

Original Research Article

A study of serum ferritin levels among voluntary blood donors

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ABSTRACT

Background: The frequent blood donations may lead on to iron deficiency and iron deficiency anaemia. Estimation of haemoglobin and hematocrit levels alone in voluntary blood donors may not be adequate. Hence this study was taken to estimate the serum ferritin level among voluntary blood donors with different frequency of donation and compare with hemoglobin levels.

Methods: A Cross sectional study consisted of 314 voluntary blood donors, they were grouped into control groups donating blood for the first time and group donating blood once, twice and thrice in a year. The red cell parameters were measured by automatic cell count analyzer and estimation of serum ferritin by ELISA method.

Results: There were 88.2% males and 11.8% females. The distribution of donors on the basis of the frequency of donation per year were 50% first time, 23.9% once a year, 19.7% twice a year and 6.4% thrice a year donation. A statistically significant correlation was seen between frequency of donation and total number of life time donations and serum ferritin levels. Distribution on the basis of number of donations per year and serum ferritin <15 ng/ml in male donors were 6.9 % in first time, 19.4 % in once a year, 26.7% in twice a year and 50% in thrice year donation. Among female donors 40.7% in first time, 50% in once a year, 50% in twice a year donation had serum ferritin levels <15 ng/ml.

Conclusions: In this study, there was a definite correlation between dwindling of serum Ferritin level and the frequency of donation. As a part of donor haemovigilance program, our study suggests estimation of serum ferritin level, iron supplementation and donor health education on balanced nutritious diet for at least female donors and regular male donors to maintain adequate donor pool.

Keywords: Depleted iron stores, Frequency of donation, Serum ferritin

INTRODUCTION

A properly organized Blood Transfusion Service (BTS) is an important component of the health care system. BTS plays a vital part of the modern health care system without which an efficient health care is not possible. In a country where comprehensive blood donation is neither possible nor practical, the regular donors are comparatively safer as they are screened for transfusion transmitted diseases more frequently. The safety and

availability of the national blood supply depends on individual who can provide repeated blood donation. Donor screening criteria are formulated so that both donor and the patient are safe.

Voluntary blood donation is considered as a noble and lifesaving act. The vision of WHO is 100% voluntary blood donation and to slowly phase out the replacement and totally eliminate paid donors. WHO definition of a voluntary non-remunerated blood donor is "a person who gives blood, plasma or cellular components of his or her

own will and receives no payment either in the form of cash or in kind which could be considered a substitute for money".¹ A regular voluntary non-remunerated blood donor is the one who has donated at least three times, the last donation being within the previous year, and continues to donate regularly at least once per year.² There are wide variations in the recommended minimum interval between donations. The WHO recommends that the interval between donations can be as short as 8 weeks and a maximum of 3 liters of blood can be collected per year. In Netherlands men and women donate blood once in every 3 months and 6 months respectively.

In men iron lost from a 450ml donation (i.e. 242±17mg), is made up in 3 months by means of enhancement of dietary iron absorption. In women with iron loss of 217±11mg about 1.5 years would be required to replenish the lost iron.³ The council of Europe allows maximum donation of 6 whole blood units per year for male and 4 per year for female with a minimum interval between standard donation of two months.⁴ In Italy donors donate once in every 90 days. Men may donate maximum of four times a year and women of child bearing age only twice a year.⁵

In Brazil according to their legislation the minimum value for haemoglobin and hematocrit requirements for male is ≥13g/dl and 40% respectively and for female is ≥12g/dl and 38% respectively.⁶ According to the Council of Europe, the cut off level of haemoglobin for blood donation is 12.5g/dl for women and 13.5g/dl for men.^{7,8} In India according to the Drugs and Cosmetic Act, 1940 for blood donation the minimum acceptable haemoglobin is 12.5g/dl. They are allowed to donate with an interval between donations of 3 months.

According to the Directorate general of health services guidelines, the haemoglobin level is estimated by using the copper sulphate method which is based on the principle of specific gravity method, Sahils method, cyanmethhaemoglobin and hemo-cue methods.⁹ The altruistic donors present our richest asset. The continued presence of window period for pathogens that are transmitted by blood necessitates the need for getting blood from the regular repeat voluntary blood donors.¹⁰ The frequent donations may lead on to iron deficiency and iron deficiency anaemia.

So, there are more chances that the regular donor will leave the donor pool after being deferred for low haemoglobin. Though the current standards and practices appear adequate to protect the health and safety of donors continued hemovigilance is needed at this point of time.¹¹

Iron deficiency can occur in blood donors who pass the test for evaluating haemoglobin levels. Hence haemoglobin values above the deferral cutoff do not always predict that iron stores are in adequate amounts. A more proactive position toward education about iron deficiency is needed so that women donors, who already

have only borderline normal stores of iron, do not become depleted and deferred from further donation.¹² Safety and appropriateness of donation standards require not only protection against iron deficiency anaemia, but also possible non-hematological effects of iron deficiency. Women have a higher instance of depleted iron stores requiring reevaluation of the donation standards.¹³

The potential for a donor to donate blood without developing iron deficiency anaemia varies with the difference in nutritional iron intake, the prevalence of iron deficiency in the defined population, the menstrual loss of iron in female, the frequency of donation, capacity for iron absorption and the use of supplemental iron intake.¹⁴ Assessing Serum Ferritin levels in the blood would be the most accurate way to assess iron store as it identifies the individual most at risk for iron depletion.¹⁵ Screening of Iron deficiency by estimating the serum ferritin has been recommended by WHO as the laboratory test of choice.¹⁶

There is paucity of data in our country regarding impact of regular voluntary blood donation on iron status of donors. So, this study was undertaken to evaluate the iron stores by estimating serum ferritin levels among voluntary blood donors in Chennai. This will be of help to identify the donors in the stage of depleted iron stores before they develop iron deficiency anaemia.

METHODS

This Cross-sectional study was conducted over one and half year period from June 2011- Dec 2012 in the Department of Transfusion Medicine, The Tamilnadu Dr.MGR Medical University, Guindy, Chennai. A total of 314 voluntary blood donors were selected. Screening of donors for hemoglobin was done by copper sulphate method as per the DGHS guidelines.⁹

Eligible donors (both male and female between 18 to 60 years of age) were divided into 2 groups with group one consisting of donors donating blood for the first time representing the control group and group two consisting of donors who had donated once or more than once in the previous years. The group 2 was again sub grouped into three groups with donors donating blood once in a year, twice in a year and thrice in a year.

During the analysis of results, the donors were grouped on the basis of serum ferritin values into those with < 15ng/ml and ≥15ng/ml. This is based on the recommendation of the World Health Organization (WHO) that serum ferritin concentration <15ng/ml indicates depleted iron stores in those >5 years of age.¹⁷ Following donation, blood samples was collected into 2.0 ml EDTA tube for measurement of Mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) and RBC distribution width (RDW) by Medonic CA620 automatic cell count analyzer and 5 ml in plain

tubes for estimation of serum ferritin concentrations by ELISA method. Serum separated from the 5ml clotted blood from each donor was stored at -200 C for estimation of ferritin for further use.¹⁸

RESULTS

Demographic analysis of the 314 donors showed 88.2% (277) male and 11.8% (37) female. Age distribution among the blood donors were 22.3% in 18-20yrs, 51.6% in 21-30 years, 18.2% in 31-40 years, 5.7% in 41-50yrs and 2.2% >50 yrs. Blood group distributions among the donors were 37.3% of B positive, 28.3% of O positive, 20.1% of A positive, 8.9% of AB positive, 2.9% of O negative, 1.9% of A negative and 0.3% each of B negative and AB negative. Food habits distribution showed that 93.9% were non-vegetarian and 6.1% were vegetarian. Distribution of donors based on haemoglobin values in g/dl were 15.6% within 12.5-13.0g/dl, 40.1% within 13.1-14g/dl, 33.4% within 14.1- 15g/dl, 9.9% within 15.1-16g/dl, 0.9% with >16.1 g/dl. Distribution of donors based on the hematocrit values in percentage were 13.1% within 37-39, 41.7% within 39.1-42, 32.8% within 42.1-45, 10.2% within 45.1-48 and 2.2% were within 48.1-52. Distribution of donors based on Mean Corpuscular Volume (MCV) values in femtoliters were 15.6% within 78.5-82.5, 25.4% within 82.6-87.5, 30.9% within 87.6-92.5, 25.2% within 92.6-97.5 and 2.9% within 97.6 to 102.5.

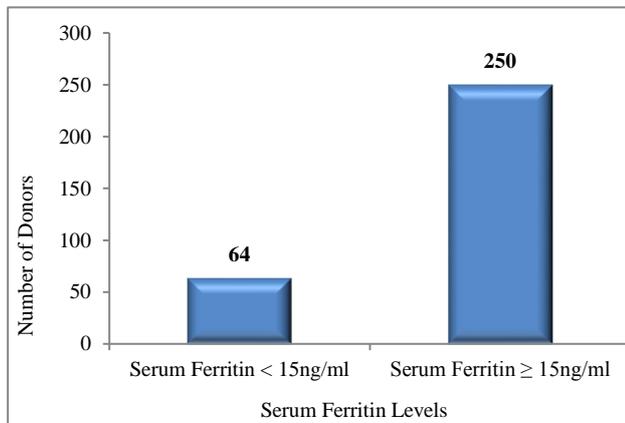


Figure 1: Distribution of donors with serum ferritin levels < 15ng/ml.

Distribution of donors on the basis of Mean Cell haemoglobin (MCH) values in picograms were 27.7% within 26-28.5, 29.9% within 28.6-31, 34.4% within 31.1-33.5 and 7.9% within 33.6-36. Distribution of donors based on Mean Cell haemoglobin Concentration (MCHC) values in g/dl were 21.3% within 31-32.5, 41.4% within 32.6-34, 31.5% within 34.1-35.5 and 5.7% within 35.6-37.

Distributions on the basis of red cell distribution width (RDW) in % were 11.5% within 12.0-13.0, 7.3% within 13.1-14, 79.6% within 14.1-15.0, and 1.6% within 15.1-

15.4 Distribution on the basis of the frequency of donation per year, 50% first time donation, 23.9% once a year donation, 19.7% twice a year donation and 6.4% thrice a year donation. Distribution on the basis of total number of life time blood donations were 50% with first time donation (control group), 36% with 1-5 donations, 8.5% with 6-10 donations, 2% each with 11-15 and 16-20 donations, and 1.5% with >20 donations.

Distribution of donors with serum ferritin levels <15 ng/ml shown in Figure 1.

Distribution of donors based on gender and serum ferritin <15ng/ml is shown in Table 1. Distribution of donors on the basis of age with serum ferritin < 15 ng/ml were 14.1% within 18-20 yrs of age, 22.2% within 21-30yrs of age, 24.6 % within 31-40yrs of age, 22.2% in 41-50yrs of age and 14.3% in >50yrs of age. p =0.464, not a significant finding.

Table 1: Distribution of donors based on gender and serum ferritin <15ng/ml.

Sex	Donors with serum ferritin < 15 ng/ml (Total donors)	%
Male	48 (277)	17.33
Female	16 (37)	43.24
P-value	0.000	

Distribution of donors on the basis of food habits and serum ferritin <15ng/ml were 20.3% in non-vegetarians and 21% in vegetarians. The p= 0.717, not a significant finding.

Distribution of donors on the basis of haemoglobin level in g/dl and serum ferritin <15ng/ml were 24.5% within 12.5-13.0g/dl, 19.8% within 13.1-14, 21%, within 14.1-15, 16% within 15.1-16 and 0% with 16.1 to 17 and more than 17g/dl. p= 0.893, not a significant finding. Distribution of donors on the basis of hematocrit in % and serum ferritin <15ng/dl were 19.5% within 37-39, 22.1% within 39.1-42, 15.5% within 42.1-45, 31.3% within 45.1 -48 and 14.3% were within 48.1-52. The p=0.468, not a significant finding.

Distribution of donors on the basis of MCV in femtoliters and serum ferritin <15 ng/ml were 28.6% within 78.5-82.5 ,16.2% within 82.6-87.5, 15.5% within 87.5- 92.5, 25.3% within 92.6-97.5 and 22.2% within 97.6-102.5. The p=0.120, not a significant finding.

Distribution of donors on the basis of Mean Cell haemoglobin (MCH) values in picograms and serum ferritin <15ng/ml were 25.3% within 26-28.5, 17% within 28.6- 31, 18.5% within 31.1-33.5 and 24% within 33.6-37.2.

The p=0.998, not a significant finding. Distribution of donors based on mean cell haemoglobin concentration (MCHC) values in g/dl and serum ferritin <15 ng/ml

were 22.4% within 31-32.5, 20% within 32.6-34, 20.2% within 34.1-35.5 and 16.7% within 35.6-37. The p=0.579, not a significant finding. Distributions of donors on the basis of red cell distribution width (RDW) in % and serum ferritin <15 mg/ml were 25% within 12.0-13.0, 17.4% within 13.1-14, 20% within 14.1-15.0, and 20 % within 15.1-15.4. The p=0.494, not a significant finding.

Table 2: Distribution of donors on the basis of number of donations per year and serum ferritin < 15 ng/ml in male donors.

Number of donations per year	Donors with serum ferritin <15 ng/ml (Total donors)	%
0	9 (130)	6.9
1	13 (67)	19.4
2	16 (60)	26.7
3	10 (20)	50
P-value	0.000	

Distribution of donors on the basis of number of donations per year and serum ferritin <15 ng/ml in male donors is shown in Table 2. Distribution of donors on the basis of basis of number of donations per year and serum ferritin <15 ng/ml in female donors is shown in Table 3.

Comparison of serum ferritin levels based on the frequency of donation for male is shown in Table 4. Comparison of serum ferritin levels based on the frequency of donation for female is shown in Table 5. Mean values of the age, haemoglobin, hematocrit and red cell indices among blood donors is shown in Table 6. Comparison of our study with other studies worldwide is shown in Table 7.

Table 3: Distribution of donors on the basis of number of donations per year and serum ferritin < 15 ng/ml in female donors.

Number of donations/year	Donors with serum ferritin <15 ng/ml (Total donors)	%
0	11(27)	40.7
1	4(8)	50
2	1(2)	50
P-value	0.000	

Table 4: Comparison of serum ferritin levels based on the frequency of donation for male.

No of donation	Serum ferritin in ng/ml		
	Mean	Standard deviation	Range
First time	47.52	37.602	7-340
Once	38.12	27.178	5-155
Twice	26.5	17.36	5-100
Thrice	20.5	16.694	5-70
P value	0.000		

Table 5: Comparison of serum ferritin levels based on the frequency of donation for female.

No of donation	Serum ferritin in ng/ml		
	Mean	Standard deviation	Range
First time	18.44	8.872	8-40
Once	18.38	11.122	8-36
Twice	13.5	4.95	10-17
P value	0.000		

DISCUSSION

The WHO recommends strong leadership of the government in establishing national transfusion network.¹¹

The blood banks are challenged with the mismatch of the increasing demand for blood transfusions and the difficulty with recruiting the new blood donors and retaining the regular blood donors.⁸ One gram of haemoglobin contains 3.4 mg of iron. Thus, in a normal person with haemoglobin of 15g/dl, 100ml of blood would contain approximately 50mg of iron. This accounts to removal of approximately 175mgs of iron with 350ml of blood donation and 225mg of iron with 450ml of donation.¹⁹

The process of donor selection is aimed to determine that the general health of the donor is in good condition to tolerate the collection procedure and he is free from transfusion transmitted diseases.

The practical significance of a single cutoff of 12.5g/dl for haemoglobin level for all donors is that women represent the vast majority of donors being deferred for haemoglobin, most of whom more likely have the chance of having normal haemoglobin concentration near this cutoff value. In contrast, men selected for donation with minimally acceptable haemoglobin for blood donation may be anemic. Haemoglobin screening does not ensure that the donor has an adequate store of iron.^{5,11,20}

There are controversies surrounding the minimum haemoglobin requirements for blood donation within different countries and different regions in the individual country.

The problem is also further compounded by the variety of test methods used for haemoglobin estimation.²¹ Because the donor may be at the latent stage of iron deficiency anaemia, wherein storage form of iron would have got depleted below normal range in spite of haemoglobin level being between 12.5 to 13.0g/dl.

According to WHO guidelines to define anaemia the cutoff value of haemoglobin for non-pregnant women is below 12 g/dl and men is below 13 g/dl.²²

Table 6: Mean values of the age, haemoglobin, hematocrit and red cell indices among blood donors.

Parameters	Donor type				Overall mean	P value
	First time donation	Once a year	Twice a year	Thrice a year		
Age	24.64±7.49 (18-52)	42.30±23.98 (12-120)	29.23±7.63 (19-49)	27.05±6.89 (19-41)	26.98±8.19 (18-52)	0.000
Haemoglobin in g/dl	13.96±0.82 (12.5-17.1)	13.82±0.76 (12.5-15.9)	14.0±0.83 (12.5-17)	14.02±0.85 (12.5-15.5)	13.94±0.81 (12.5-17.1)	0.494
Hematocrit in %	41.82±2.70 (37.2-49.6)	41.05±2.28 (37.4-47.4)	41.86±2.67 (37.3-51.6)	41.76±2.40 (38.2-45.8)	41.64±2.6 (37.2-51.6)	0.168
MCV in FL	88.42±5.07 (9.2-98.6)	89.14±5.11 (78.6±98.8)	88.31±5.17 (78.5-97.2)	86.64±6.34 (79.0-96.8)	88.46±5.20 (78.5-98.8)	0.286
MCHC in g/dl	33.51±1.19 (31.5-36.8)	33.87±1.04 (31.3-36.2)	33.62±1.14 (31.5-36.5)	33.73±1.12 (31.0-35.4)	33.63±1.14 (31-36.8)	0.169
RDW in %	14.32±0.73 (12.1-15.1)	14.16±0.90 (12.0-15.2)	14.20±0.77 (12.0-15.4)	4.08±0.88 (12.1-14.9)	14.25±0.79 (12.0-15.4)	0.841

The three methods to estimate haemoglobin or hematocrit in widespread use are the copper sulfate method, spun hematocrit and spectrophotometric method of haemoglobin measurement.²⁰ Neufeld et al assessed the comparability of the concentration of haemoglobin in venous and capillary blood and found that capillary blood has 0.5g/dl higher values than venous blood. Thus, the method of analysis and also the sampling site has to be taken into consideration.²³

Hematologic recovery after whole blood or red cell donation depends on total body iron stores. The current limitations on the donation interval and frequency reduce but do not eliminate the risk of iron depletion in regular repeat blood donors. Initially, although the haemoglobin concentration is unaffected, iron stores are depleted unavoidably with increase in the frequency of blood donation. The physiologic consequences of low iron stores in the absence of anaemia are controversial, with health reports of both beneficial and detrimental effects.²⁰ Depletion of Iron store in the absence of anaemia may be common among donors particularly mothers and menstruating females.²⁴

Iron deficiency in an individual can be detected only by estimation of serum ferritin levels. In order to fulfill the global and national drive to recruit and retain regular repeat voluntary blood donors, the iron status of the donors needs to be identified and necessary steps taken for iron supplementation.²⁵

Knowledge of pre-donation serum ferritin levels helps to decide if a donor should be offered iron supplementation or not after donation of blood.

Rosvik et al has recommended that donors with serum ferritin levels below 50µg/L should be given iron while donors with levels above 80µg/L needs no additional iron.²⁶ There are no formal recommendations in standards or regulations for the use of iron supplementation after

blood donation, but dietary advice is a relatively widespread practice in donor centers. Even casual use of iron supplementation has shown to be advantageous to blood donors.²⁰ The blood donors at risk of developing iron deficiency can be detected only by the estimation of the levels of serum ferritin levels. The iron status of the donors should be identified and necessary steps for iron supplementation need to be taken to fulfill the national and global drive for the blood requirements.²⁵

In our study we found that the p value with regard to the frequency of donation and haemoglobin levels were not a significant finding. This is similar to the study by Vahid et al, Saleh M Abdulla, Toby et al, and Finch et al.²⁷⁻²⁹ This is in accordance with the study by Vahid et al who also found similar findings between haemoglobin and MCV with donation intervals.²⁷ Saleh M Abdulla also found that the MCV and MCH values when comparing all donor groups with each other were not statistically significant.²⁸

Toby et al, Natarajan et al, Noraskin et al, Finch et al and Rodolfo et al also found similar findings.^{6,30-32} This is with contrast with Vilsu et al who found gradual decrease in haemoglobin, MCV MCH and RDW as number of donation increased and observed significant correlation in donors donating 21-50 and >50 times.³³ Zahra et al found statistically significant difference between groups when the mean values of haemoglobin and MCV were considered.³⁴

We found a statistically significant correlation between frequency of donation (control groups and donating once or twice or thrice in a year) and serum ferritin levels. This is in correlation with the finding of Noraskin et al, Romaila Mittal et al, Saleh M. Abdullah, Rodolfo et al, Zahra et al, Natarajan et al, Ahmed Badar et al, Finch et al, Boulahriss et al and Krishna et al who found a similar significant relationship between frequency of donation and serum ferritin levels.^{6,19,28,30-34,36,37}

We found a statistically significant decrease in serum ferritin levels with the total number of donations in the life time. This finding correlated with the study by Vilsu et al.³³

However, it is in contrast to the study by Toby et al and Romilla Mittal et al who found no statistical significant findings.^{29,35}

We found no significant association between dietary history and serum ferritin levels. Most of our donors gave history of intake of non-vegetarian food once or twice in a week. This is similar to the study by Romilla Mittal et al and Vilsu et al who also found no difference in iron profile of vegetarian and non-vegetarian.^{32,33} However, Richard et al and Leggett et al had showed that ferritin concentration was related to the amount of meat consumed in the diet, with vegetarians having lower concentrations of serum ferritin.^{38,39} Robert et al found that normal men consuming mixed diet containing 15 mg of iron and having the phlebotomy loses did not compensate for the iron loss by increasing the iron absorption sufficiently.⁴⁰

In our study we found that the mean \pm standard deviation of serum ferritin similar to the study by Romilla Mittal et al but markedly lower than the studies by Saleh M Abdulla and Rodolfo et al.^{7,28,35} Romilla mittal et al found that among the first time donors the frequency of decreased iron stores were seen in 8% and 50% of male and female donors respectively, in donors donating blood once in a year decreased iron stores were seen in 21% and 46% respectively, in donors donating twice in a year decreased iron stores were seen in 29% and 27% respectively and in donors donating blood thrice in a year decreased iron stores were seen in 49% and 100% respectively.³⁵

Norashikin et al has showed that 11 % of the regular donors had depleted iron stores of <15 ng/ml. Boulahriess et al found that prevalence of iron deficiency was seen in 60% of female regular donors compared to 14% of first time female donors.^{32,36} Krishna et al showed that prevalence of iron deficiency was seen in 14.1% of overall donors with 19.9% of females and 25.1% of those who donated 3-4 whole blood units during the previous 12 months.³⁷

CONCLUSION

In our study, there was a definite correlation between increase in frequency of donation and fall in serum ferritin level. Haemoglobin levels of the donors were not matched with corresponding serum ferritin levels. The haemoglobin level of ≥ 12.5 g/dl in donors with serum ferritin of <15 ng/ml could probably be explained by different stages in development of iron deficiency anaemia, in particular pre-latent and latent stages. The same explanation could be given for the lack of changes in Red Cell Indices in these donors.

In our study population even, the first-time donors had shown low serum ferritin levels. This is most probably due to their dietary habits and low socioeconomic status. There is a definite relationship between low serum ferritin levels and female donors in reproductive age group. This is because of their lack of dietary replenishment to the physiological demand required. As a part of donor haemovigilance program, our study suggests estimation of serum ferritin level, iron supplementation and donor health education on balanced nutritious diet for at least female donors and regular male donors to maintain adequate donor pool.

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