IRON DEFICIENCY STATUS IN FIRST TIME, REPLACEMENT, VOLUNTARY AND REGULAR MALE BLOOD DONORS AT TERTIARY CARE HOSPITALS OF PESHAWAR, PAKISTAN

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ABSTRACT

OBJECTIVES: To determine iron deficiency in first time, replacement, voluntary and regular male blood donors and to detect pre-clinical iron deficiency in blood donors at tertiary care hospitals of Peshawar, Pakistan by assessing serum ferritin levels.

METHODS: In this cross-sectional descriptive study 152 male blood donors from North West General Hospital and Hayatabad Medical Complex, Peshawar, Pakistan were recruited from 1st December, 2012 to 30th May, 2013. Donors were divided into regular and non-regular (1st time, replacement and voluntary) groups based on number of donations in the past. Quantitative determination of serum ferritin levels was performed by Chemiluminescence immunoassay. Serum ferritin level >30μg/L were taken as normal, 15-30μg/L were reduced and <15μg/L were iron deficiency. Data was analyzed using descriptive statistics in SPSS version 20.

RESULTS: Out of 23 regular donors, 17 (73.9%) while out of 129 non regular donors, 13 (10.1%) developed iron deficiency. The mean number of donations for all donors was 2.8±2.6 (range 0-20). Among non-regular blood donors, 09% 1st time donors, 9.3% replacement donors and 15.8% voluntary donors had iron deficiency. Iron deficiency was recorded in 19.7% of the whole study sample. Statistically significant inverse relationship existed between number of donations and serum ferritin levels (r=-0.193, p 0.017). Also a weak positive relationship between time since last donation (months) and serum ferritin levels (r=0.109, p 0.18).

CONCLUSION: Regular blood donations in males cause serious iron deficiency. Pre-donation serum ferritin analysis identifies and prevents iron deficiency in both regular and non-regular blood donors.

KEY WORDS: Blood Donors (MeSH), Anemia (MeSH), Ferritin (MeSH), Iron (MeSH).

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INTRODUCTION

Blood is donated worldwide so it is our ethical duty to prevent the blood donors from harm.[1] Iron deficiency in first time and repeat blood donors is challenging in transfusion medicine.[2] The influence of blood donation on the body's iron status has been a subject of interest since 1970's.[3] Blood can be donated safely, at a minimum of eight weeks interval but at the risk of developing iron deficiency with repeated donations.[4,5] A strong association has been observed between donation frequency, time since last donation and iron stores.[4] The Hemoglobin (Hb) reaches the pre-donation level by 30 to 50 days in first time donors.[1] There is no major risk associated with blood donation, however, studies have documented that regular blood donors are iron depleted.[6,7] Inadequate dietary iron intake cannot resume iron balance in blood donors.[2] Eligibility criteria for blood donation is a cut-off Hb value of 12.5g/dL.[8] Use of Hb as a screening tool to exclude anaemic donors sometimes fails to identify iron deficient donors whose Hb is above the cutoff limits.[9]

The reticulocytes, Hb content and percentage of hypochromic red cells are very helpful in detecting functional iron deficiency but they have not been validated in the past.[6] Each 1 mL of blood contains 0.5 mg of iron roughly, hence donation of one unit of whole blood removes 4-10% (approximately 250 mg) of the body iron and with resulting fall in Hb after 3 days.[8,10] It takes about 150 days to replenish 220-320 mg of iron lost by donation. Hence repeated donations cause further iron depletion.[1,11]

Hemoglobin levels may not correlate significantly with the underlying iron status of the donor and is not a sensitive test to rule out the early stages in the development of iron deficiency.[6,12] For precise assessment of the body's iron level and diagnosis of iron deficiency,

different blood parameters have been recommended.[9,13,14]

Serum ferritin (Fe) level is considered most consistent test for the assessment of iron status of the body. Low levels of serum ferritin occur when there is a reduction in iron stores of the body.[6,12] However, ferritin is an acute phase reactant as well. Therefore; a high level of serum ferritin may show a false result unless presence of any infectious or inflammatory condition is not ruled out.[15,16]

Keeping in mind, the widespread incidence of iron deficiency in blood donors, this study was conducted to determine iron deficiency in first time, replacement, voluntary and regular male blood donors and to detect pre-clinical iron deficiency in blood donors at tertiary care hospitals of Peshawar, Pakistan by assessing serum ferritin levels.

METHODS

A cross-sectional descriptive study was conducted in the Department of Pathology, North West General Hospital and Research Centre, Peshawar, Department of Haematology, Hayatabad Medical Complex (HMC), Peshawar and Institute of Basic Medical Sciences (IBMS), Khyber Medical University (KMU), Peshawar from December 1, 2012 to May 30, 2013. Ethical approval was taken from the institutional research ethical committee.

After taking informed consent healthy male blood donors, aged between 17-60 years, weight more than 50kg & with hemoglobin (Hb) level > 13.0g/dl were included in the study. Selected donors were asked certain questions according to a pre-designed questionnare. Smokers, tobacco users, known anemics, iron deficient; those on iron supplementations were excluded. Also donors with any acute condition or inflammatory disease or history of hospitalization in the past 6 months were excluded.

Non-probability purposive sampling technique was used. The total sample was divided into four main categories, according to the number of blood donations and frequency of donations. Group A: 1st time blood donors (they had not given any previous blood donation) Group B: Voluntary donor (those who donated blood without remuneration or any family relation). Group C: Replacement donor (they were patient's relatives or friends who had given ≥ 1 donations in last 12 months), Group D: Regular donors (they had donated blood 3-4 times previously, in last 12 months).

From all the included 152 male blood donors, from the afore mentioned Tertiary Care Hospitals a sample of venous blood was obtained and tested in the laboratory of KMU-IBMS for certain hematological and biochemical parameters.

Blood samples were taken in two vacutainer tubes, Ethylene Diamine Tetra Acetic Acid (EDTA) and a plain tube with gel. Complete blood count was performed on the same day on Automated Hematology Analyzer (Sysmex XS-1000i, Sysmex Corporation, America). To exclude any acute condition or inflammatory condition, qualitative CRP analysis was done using CRP-latex test based on slide agglutination method using the kit (SPINREACT, Spain). Only CRP negative blood samples were included for further analysis. Quantitative determination of circulating ferritin concentrations in human serum was done by Chemiluminescence immunoassay (CLIA) (Ferritin Acculite CLIA kit).

Blood smears of all donors were made and examined for red cell morphology. In iron deficiency red blood cells appear microcytic and hypochromic.

For diagnosing iron deficiency in male blood donors, various cut-off vaues were set. In this study iron stores were considered normal for serum ferritin level above 30 μg/L, values between 15-30 μg/L were reduced and < 15 μg/L were iron deficiency.[12,17]

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 20. Comparison between groups was done using chi-square test. For quantitative variables, mean ± standard deviation was designed. Pearson's correlation coefficient was applied on different iron parameters to measure the degree of linear relationship between variables.

RESULTS

The study was conducted on 152 male blood donors of which 129 (84.9%) were non-regular blood donors while 23 (15.1%) were regular blood donors. Among 129 non-regular blood donors, 67 (51.9%) were 1st time blood donors, 43 (33.3%) were replacement donors and 19 (14.7%) were voluntary blood donors. The baseline characteristics of the included sample are detailed in Table I:

Table II elaborates various parameters tested on donor blood sample

TABLE I: BASELINE CHARACTERISTICS OF BLOOD DONORS

Donor type		Age in years (range)	No. of donations
Non regular donors (n=129)	1st time donor (n = 67)	17-55	0
	Replacement donor (n = 43)	18-45	1.6±1.1 (1-5)
	Voluntary donor (n = 19)	19-48	2.2±1.9 (1-8)
Regular Donors	Regular donor (n = 23)	18-47	5.6±3.3 (4-20)
Total (n = 152)		17-55	2.8±2.6 (0-20)

TABLE II: COMPARISON OF BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS AMONG BLOOD DONOR GROUPS

Parameter	Non Regular Donors			Regular donors (n = 23)	One way ANOVA (P-value)
	1st time donor (n = 67)	Replacement donor (n = 43)	Voluntary donor (n = 19)		
MCV (fl)	81.7±4.4	81.5±4.2	82.5±3.8	78.8±4.9	0.02
MCH (pg)	27.4±2.3	27.8±2.0	27.9±1.1	26.5±2.9	0.1
RDW (%)	10.7±0.8	10.5±0.7	11.8±1.0	10.9±0.9	0.005
S. Ferritin (ug/L)	77.9±72.5	92.7±79.3	66.7±61.5	23.7±30.2	0.001
Platelets (10^9/L)	269.5±62.1	271.4±56.8	278.9±65.6	257.1±52.4	0.68
Pre donation Hb (gm/dl)	14.8±0.8	14.8±0.7	14.8±0.8	14.6±0.9	0.7
Hematocrit (%)	44±2.7	43.2±2.8	43.4±2.5	43.3±2.7	0.42

MCV= Mean corpuscular volume , MCH= mean corpuscular hemoglobin , RDW= red cell distribution width

TABLE III: IRON STATUS AMONG BLOOD DONOR GROUPS

Iron Status	Non Regular Donors			Regular donor (n = 23)	P-value
	1st time donor (n = 67)	Replacement donor (n = 43)	Voluntary donor (n = 19)		
Iron deficiency present n (%)*	6 (9%)	4 (9.3%)	3 (15.8%)	17 (73.9%)	< 0.001****
Reduced iron levels n (%)**	14 (20.9%)	8 (18.6%)	4 (21%)	1 (4.4%)	
No iron deficiency n (%)***	47 (70.1%)	31 (72.1%)	12 (63.2%)	5 (21.7%)	
Total	67 (100%)	43 (100%)	19 (100%)	23 (100%)	

*Iron Deficiency: (<15ug/l); **Reduced Iron Level: (15-30ug/l); **No iron Deficiency: (>30ug/l); ****at 5% significance level

TABLE IV: RELATIONSHIP BETWEEN IRON DEFICIENCY AND DONOR TYPE

		Donor type		Total	P-value
		Non Regular Donor	Regular Donor		
Iron Deficiency	Yes	13 (10.1%)	17 (73.9%)	30 (19.7%)	<0.001*
	No	116 (89.9%)	06 (26.1%)	122 (80.3%)	
	Total	129	23	152	

*Chi square test at 5% significance level

before the blood donations is executed. The mean MCV of the whole study sample was 81.3±4.4 fl, mean MCH was 27.4±2.2pg, mean RDW was 10.8±0.8%, mean serum ferritin was 72.5±71.6 ug/L, mean platelets count was 269.3±59.5 x 10^9/L, mean Hemoglobin was 14.7±0.8gm/dl and mean hematocrit was 43.6±2.6%.

On applying one way ANOVA at 5% significance level, we observed a statistically significant difference between the donor groups and MCV (p 0.02), RDW (p 0.005) and serum ferritin (p 0.001). (Table II)

Using a cutoff point of <15ug/l for serum ferritin, iron deficiency was recorded in 10.1% of non-regular blood donors while it was recorded in 73.9% of regular blood donors (p < 0.001). (Table III and Table IV). Overall, iron deficiency was recorded in 19.7% of the whole study sample of 152.

Pearson correlation test was applied at 5% level of significance to study the bivariate relationship between number of donations and its correlation with serum ferritin levels. It was observed that a weak but statistically significant inverse relationship existed between number of donations and serum ferritin levels. (r = - 0.193, p 0.017). Moreover, there was also a weak positive relationship between time since last donation (months) and serum ferritin levels (Pearson r = 0.109, p 0.18).

In this study, out of 62.5% blood donors with normal ferritin levels, 85.3% showed normal red cell morphology while 14.7% showed microcytic and hypochromic blood picture. Among iron deficient blood donors and those with reduced iron levels, 66.7% and 22.2% blood donors respectively showed microcytic hypochromic blood picture.

DISCUSSION

Blood is donated as a "gift of life" therefore; donor's safety and protection should be of prime importance. A number of studies have shown that frequent

blood donation can cause sub-clinical iron deficiency.[6] To protect the donors from depletion of iron stores and development of iron deficiency, the donor selection criteria should have been revised but still current guidelines in most of the countries only require pre-donation hemoglobin measurement for donor selection.[6,18,19]

The frequency of iron deficiency among blood donors differs, depending on many factors. The REDS-II Donor Iron Status Evaluation (RISE) study revealed that 47% of frequent male donors were iron deficient.[4] The prevalance of iron deficiency was higher in RISE study, compared to this study as 19.73% of our study population were iron deficient. This can be due to number of reasons i.e. RISE study used a number of iron parameters with different reference ranges, also hemoglobin level set for donation was low 12.5g/dl compared to current study.

Descriptive analysis was done, first among regular and non-regular blood donors and then between the subgroups-of non-regular donors. Taking out the mean value of different biochemical and hematological parameters used in this study, it was recorded that the mean values were lower for all the variables in blood samples of the regular donors as opposed to non-regualr donors. Same results were observed in blood donors of Saudi10 and Nigeria.[3]

The comparison of serum ferritin values among sub-groups of non-regular donors showed that 1st time donors and replacement donors are safer groups for blood donation compared to voluntary donors. This may be because voluntary donors had overall more donations done as compared to the other two groups. Also their time since last donation was also less as comapred to the other groups.[4,10] Our study shows that depletion of iron stores is related to increasing number of blood donations in last 12 months. This is comparable to a study done in Hong Kong.[19]

In this study 19.7% of the male blood donors, meeting the selection criteria with normal haemoglobin level had sub-clinical iron deficiency. This shows that haemoglobin level does not directly associate with iron status.[4,18,19]

Current study also shows that serum ferittin levels are much lower in regular donors as compared to non-regualr donors. This finding also correlates with the results reported in a number of other studies.[8,18] Similarly a local study done in Pakistan demonstrated that, blood donors who have donated blood four times or more in last two years, are likely to develop iron deficiency and iron deficiency anemia as compared to those who donated less frequently.[20]

This study demonstrated that the total number of blood donations also affects the iron status as 73.9% of regular blood donors while 15.8% voluntary donors and 9% each of the 1st time and replacement donor were found to be iron deficient. A similar study done in Iran favours our findings.[21]

Further large scale studies with multiple parameter analysis including haemoglobin, ferritin, iron binding capacity, hepcidin, erythropoietin, soluble transferrin before donation and after donation are recommended for future research to determine the exact time needed for these parameters to return to normal.

CONCLUSION

Blood donors are at serious risk of developing iron deficiency with repeated donations. Predonation measurement of serum ferritin, identifies sub-clinical iron deficiency in regular as well as the first time, voluntary and replacement blood donors. Many blood donors with acceptable Hb level have either reduced iron stores or iron deficiency.

RECOMMENDATIONS

Government should bear the cost of pre-donation ferritin assesment to keep flow of donors. This free of cost investigation will encourge blood donation, as we only have 15.1% regular blood donors. Prolongation of donation interval or provision of free iron supplements is necessary for donor welfare.

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CONFLICT OF INTEREST

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Following authors have made substantial contributions to the manuscript as under:

KH: Acquisition of data, drafting the manuscript, final approval of the version to be published

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SF: Drafting the manuscript, final approval of the version to be published

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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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