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ORIGINAL RESEARCH

Serum ferritin and blood pressure modulation in first-time and regular blood donors

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Abstract

Background: The health benefits of blood donation are well known. However, the overall effect of long term regular blood donation on body iron store and blood pressure need to be evaluated among voluntary blood donors.
Objective: To determine the effect of long term, regular blood donation on body iron store and blood pressure among regular voluntary non-remunerated blood donors in Lagos, Nigeria.
Methods: Consenting adult blood donors (n = 320), ranging from the first time to regular blood donors were studied over six months. Supine blood pressure (BP) readings were taken twice at 30 minutes interval with a mercury sphygmomanometer. Venous whole blood was drawn into EDTA anti-coagulated and plain tubes for haematological parameters and serum ferritin estimation using Enzyme-linked Immunosorbent Assay (ELISA) method.
Results: The mean serum ferritin levels declined significantly from 95.5ng/mL among first time donors to 68.9ng/mL among Category III donors (p = 0.035). Male voluntary blood donors had increased risk of low serum ferritin level (OR = 5.02; 95%CI= 1.12-22.51; p = 0.035). Lower values of serum ferritin were recorded more frequently among donors within the 21-30 year age category (OR = 1.54; 95%CI = 1.0-2.71; p= 0.042). Long term regular voluntary blood donation was associated with significant reduction in mean systolic blood pressure (p = 0.01).
Conclusion: Long term blood donation resulted in the reduction of blood pressure. Progressive increase in the duration of donation resulted in reduced iron stores even as haemoglobin concentration levels remained acceptable for blood donation.

Keywords: Blood pressure, Long term blood donation, Serum ferritin, Voluntary blood donors.

Introduction

In 1975, the Twenty-eighth World Health Assembly in the resolution WHA28.72 (later endorsed in resolution WHA58.13), made a call for the development of national blood transfusion services.[1] These blood transfusion services were meant to be based on voluntary, non-remunerated blood donation to ensure safe, adequate and sustainable blood supplies and to protect the health of blood donors and recipients. [1 - 4] It is important to note that, building a pool of regular voluntary blood donors is also more cost-effective than recruiting new donors.[5] In order to achieve the desired objectives, the WHO estimates that blood donation by 1% of the population is regarded as

the minimum proportion of the population needed to meet a nation's most basic requirements for blood. [3] In Nigeria, voluntary blood donation accounts for far less than the target set by the WHO,[6] a situation which has led to the reliance on family replacement donors over the years. However, there has been an upsurge in blood transfusion requirement in Nigeria along with factors such as the need to conform with international best practices and the recent efforts by tertiary centres. The national and state blood transfusion committees have stepped up efforts to increase the number of voluntary blood donors via public enlightenment, setting up of the National Blood Transfusion Guidelines and enactment of laws regulating blood transfusion practices. These efforts also include the establishment and support of youth organizations such as the Club 25, in its attempt to entrench a tradition of voluntary blood donation. [7,8] Though the WHO and other organizations with interest in blood transfusion have recommended voluntary blood donation as the gold standard, this initiative poses peculiar challenges for donor protection. [9, 10]

Few reports on the iron status of voluntary blood donors have been documented in our environment. In the USA, with over five million voluntary donors, iron studies have been regularly done on this group of donors. [10] In the RISE Study report, two-thirds of the voluntary female blood donors and almost half of the voluntary male blood donors were found to be iron deficient. [10,11] Blood donors provide life-saving blood products, but in doing so, they risk suffering adverse consequences where an average of 250 mg of iron is lost with every unit of blood donated. [12] Reports on the iron status of blood donors available from the few reports in the literature have been mixed. While most researchers have reported reduced serum ferritin levels among regular blood donors, [13 - 15], a few others have reported no significant difference in serum ferritin levels. [16,17]

As part of donor selection criteria in most blood donor clinics in Nigeria, individuals with elevated blood pressure are still routinely differed. However, available systematic reviews have not established any association between blood pressure levels and the occurrence of adverse outcomes in blood donation. [18] In the year 2005, the United Kingdom blood transfusion services, after a critical review, recommended that donors with well-controlled hypertension should be accepted as blood and blood component donors. [19] In the year 2009, the American Association of Blood Banks modified its standards and eliminated the requirement to measure blood pressure or pulse rate as part of the determination of eligibility for blood donation.[20]

Most blood banks in Nigeria currently face a considerable challenge in maintaining adequate blood supply. [6, 9] More so, most blood donor clinics are yet to review the available donor selection criteria over the years. Therefore, there is an urgent need to research on the long term benefits and challenges of blood donation in our immediate environment and provide documented evidence for revising the guidelines on safe, voluntary donation practices in Nigeria, while adequately informing and protecting blood donors. In order to expand the existing donor base in Lagos, south-west, Nigeria, targeting 1% of the over 21million people living in Lagos (as required by WHO), may translate to an approximate 210,000 potential voluntary blood donors with various environmental and socio-economic peculiarities. [18] The objective of this study was to assess the iron status and haematological parameters of first time and regular blood donors, and determine the effect of regular blood donation on systemic blood pressure (BP).

Methods

Study design, Sites and Period

This was an observational, cross-sectional study. Three hundred and twenty (320) voluntary blood donors were selected by systematic random sampling from donors at the Blood Donor Clinic of the Lagos University Teaching Hospital (LUTH), members of Club 25 of both the Lagos State Polytechnic (LASPOTECH) and the Lagos State School of Health Technology (LASCOHET) over a period of seven months starting from October 2015 to April 2016.

Ethical clearance for the study was obtained from the Health Research and Ethics Committee of LUTH. The blood donors were the first time and regular blood donors who gave informed consents for recruitment into the study. All the selected donors were apparently-healthy individuals who fulfilled the eligibility criteria for donation. Donor questionnaires were administered to obtain information on age at first donation, the total number of donations, interval between donations, date of last donation/previous donations, and dietary and drug history.

Procedures

Donors who were included in this study included healthy, consenting males, and non-pregnant, non- lactating females aged 18 - 60 years, weighing ≥ 50kg with minimum haemoglobin concentration levels of 12.5g/dl for females and 13.5g/dl for males. Only voluntary donors who have been donating once every 3 to 4 months as recommended by the World Health Organization were recruited and categorized as regular voluntary blood donors for the study. [21] Donors with any history of long-term medication use, acute or chronic systemic disease, menstruating females, and all first-time blood donors who did not meet the standard donor selection criteria were excluded from this study.

The donors were divided into four categories according to the number of donations per year. The blood donors in Category 0 (n = 215) were first- time donors with no previous history of blood donation. Donors in category I (n = 66) were regular donors who have been donating for the last 1 to 2 years. Category II donors (n = 15), were regular donors who have regularly been donating in the previous 3 to 4 years. Category III donors (n=24) were regular blood donors who have been donating for more than four years. Blood pressure measurements were taken twice in the sitting position at 30 minutes intervals, using a mercury sphygmomanometer (KENZ 600, SUZUKEN Co., Ltd, Japan), and mean BP was documented for each participant. Three millilitres of whole blood was drawn each into K-EDTA anticoagulated tubes and plain tubes at the end of donation. The EDTA anti-coagulated blood was used to determine the Full Blood Count (FBC) and other to basic haematological parameters such as white cell count –WBC; % lymphocyte and % granulocyte and red cell indices such as mean cell haemoglobin - MCH; mean cell haemoglobin concentration – MCHC; mean cell volume- MCV and haemoglobin concentration –Hb within six hours of blood sample collection using the BC-3200 Auto-haematology analyzer manufactured by Mindray (China). The serum obtained was used for serum ferritin estimation using AccuBind™ ELISA Microwells, Chicago, IL, USA. Standard minimum haemoglobin of 13.5 g/dl for men and 12.5 g/dl for women donors were adopted as fit for donation. [21]

Statistical Analysis

Statistical analyses were performed using the IBM SPSS Software for Windows, Version 20.0 (Armonk NY: IBM Corp. USA). The data were then summarized as simple proportions. Associations between mean values of

continuous variables were tested for statistical significance using the Student's t-test for two variables, and Analysis of Variance (ANOVA) for three or more variables, where appropriate. Discrete variables were tested for relationships using the Chi-Square test. A p-value of less than 0.05 was considered statistically significant. Logistic regression model was used to evaluate the degree of association between some independent variables and the occurrence of low serum ferritin levels among blood donors in a dichotomous response (normal or low serum ferritin).

Results

The age of recruited donors ranged from 18 years to 60years (Table I). Of the 320 blood donors, 309 (96.6%) were males, and 11 (3.4%) were females. The modal age group for regular donors and first-time donors was 21-30 years. The majority of the subjects were single (189; 59%) while 93.1% (298/320) had up to tertiary education.

A higher proportion of blood donors with low serum ferritin was demonstrated within the age group 21-30 years (Figure 1). Low serum ferritin was least observed among donors within the extreme age groups: 18-20 years and 51-60 years.

Table I: Demographic characteristics of blood donors

Demographic variables	Donor category				Total
	Group 0 n = 215 (%)	Group I n = 66 (%)	Group II n = 15 (%)	Group III n = 24 (%)	
Age Groups (Years)					
≤ 20	12 (5.6)	8 (12.1)	0 (0.0)	0 (0.0)	20
21-30	106 (49.3)	26 (39.4)	8 (53.3)	12 (50.0)	152
31-40	76 (35.3)	18 (27.3)	5 (33.3)	6 (25.0)	105
41-50	20 (9.3)	11 (16.7)	2 (13.3)	2 (8.3)	35
51-60	1 (5.0)	3 (4.5)	0 (0.0)	4 (16.7)	8
Sex					
Female	5 (2.3)	5 (7.6)	1 (6.7)	0 (0.0)	11
Male	210 (97.7)	61 (92.4)	14 (93.3)	24 (100.0)	309
Marital Status					
Single	132 (61.4)	36 (54.5)	8 (53.3)	13 (54.1)	189
Others	83 (38.6)	30 (45.5)	7 (46.7)	11 (45.9)	131
Educational status					
No formal education	5(2.3)	0 (0.0)	0 (0.0)	3 (12.5)	8
Primary	2 (9.0)	0 (0.0)	0 (0.0)	0 (0.0)	2
Secondary	8 (3.7)	1 (1.5)	1 (6.7)	2 (8.3)	12
Tertiary	200 (85.0)	65 (98.5)	14 (93.3)	19 (79.2)	298

Key: Group 0 (First time blood donors); Group I (donors who have been donating blood regularly for the past 1 to 2 years); Group II (donors who have been donating blood regularly for the past 3 to 4 years); Group III (donors who have been donating blood regularly for more than 4 years).

The mean values of haematological parameters were compared across study categories, as shown in Table II. The mean values of % lymphocyte count, % granulocyte count and platelet count varied significantly among participants from category 0 to III (F = 3.128, p =

0.026; F = 5.593, p = 0.001; F = 5.127, p = 0.002 respectively). Likewise, post hoc evaluation (for % lymphocyte count, % granulocyte count and Platelet count across study categories) show greater mean values of % lymphocyte count in category III donors compared to category 0 donors (P = 0.019). A greater mean % granulocyte count was greater in category I donors compared to category III donors (P = 0.045). The mean platelet count also differed significantly (F = 5.127, p = 0.002) across donor categories, such that the mean platelet count in category III blood donors (154.3 ± 38.9 $x10^{12}$/L) was significantly lower compared to the mean value for category 0 subjects (202.5 ± 56.1 $x10^{12}$/L) and category I subjects (199.7 ± 70 $x10^{12}$/L) following post hoc analysis (p = 0.037 and p = 0.041 respectively). There were no significant variations in mean values of haemoglobin concentration, red cell count and Total white cell counts across the subject groups (P = 0.970).

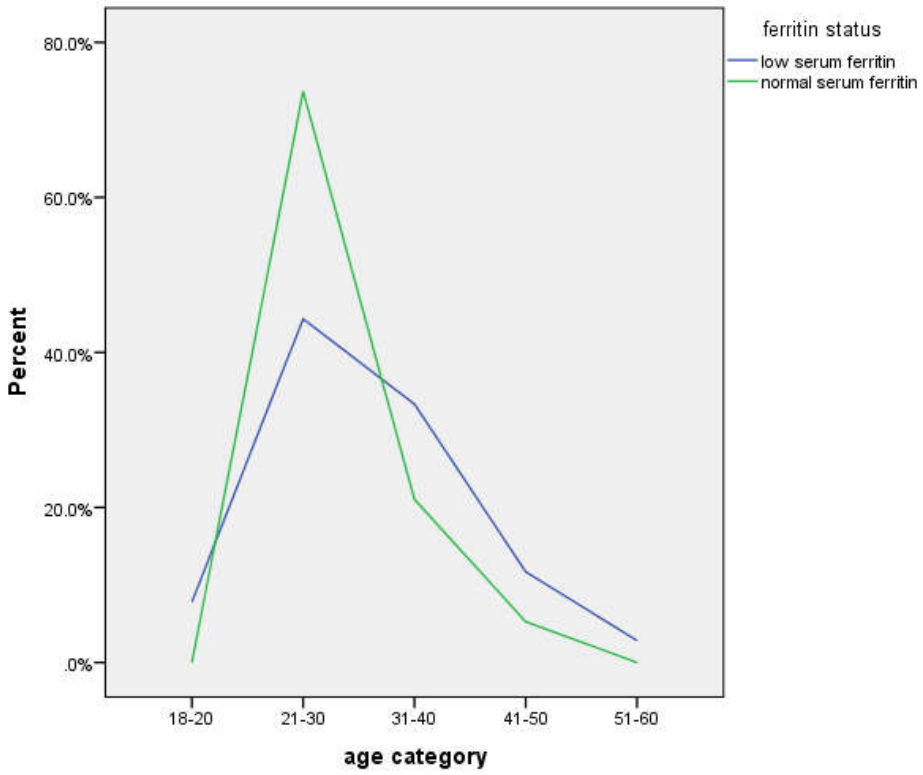

Figure1: Distribution of serum ferritin in relation to the age of voluntary blood donors

The data for MCV, MCH, MCHC and serum ferritin were not normally distributed among subjects (p=0.021; 0.01; 0.047 and 0.04 respectively) using Shapiro-Wilk test for normality, and the median values were then compared across study categories of donors for each variable using Kruskal Wallis non-parametric analysis and Mann-Whitney U test as post hoc. The median values for MCV, MCH and MCHC did not vary significantly across donor categories (p = 0.138, p = 0.304 and p = 0.197 respectively).

There was a statistically significant progressive decline in the median serum ferritin levels across the different study categories (95.5ng/mL

> 90.0ng/mL > 71.0ng/mL > 68.9ng/mL for category 0 to III respectively [p = 0.035]). Post hoc analysis showed multiple donors in Category III (68.9ng/mL) had significantly lower median serum ferritin levels compared to Category I donors (90.0ng/mL, p = 0.045) and first time donors had a significantly higher mean serum ferritin levels (95.5ng/mL) compared to Category II donors (71.0ng/mL, p = 0.023).

The male sex was significantly associated with low serum ferritin level (OR= 5.023, 95%CI 1.121- 22.513; p = 0.035) as shown in Table III. The risk of low serum ferritin was also associated with younger blood donors aged 21-30 years (OR=1.542, 95%CI 1.015-2.716; p= 0.042). The risk of low serum ferritin appeared to increase progressively as the duration of blood donation increased from Category I donors through Category III donors (OR= 1.185, 1.521 and 5.003 respectively). However, the risk of low serum ferritin was significantly increased only among Category III donors (OR=5.003, 95%CI 1.428 - 8.487; p = 0.034).

Table II: Comparison of the values of some haematological parameters and serum ferritin levels across blood donor categories

Parameters	Donor Category				F	*P* value	Post Hoc (*p* value
	0	I	II	III			
FBC Mean values							
WBC ($x10^9/L$)	5.06±1.2	5.0±1.2	4.9±1.3	5.1±1.5	0.082	0.970	
Lymph %	44±9.7	45±10.5	43±9.6	51±9.6	3.128	0.026*	III>0 (p = 0.019)
Gran %	47±10.2	45±13	47±11.1	38±12.7	5.593	0.001*	I>III (p = 0.05)
Hb (g/dL)	13.5±1.8	13.1±2.2	13±1.9	14.1±1.3	1.893	0.131	
Platelet($x10^{12}/L$)	202.5±56.1	199.7±70	187.1±59	154.3±38.9	5.127	0.002*	III<0&I (p<0.05)
Red cell indices and serum ferritin levels (median values)							
MCV(fl)	79.2	79.4	82.5	82.7	0.138		
MCH(pg)	26.6	25.5	25.0	26.2	0.304		
MCHC(g/dl)	32.2	32.05	31.1	31.7	0.197		
SF (ng/ml)	95.5	90.0	71.0	68.9	0.035	0.035**	0>II&III (p < 0.05)

Key: SF (serum ferritin); p* (significant p-value for ANOVA); p (significant p-value for Kruskal-Wallis analysis).**

Table III: Association between some independent variables and the occurrence of low serum ferritin among blood donors

Variables	Odd Ratio	95%Confidence Interval		*P* value
		Lower	Upper	
Age (21-30 years)	1.542	1.015	2.716	0.042
Sex (Male)	5.023	1.121	22.513	0.035
Blood donor Categories				
I	1.185	0.137	10.237	0.877
II	1.521	0.153	15.123	0.720
III	5.003	1.428	8.487	0.034

A consistent decline in mean systolic blood pressure was demonstrated in Table IV. The systolic blood pressure dropped from 130mmHg among the first time donors to 122mmHg among the category III participants (p = 0.01). Post hoc analysis showed significant mean

differences between systolic BP for Category 0 donors (130 ± 11.2 mmHg) when compared with systolic BP for Category II donors (124 ± 8.2 mmHg) (p = 0.021) and also when compared with systolic BP for Category III donors (122 ± 7.4 mmHg; p = 0.019).

Table IV: Mean systolic and diastolic blood pressure values across donor categories

Donor Category	Sample size	Mean Systolic BP (±SD mmHg)	Mean Diastolic BP (±SD mmHg)
0	215	130 ± 11.2	84 ± 7.2
I	66	129 ± 29.1	81 ± 17.8
II	15	124 ± 8.2	82 ± 6.4
III	24	122 ± 7.4	78 ± 9.2
p values		0.01	0.112
Post hoc 0>2 and 3	(p = 0.021 and 0.019)		

Discussion

Although blood donation is highly beneficial, one of the most frequent concerns is the effect of repeated blood donation on iron stores. This study demonstrated that the median serum ferritin levels in the donors declined significantly with their duration of donation. The risk of serum ferritin deficiency was observed to increase significantly with increased duration of blood donation. This observation was similar to the findings reported by Adewumi *et al*. [14] Similar results have also been reported in a study of Saudi blood donors. [22] Significant decrease in mean serum ferritin levels with increasing frequency and duration of blood donation have also been reported in a study conducted at Calabar, southern Nigeria [23]

The reasons for iron deficiency among the blood donors with repeated donations may be related to increased iron demand and inadequate iron replacement/supplementation with increased numbers of blood donation. This may be more serious in an environment where socio-economic indices are poor. Males appeared to have lower serum ferritin levels compared to females in the present study and the risk of low serum ferritin levels also increased with their duration of blood donation. This finding was similar to the reports made by Richard *et al.,* where a marked decrease in serum ferritin levels among males was observed compared to females. [24] However, Deepa *et al.,* reported low serum ferritin levels in females compared to males. [25] The difference in serum ferritin levels observed among both sexes in the present study could be attributable to increased duration of blood donation among males, as more males were documented to donate for more extended periods in this study. The study also demonstrated an increased proportion of subjects with low serum ferritin level in the age group of 21-30 years compared to the extreme age categories (18-20 years and 51-60 years). This was similar to the report by Parasappa and Harish, [16] among similar age groups. This trend could result from the fact that blood donors in the 21-30 years age category accounted for the largest number of blood donor population in the environment and generally, most active voluntary regular blood donors also fall into this age category.

The mean values of lymphocyte and granulocyte counts varied significantly across subject groups. Regular donors in group III showed significantly higher proportions of absolute lymphocyte count above first-time donors, and conversely, the percentage granulocyte count was significantly lower for long term donors compared to the new or short term blood

donors. Likewise, platelet count among regular long term blood donors (Group III) decreased significantly compared to first-time donors and Group I donors. These findings are in agreement with a previous study of iron stores among blood donors in Lagos. [14] This study could not demonstrate a significant difference in hemoglobin concentration between long term regular blood donors and first-time donors, as similarly reported by Adewumi *et al.*[14] However, a contrary view was expressed by Vilsu *et al.*, who reported a gradual decrease in haemoglobin concentration, as the duration of blood donations increased among regular blood donors studied. [26]

Although the red cell indices (MCV, MCH and MCHC) have been reported to be useful indices of iron deficiency, the median values for MCV, MCH and MCHC in the present study did not vary significantly across donor categories. This pattern was similar to a report made among Arabs irrespective of the duration of blood donation. [22] This indicates that the reduction in serum ferritin may not be severe enough to deplete the total iron store to such level as to affect normal erythropoietic activities.

This study also demonstrated the reduction of systemic blood pressure among long term regular blood donors when compared with first time blood donors in agreement with previous reports made by Kamhieh-Miz *et al.*, and France *et al.*, in separate studies where significant reductions in blood pressure among individuals who were hypertensive at initial donation were observed compared to subsequent donations.[27,28] Regular blood donation may reduce red cell concentration and plasma protein levels such as fibrinogen and consequently, reduce whole blood viscosity and by extension, reducing blood pressure. [29, 30] Some researchers, however, have only demonstrated a reduction in blood pressure among subjects with pre-donation hypertension, while no significant changes were observed among subjects with normal pre-donation blood pressure. [28] However, available data on this subject matter are mainly from the non-African population. Although the reduction in diastolic blood pressure as observed with the duration of blood donation did not attain statistical significance in the present study, some literature have indicated a significant reduction in diastolic blood pressure of consistent blood donors. [29] This might be related to a possible reduction in vascular arteriosclerotic changes [30] resulting from reduced serum lipids as reported in long term donors. [31,32] This observation could contribute to a lowering or stability in the diastolic blood pressure of long term blood donors.

Limitation of the study: A longitudinal study may be needed to fully highlight the pattern of serum ferritin changes per unit time, and subsequently indicate how long a regular donor can sustain iron stores before the need for therapeutic interventions. Likewise, the effect of regular donation on blood pressure may be confounded by several factors which were not controlled for in the present study. A longitudinal multicenter study may be needed to evaluate blood pressure changes in African blood donors fully.

Conclusion

Prolonged regular donations may result in reduced blood pressure of blood donors in Nigeria. The study also indicated that long term blood donation might reduce iron stores while haemoglobin levels remained acceptable for blood donation. Though low iron stores may be beneficial among subjects who are prone to iron overload, it may need to be reviewed from time to time in voluntary donors to avoid states of deficiency in long term donors as part of donor protection.

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