437	0.644	0.018-642.284
Secondary	1.619	0.456	0.456-5.747
Uneducated	9.405 E-8	0.0.974	-
Tertiary*			
Number of donations			
1-2	1.846	0.431	0.401-8.494
≥3	6.297	0.016	1.401-28.295
None*	-	-	-
Iron supplements			
No	17.553	0.078	0.728-423.157
Yes*	-		
Weight (Kg)			
50-70	-	-	-
>70	0.240	0.049	0.058-0.995
MCV (fL)			
<80	1.868	0.364	0.485-7.198
≥80	-	-	-
Platelet (×10^9/L)			
<150*	-	-	-
≥150	2.689	0.354	0.332-21.754

*indicates variable used as the referent. aOR=Adjusted odds ratios, MCV=Mean cell volume, CI=Confidence interval

Upper West region [UWR]]; $P < 0.01$ [ER vs. UWR]). In addition, serum ferritin levels increased with advancing age of the blood donor.

Discussion

The donation of one unit of blood (~500 mL) is estimated to be associated with a loss of 250 mg of iron. Thus, blood donors stand an increased risk of negative iron balance. This is particularly an important public health concern in developing countries where iron deficiency anemia is endemic in the general populace. Identification of factors that could be predictive of negative iron balance would assist blood donor recruiting centers to exclude at-risk groups to protect such donors from sideropenia in the postdonation period. Herein, using serum ferritin measurement, we show that respectively, 27.4% and 20.3% of blood donors in our study population were iron depleted (ferritin <15 ng/mL) or had iron deficient erythropoiesis highlighting an inherent negative iron balance in these voluntary donors that may be compounded by the blood donation process. The potential adverse erythropoietic effects in the postdonation period remains to be studied considering that the postdonation care in Ghana does not include routine iron supplementation. However, calculated red cell indices only poorly predicted prospective donors with negative iron balance suggesting the need for further research to devise algorithms that could be used to identify such prospective donors to ensure their deferral during the predonation screening.

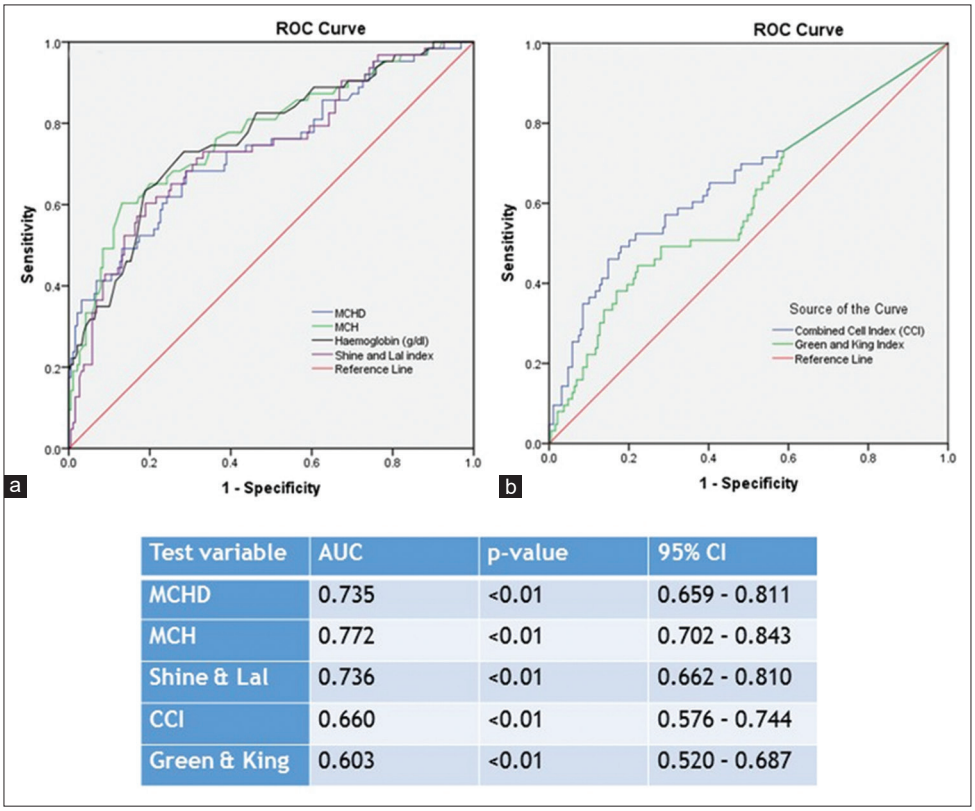
A previous study in Port Harcourt, Nigeria, that used serum ferritin cutoff value of 12 ng/mL found 20.6% (compared to 27.4% in the present study) of

blood donors being iron depleted.[16] Considering that the serum ferritin cutoff value of 15 ng/mL was used in the present study, the findings may be comparable. Previously, the RISE study in the USA showed that 15% of blood donors had depleted iron stores with a further 41.7% having iron-deficient erythropoiesis.[17] Our finding of 27.4% of the blood donors having depleted iron stores is higher than the reported 15% in the RISE study, perhaps underscoring the differences in the iron deficiency anemia in the general populace between Ghana and the USA.[18] One can also argue that the differences in the donor hemoglobin screening methods may also be a factor as one of our study sites still used copper sulfate density method. Although hemoglobin estimation is widely used as a guide for donor recruitment, various reports have shown this criterion to have poor sensitivity in detecting those with negative iron balance.[6,7] This is compounded in cases where Copper sulfate density-based procedure is used instead of actual hemoglobin measurement. This was highlighted in this study in which the study site that employed the copper sulfate hemoglobin screening protocol had significantly reduced serum ferritin levels compared to the other regions where automated hemoglobin estimations were employed. As the copper sulfate density-based hemoglobin screening procedure has been demonstrated to be fraught with low sensitivity in detecting negative iron balance,[19,20] blood donor recruitment centers should be encouraged to adopt hemoglobin meters for hemoglobin screening

Table 6: Correlation analyses between serum ferritin and various calculated red cell indices

	Hgb	Ferritin	CCI	MCHD	S and L	G and K
Hgb						
r	1					
P						
Ferritin						
r	0.434**	1				
P	<0.001					
CCI						
r	−0.529**	−0.222**	1			
P	<0.001	<0.001				
MCHD						
r	0.635**	0.341**	−0.659**	1		
P	<0.001	<0.001	<0.001			
S and L						
r	0.479**	0.344**	−0.506**	0.354**	1	
P	<0.001	0.000	<0.001	<0.001		
G and K						
r	−0.426**	−0.085	0.715**	−0.643**	0.107	1
P	<0.001	0.164	<0.001	<0.001	0.078	
MCH						
r	0.640**	0.364**	−0.672**	0.710**	0.886**	−0.314**
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

**indicates *P* <0.01. G and K=Green and King, S and L=Shine and Lal, MCHD=Mean cell hemoglobin density index, CCI=Combined cell index, MCH=Mean cell hemoglobin, Hgb=Hemoglobin



Test variable	AUC	p-value	95% CI
MCHD	0.735	<0.01	0.659 - 0.811
MCH	0.772	<0.01	0.702 - 0.843
Shine & Lal	0.736	<0.01	0.662 - 0.810
CCI	0.660	<0.01	0.576 - 0.744
Green & King	0.603	<0.01	0.520 - 0.687

Figure 1: (a) is ROC for variables (MCHD, MCH, Shine & Lal) directly correlated with serum ferritin. (b) is ROC for variables (CCI, and Green & King) inversely correlated to serum ferritin

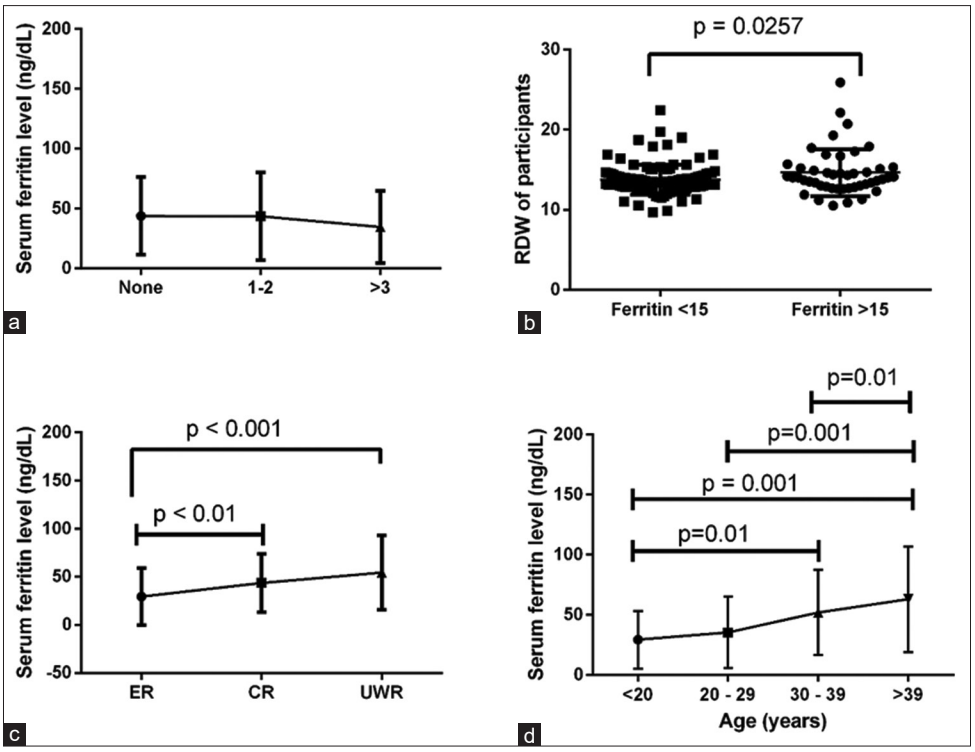


Figure 2: (a) is a line graph showing the trend of serum ferritin in donors per donation history. (b) is unpaired *t*-test used to compare means of RDW of donors per serum ferritin level. (c) compares the mean serum ferritin levels of donors per region of residence. (d) compares mean of serum ferritin per age categories. [three or more variables were compared using One-Way analyses of variance]

during mobile sessions to ensure adequate protection of prospective donors.[21]

Countries having anemia prevalence >20% have been encouraged to adopt mandatory iron supplementation as a public health measure to address the adverse physical and mental consequences of anemia.[22] Even though Ghana with a 42%–78.4% anemia prevalence (among children under 5 years and 15–45-year old women, respectively)[23,24] falls into this category, our study found that only 11% of the blood donors routinely took iron supplementation. This clearly indicates that the recommended iron supplementation is not being adopted at the individual level. The adolescent stage has been noted to require large amount of iron to support mental and physical growth spurts.[25,26] Not surprisingly, this study found that the highest proportion of donors with depleted iron stores were adolescents, and a trend towards increasing serum ferritin level with advancing age of participants. We propose that in countries where anemia is an endemic public health problem, measures should be taken to protect/restrict adolescent blood donation in the light of their unique vulnerability to negative iron balance.

The multinomial logistic regression exploration of the sociodemographic characteristics of the blood donors revealed that being female (AOR: 7.407), having primary (AOR: 3.437)/secondary (AOR: 1.619) education, a history of previous donation (AOR: 1.846 [1–2 donations], AOR: 6.297 [≥3 donation]) or not taking iron supplementation (AOR: 17.53) was associated with increased odds of a blood donor having depleted iron stores. Iron deficiency anemia has been demonstrated to be particularly common in reproductive age women due to the added demands of menstruation.[25,27] Other cross-sectional studies in Saudi Arabia,[4] Norway,[28] Germany,[29] and Nigeria[16,30] have demonstrated that multiple blood donations are associated with negative iron balance. The findings presented herein are suggestive of urgent consideration in implementing a mandatory iron supplementation therapy as a postdonation care in countries where anemia is endemic. In the light of this increased odds of negative iron balance associated with blood donations from reproductive age women in Ghana, we also suggest that this particular group of donors should be considered only in the emergency situations or when their blood types are rare and are the only compatible type available.

Although screening of body iron stores of prospective blood donors will be the ideal strategy to exclude donors with negative iron balance from the adverse outcomes of deficient iron metabolism, this is not practicable on a routine basis. In line with this, others have postulated the use of various calculated blood indices as a surrogate to identify such donors.[10,12,31] Using ROC analysis, Vuk *et al*. identified CCI to be inversely correlated to serum ferritin and to have a

good-to-excellent diagnostic efficacy in identifying depleted iron stores among blood donors in Zagreb.[10] Although our study also found a significant negative correlation between serum ferritin and CCI ($r = -0.222$; $P < 0.001$), we could only detect a poor predictive value for CCI in identifying depleted iron stores among blood donors in our study area ($P < 0.01$; AUC = 0.660; CI [0.576–0.744]). Whereas we used a serum ferritin cutoff value of 15 ng/mL and a sample size of 281, the Vuk *et al*. study used a serum ferritin cutoff value 12 ng/mL and a large sample size of 1876. These differences might have contributed to the variance in the two studies especially as large sample sizes increase statistical power. Our study rather found both MCHD ($r = 0.341$; $P < 0.01$) and MCH ($r = 0.364$; $P < 0.01$) to have fair diagnostic sensitivity in predicting depleted iron stores (AUC 0.735 or 0.772 for MCHD and MCH, respectively). Larger sample size studies exploring these two indices may assist in the potential usefulness of these two indices in identifying candidate blood donors with negative iron balance as well as establishing cutoff values that could be adopted in blood donor centers for deferring such prospective donors. However, the differences in the key findings in the present study and that of Vuk *et al* may not necessarily be a function of sample size alone but also other co-inherited genetic variables like hemoglobinopathies and enzymopathies that affect red cells. For example, a cross-sectional study that recruited 179 blood donors in Malaysia found another red cell index RBC-Y (a mean value of the forward light scatter histogram of matured red blood cells) to have good diagnostic utility in identifying iron deficiency.[31] That variable was however not available on the analyzers used in the present study and could not therefore compare. We speculate that even though our donor population were healthy, it is possible that some might have had inherited hemoglobinopathies due to the high prevalence of these in sub-Saharan Africa. As hemoglobinopathies affect red cell size, it is tangible to suppose that these may have contributed to the variance in the reported usefulness of red cell indices in detecting depleted iron stores. Future studies must take this into consideration.

Conclusions

The finding of more than a quarter of blood donors having depleted iron stores is suggestive that most blood donors suffer sideropenia in the postdonation period and must be addressed either by iron supplementation or intake of iron-rich foods. Calculated red cell indices should be investigated in different settings to validate their global usefulness in detecting depleted iron stores.

Ethical approval and consent to participate

All protocols for the study were approved by the institutional review board, University of Cape Coast (ethical clearance ID: UCCIRB/CHAS/2016/46). Also, approval was sought from the heads of the various hospitals before commencing the study. Although the study sought to recruit 130 participants from each zone, only participants who gave written informed consent before being enrolled for the study. Participants read and signed written informed consent before being enrolled unto the study. Participants were also made aware that they can withdraw from the study at any point in time and also their medical records will be kept and treated with strict confidentiality.

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Conflicts of interest

There are no conflicts of interest.

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