TERUMO PENPOL REVIEW
ON BLOOD MANAGEMENT SYSTEMS

APR-JUN 13 NUMBER 74

Rev Bras Hematol Hemoter. 2012;34(5):356-60

Published in every quarter by TERUMO PENPOL Limited

TERUMO PENPOL®

Etiology of anemia of blood donor candidates deferred by hematologic screening

Michel Alves da Silva[1]
Renata Andréia Volpe de Souza[2]
Aline Meneses Carlos[2]
Sheila Soares[2]
Helio Moraes-Souza[2]
Gilberto de Araujo Pereira[2]
[1]Universidade Federal de Minas Gerais - UFMG, Belo Horizonte, MG, Brazil
[2]Universidade Federal do Triângulo Mineiro - UFTM, Uberaba, MG, Brazil

Objective : Iron deficiency is the most common cause of anemia and one of the main factors in the clinical deferral of blood donors. This fact prompted the current study that aimed to determine the prevalence and etiology of anemia in blood donor candidates and to evaluate the hematological screening technique used for the exclusion of these donors.

Methods : This was a prospective study that compared two groups (Anemic and Non-anemic). Initially screening for anemia was performed by manually measuring hemoglobin (Bioclin® Kit); the results were subsequently compared with an automated screening method (Coulter T-890). The etiology was investigated by hemoglobin electrophoresis in alkaline and acid pH, Hb

A2 dosage and measurement of the ferritin concentration by immunoagglutination. Differences and associations of interest were analyzed using the Yates and McNemar's Chi-square tests and the Fisher, Mann-Whitney, Wilcoxon and Kruskal-Wallis tests.

Results: The deferral rate due to anemia was 4.2%; iron deficiency was identified in 37.5% and beta thalassemia in 9.3% of the excluded candidates. There was a significant discrepancy between the two techniques used to measure hemoglobin with 38.1% of initially deferred donors presenting normal hemoglobin levels by the automated method.

Conclusion: The results show a high rate of blood donors being deferred for anemia and confirm that iron deficiency is the most prevalent cause. The discrepancies found by comparing screening methods suggest that hemoglobin and hematocrit levels should be confirmed before deferring a donor due to anemia; this may increase supplies in blood banks.

Keywords: Iron deficiency; Blood donors; Donor selection; Anemia

Introduction

There are several factors that lead to the deferral of candidates from donating blood including anemia, in particular iron deficiency anemia which is strongly linked to the frequency of donations[1,2]. In Brazilian blood banks, about 100,000 blood units are not collected annually due to anemia; this significantly affects the blood stocks in the country[3]. This has also been reported in other countries. A recent multicenter study carried out in several American states reported alarming levels of iron deficiency among repeat donors; two thirds (66%) of women and almost half (49%) of men were iron deficient[4].

Besides iron-deficiency anemia, hemoglobinopathies are common in blood donors and so the early detection of these blood disorders benefits both donors and recipients of blood products. Donors will benefit by the prompt correction of iron deficiency and proper guidance about the disease and recipients by receiving good quality blood[1,2,5-8].

In several countries of the world, including Brazil, screening for anemia is essential for blood donation

and for the subsequent protection of the donor. Hemoglobin levels should be above 12.5 g/dL and 13.0 g/dL and hematocrit concentrations above 38% and 39% in women and men, respectively[9,10].

The most frequently used technique to screen blood donors is a manual measurement of hemoglobin or hematocrit of a blood sample obtained by finger prick[1]. The copper sulfate method has also been used in some countries, although there are still doubts about its sensitivity, specificity and accuracy[11]. Although there is no consensus among blood banks about what is the best method, the International Committee for Standardization in Hematology proposes the measurement of hemoglobin by an automated technique using the cyanmethemoglobin method[12].

Hematological screening of donors in the Uberaba Regional Blood Bank (HRU-MG) was made in the period of this study by manually measuring hemoglobin using the cyanmethemoglobin method (Bioclin kit®, Belo Horizonte, Brazil) in a sample taken from the digital pulp. However, on the possibility of deferral, additional laboratory methods were used for confirmation, investigation of the etiology and to provide guidance, which is done with the individual's transfer to an appropriate referral service.

In 2003, anemia occurred most often in candidates on their first attempt to donate and this was the commonest reason for the clinical deferral of blood donors (4% according to the production report of HRU-MG - data not shown). Thus, the current study aimed to determine the prevalence and etiology of anemia in blood donor candidates and evaluate the screening technique used for the identification and deferral of individuals unsuitable for donation due to anemia.

Methods

This study, carried out in blood donor candidates of HRU-MG, was approved by the Research Ethics Committee of the Universidade Federal do Triângulo Mineiro (UFMG - Protocol #4532004).

In the period from August 2005 to March 2006, the HRU-MG received 13,416 candidates for blood

donation, of which 2170 (16.2%) were considered clinically unfit and the remaining 11,246 were referred for hematological screening using a sample obtained from digital pulp and processed by the manual cyanmethemoglobin technique employing the Bioclin® kit.

According to this test, 473 (4.2%) had hemoglobin levels below the minimum reference levels and were therefore unsuitable for donation due to anemia; 373 (3.3%) were female and 100 (0.9%) were male.

Of this total (473), 97 blood donor candidates (21 men and 76 women) were invited and agreed to participate in this study. These participants (Anemic Group) were matched for gender and age with 103 successive donors suitable for donation (33 men and 70 women – Non-anemic Group).

After reading and signing an informed consent form, blood samples were collected from both groups (Anemic and Non-anemic) to perform laboratory tests and to investigate the causes of anemia: hematimetry, measurement of ferritin, qualitative hemoglobin electrophoresis in alkaline and acid pH and quantitative electrophoresis for hemoglobin (Hb) A_2 [13,14].

For controls, samples were obtained at the end of donation direct from the distal tube of the blood bag system.

The identification of abnormal hemoglobins was verified by quantitative hemoglobin electrophoresis on cellulose acetate in basic pH (8.4) and on agar in acidic pH (6.2)[13]. The Hb A2 fractions were obtained by segmentation, elution and dosage using a densitometry of the bands resulting from electrophoresis in cellulose acetate and a buffer solution at pH 8.5[14].

The serum ferritin level (ng/dL) was measured using an automated technique based on the principle of immunoagglutination with amplification of the reaction by latex and measurement by turbidimetry. Normal ferritin values using this method are from 12 to 120 ng/dL for women and from 20 to 300 ng/dL for men.

To evaluate the method of screening for anemia employed by the HRU-MG (manual), the hemoglobin levels of both groups were measured by an automated method using a Coulter T-

890 automated blood analyzer (Florida, USA), which also uses the cyanmethemoglobin method. As the reproducibility of this test is more accurate, the patients were regrouped for all other analyses as anemic and non-anemic based on the results.

For statistical analysis, the correlation of the results of anemia concentrations (low Hb) between the manual and automated screening methods was assessed employing McNemar's chi-square test (χ^2_{McN}). The proportions of cases of anemia due to hemoglobinopathies or iron deficiency were initially established according to gender and compared between the Anemic and Non-anemic Groups using the chisquare test with Yates correction (χ^2_{Yates}) or Fisher's exact test (p_{Fisher}). Measurement of the hemoglobin (g/dL) and ferritin (ng/dL) levels were also evaluated according to gender and compared between the Anemic and Non-anemic Groups using the Mann-Whitney test (MW) and within each group the hemoglobin levels (g/dL) were compared between the automated and manual methods using the Wilcoxon signed-rank test (W). Ferritin (ng/dL) was assessed according to gender, group (Anemic and Non-anemic) and number of donations (< 6 and > 6 donations) using the nonparametric Kruskal-Wallis test (KW) followed by Dunn multiple-comparison testing (p_{Dunn}). The choice of a nonparametric test was because the assumption of data normality and the homogeneity of variances for independent samples were not met. Differences of 5% were considered statistically significant in all tests. The STATISTICA computer program (version 6.0) was used to perform all analyses.

Results

On comparing the results obtained by the two screening methods, 37 (38.1%) candidates [13 (61.9%) men and 24 (31.6%) women], originally considered unfit for donation by the manual technique (Bioclin® Kit) were considered fit by the automated method (Coulter T-890). According to the automated test, these 37 candidates had hemoglobin levels within the normal range and thus this change in diagnosis was statistically significant (χ^2_{McN} = 35.1: p < 0.0001, χ^2_{McN} = 11.1: p =

0.0009 and χ^2_{McN} = 22.04: p < 0.0001 for the total, for men and for women, respectively). Of the donors originally considered suitable for donation, 15 (14.6%) individuals, all female (21.4%), had hemoglobin levels below the normal range according to the automated test; this was a statistically significant difference (χ^2_{McN} = 13.1; p = 0.0003). For the other analyses, the donors were regrouped as anemic (n = 75) and non-anemic (n =125) according to the results of the automated method. When the hemoglobin levels (g/dL) were compared between the automated and manual techniques, the levels of the automated test were significantly higher for both genders in the Non-anemic Group (p_W = 0.002 and p_W = 0.0001 for men and women, respectively) compared to the manual method. While on comparing the Anemic Group this difference was not significant (p_W = 0.353 and p_W = 0.810 for men and women, respectively). The hemoglobin levels were significantly higher in the Non-anemic Group than the Anemic Group for both genders (Table 1).

The total rate of iron deficiency of all four groups together was 20.5%. On analyzing the iron deficiency between the groups (Anemic and Non-anemic), six men (75.0%) of the anemic blood donor candidates suffered from iron deficiency while among the non-anemic blood donor candidates this rate was 15.9%, i.e. iron deficiency was significantly associated with anemia in male donors (χ^2_{Yates} = 9.7; p = 0.002). For the females, 32.8% (n = 21) of blood donor candidates in the Anemic Group had iron deficiency; this was significantly higher (χ^2_{Yates} = 13.1; p = 0.0003) than the female candidates in the Non-anemic Group (7.6%; n = 6 - Table 2).

Table 1 - Hemoglobin levels (g/dL) of 200 blood donor candidates grouped as anemic (n = 75) and non-anemic (n = 125) by the automated test and stratified according to gender (male and female) and technique (manual and automated)

		Method			
		Manual		Automated	
Group		**Male**	**Female**	**Male**	**Female**
Non-anemic	**n**	46	79	46	79
	P 2.5%	12.8	12.0	13.7	12.8
	Median	14.0	12.8	14.6	13.2
	P 97.5%	15.2	13.4	15.8	13.8
	*	$p_W = 0.002$	$p_W < 0.0001$	-	-
	#	$p_{MW} < 0.0001$	$p_{MW} < 0.0001$	$p_{MW} < 0.0001$	$p_{MW} < 0.0001$
Anemic	**n**	8	67	8	67
	P 2.5%	11.6	11.2	10.8	11.3
	Median	12.3	11.7	12.3	11.8
	P 97.5%	12.5	12.2	12.5	12.2
	*	$p_W = 0.353$	$p_W = 0.810$	-	-

*: Comparison between the techniques (Manual and automatic) for each group and gender; #: Comparison between groups (Anemic and Non-anemic); p_W: p-value for the paired Wilcoxon test; p_{MW}: p-value for the Mann-Whitney test; n: number of donors; P 2.5%: 2.5% percentile; P 97.5%: 97.5 % percentile

Table 2 - Occurrence of iron deficiency in blood donor candidates according to the groups (Anemic and Non-anemic) by gender

		Anemic		Non-anemic			
	Iron deficiency	**n**	**%**	**n**	**%**	χ^2_{Yates}	**p-value**
Male	Yes	6	75.0	7	15.9	9.7	0.002
	No	2	25.0	37	84.1		
	Total	**8**	**100**	**44**	**100**		
Female	Yes	21	32.8	6	7.6	13.1	0.0003
	No	43	67.2	73	92.4		
	Total	**64**	**100**	**79**	**100**		

§: the ferritin of 5 donors was not measured (2 Non-anemic and 3 Anemic)

Of the group of anemic blood donor candidates, 9.3% (n = 7) presented electrophoretic profiles with alterations that might justify the presence of anemia due to a hemoglobinopathy; Hb A2 was elevated in 8.0% (n = 6) and Hb A1S together with Hb A2 was elevated in 1.3% (n = 1). In the Non-anemic Group, 7.2% (n = 9) of candidates presented with elevated Hb A_2. No statistically significant difference was observed in the percentage of hemoglobinopathies between the groups ($p_{Fisher} = 0.212$ – Table 3).

Table 3 - Electrophoretic profile and Hb A2 dosage according to the groups of candidates (Anemic and Non-anemic)

	Group				Total	
	Anemic		Non-anemic			
Hemoglobin	**n**	**%**	**n**	**%**	**n**	**%**
(A1) (A2 normal)	65	86.7	116	92.8	181	87.6
(A1) (A2 elevated)	6	8.0	9	7.2	15	10.3
(A1S) (A2 normal)	3	4.0	0	0.0	3	1.6
(A1S) (A2 elevated)	1	1.3	0	0.0	1	0.5
Abnormal	10	13.3	9	7.2	19	9.5
Total	**75**	**100**	**125**	**100**	**100**	**100**

The abnormal cases - (A1) (A2 elevated) + (A1S) (A2 normal) + (A1S) (A2 elevated) - are not included in the sum of the columns; $p_{Fisher} = 0.212$ [test performed considering the categories A1 (A2 normal) versus abnormal]

The ferritin level was lower in individuals with a high number of donations. This difference was significant for both men and women in the Non-anemic Group ($p_{Dunn} < 0.0001$ and $p_{Dunn} = 0.0357$, respectively) while in the Anemic Group, a significant difference was observed only for women ($p_{Dunn} < 0.0001$). In addition, the levels of ferritin (ng/dL) were significantly lower in the Anemic compared to the Non-anemic Group for both genders and for the number of donations ($p_{Dunn} < 0.0001$).

Discussion

The high rate of candidates who were unfit to donate due to anemia (4.2%), which was as high as 11.3% in women, confirms reports in the literature[14,15] that identify woman as being more predisposed to anemia due to menstruation and pregnancy which is intensified by blood donations. Such a level of unsuitability, as has already been observed in other studies, compromises the blood supply[1].

The significantly higher hemoglobin levels by the automated method points to discrepancies between the methods used. Despite this, the differences in the means obtained varied between 0.1 g/dL and 0.6 g/dL. This difference is considered acceptable for the screening method used (Bioclin® kit) as, according to the instructions of the kit, errors of up to 5.0% are permissible, which in the case of male (13.0 g/dL) and female (12.5 g/dL) donors corresponds to 0.7 g/dL and 0.6 g/dL, respectively. These differences, based on the specifications of the instructions, do not characterize failure of the technique employed and are in accordance with the study of Rosenblit et al.[16] who found a difference of 0.6 g/dL between two automated techniques. Research carried out in Northern England, employing the copper sulphate precipitation technique to screen blood donors also observed differences between tests of 0.24 for men and 2.8 for women[17]. It is recommended that the variations should not exceed 0.3 g/dL when employing the cyanmethemoglobin method[18].

It is interesting that 38.1% of individuals considered unsuitable by the finger prick technique, would have been considered fit by the automated technique using a

sample obtained by venipuncture. These findings reinforce the need for stringent controls and periodic evaluations of the screening technique as, with this false positive rate, if extrapolated to the total number of individuals excluded for anemia every year in Brazil, would represent the inclusion of approximately 40,000 donors.

The general index of iron deficiency in the tested blood donor candidates (anemic and non-anemic) was 20.5% with a slightly higher prevalence in men (25.0%) than in women (18.9%), and significantly higher in the Anemic Group, for both genders as expected. Iron deficiency was responsible for anemia in 37.5% of the Anemic Group. The worryingly high iron deficiency rate observed in this study was similar to the result found in 348 male and female blood donors in Port Harcourt in Nigeria (20.6%)[19]

– a country in worse economic conditions than Brazil - and much higher than the results of a study carried out in the blood bank of Santa Casa de São Paulo[1], in which 11% of 300 blood donors of both genders had iron deficiency[5], and in an Iranian study of male blood donors (14.1%)[20]. However, alarming results on iron deficiency were also found in a North American study on repeat donors in which two-thirds (66%) of women and almost half of men (49%) had iron deficiency[4].

The fact that the non-anemic individuals in this study presented ferritin levels higher than anemic candidates, although expected, reinforces the importance of this test in the propedeutics of anemic donors. In addition, identifying non-anemic donors with low levels of ferritin (10.6%) should be the reason for prompt intervention to prevent anemia; this supports the position of some authors who suggest that ferritin should be measured in the screening of donors[19-23], particularly those who donated more than five times[5,19] as well as iron supplementation for iron deficiency[24,25].

Studies have shown that ferritin levels drop with the number of donations[2,5,6,20] and the greater frequency in male and female donors than in individuals who are not donors[5]. In this study, the ferritin levels dropped

parallel to the number of donations with more consistent declines being observed in individuals who made six or more donations when compared to those who donated less than six times, thus proving the influence of the number of donations on serum ferritin levels.

Besides iron-deficiency anemia, beta thalassemia was identified as a possible cause of anemia in 9.3% of the anemic individuals in this study. Elevated Hb A2 was also found in 7.2% of the candidates in the Non-anemic Group even though they did not present with anemia. Published data show that beta thalassemia varies between regions and that heterozygosity for thalassemia is responsible for the greatest difficulty of diagnosing anemia followed by rare variants, and interactive forms of hemoglobinopathies[26,27]. A study of the etiology of anemia in 58 patients without iron deficiency and 235 controls demonstrated that 32.8% of the patients and 0.9% of the controls were beta thalassemia carriers[28]. Hence, our findings of 7.2% of individuals in the Non-anemic Group with suspicion of beta thalassemia are well above what would be expected.

However, researchers recommend caution when diagnosing beta thalassemia only by the dosage of Hb A2. They point out that elevated levels can also be detected in other acquired and congenital conditions and suggest repeating the test before arriving at any diagnostic conclusion[7,29]. Thus, we recommend further studies to confirm these findings.

The results demonstrated evidence of a high rate of deferral of donors due to anemia, and the discrepancies observed between the manual screening technique used and automated screening suggest the need for standardization, constant control of the hematological screening technique employed and confirmation of hematimetric levels before deferring a candidate due to anemia. Iron deficiency has been confirmed as the leading cause of deferral of blood donor candidates due to anemia; this increases as the number of donations increases suggesting that the measurement of ferritin levels should be included in the screening process,

especially after multiple donations and for individuals with hematimetric levels close to cut-off limits. Additionally, iron supplementation should be provided to all repeat donors and donors with hemoglobin or hematocrit levels below or even near to the normal cut-off limit.

References

1. Cançado RD, Chiattone CS, Alonso FF, Langhi Júnior DM, Alves Rde C. Iron deficiency in blood donors. São Paulo Med J. 2001;119(4):132-34.
2. Addullah SM. The effect of repeated blood donations on the iron status of male Saudi blood donors. Blood Transf. 2011;9:167-71.
3. Brasil. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (ANVISA). Relatório de produção da hemorrede em 2002: perfil sorológico dos doadores [Internet]. 2002 [cited 2011 March 10].Available from: http://portal.anvisa.gov.br/.
4. Cable RG, Glynn SA, Kiss JE, Mast AE, Steele WR, Murphy EL, Wright DJ, Sacher RA, Gottschall JL, Vij V, Simon TLCable R, Rios J, Benjamin R, Roback JD, Sacher RA, Wilkinson SL, Carey PM, Murphy EL, Custer B, Hirschler N, Triulzi D, Kakaiya R, Kiss J, Gottschall JL, Mast AE, Schulman J, King M, Nemo GJ, Busch MP, Norris P; NHLBI Retrovirus Epidemiology Donor Study-II. Iron deficiency in blood donors: analysis of enrollment data from the REDS-II Donor Iron Status Evaluation (RISE) study. Transfusion. 2011;51(3):511-22. Comment in: Transfusion.2011;51(3):458-61.5. Garcia-Casal MN. La deficiência de hierro com problema de salud pública. An Venez Nutr. 2005;18(1):45-8.
6. Alvarez-Ossorio L, Kirchner H, Klüter H, Schlenke P. Low ferritin levels indicate the need for iron supplementation: strategy to minimize irondepletion in regular blood donors. Transfus Med. 2000;10(2):107-12. Comment in: Transfus Med. 2001;11(1-59-60.
7. Lisot CL, Silla LM. Triagem de hemoglobinopatias em doadores de sangue de Caxias do Sul, Rio Grande do Sul, Brasil: prevalência em área de colonização italiana. Cad Saúde Pública. 2004;20(6):1595-1601.
8. Piedras J, Alvarez E, Herrera FM, Córdova MS. Clinical usefulness of mean corpuscular volume and red cell distribution width in iron deficient blood donors. Rev Invest Clin. 1993;45(5):469-72.
9. Mendrone Jr A, Sabino EC, Sampaio L, Almeida Neto C, Schreiber GB, DA Chamone, Dorlhiac-Llacer PE. Anemia screening in potential female blood donors: comparison of two different quantitative methods. Transfusion. 2009;49(4):662-68.
10. Brasil. Ministério da Saude. Agência Nacional de Vigilância Sanitária (Anvisa). Resolução RDC nº 57, de 17 de outubro de 2010. Diário Oficial da União. 2010 Dez 16. [cited 2011 Oct 11]. Available from: http://portal.anvisa.gov.br/.
11. Russel BL, Martin SM. Blood donor rejection rate: HemoCue® hemoglobin analyzer vs. microhematocrit. Clin Lab Sci.1997;10(6):321-4.
12. Zwart A, van Assendelft OW, Bull BS, England JM, Lewis SM, Zijlstra WG. Recommendations for reference method for haemoglobinometry in human blood (ICSH standard 1995) and specifications for international haemiglobincyanide standard (4th ed). J Clin Pathol. 1996;49:271-4.
13. Naoum PC. Eletroforese: técnicas e diagnósticos. 2rd ed. São Paulo: Editora Santos; 1999.
14. Abu-Sitta AR, Dalton HR. Anaemia in a 17 year old student. BMJ. 2008;337:a1845.
15. Lorenzi TF, Amico ED, Daniel MM, Silveira PA, Buccheri V. Manual de hematologia: propedêutica e clínica. 3rd ed. São Paulo: Medsi; 2003. p.193-288.

16. Rosenblit J, Abreu CR, Szterling LN, Kutner JM, Hamerschlak N, Frutuoso P, et al. Evaluation of three methods for hemoglobin measurement in a blood donor setting. Sao Paulo Med J. 1999;117(3):108-12.

17. Oliveira RA, Poli Neto A. Anemias e leucemias: conceitos básicos e diagnóstico por técnicas laboratoriais. São Paulo: Roca; 2004. p. 389-410.

18. Lloyk H, Collins A, Walker W, Fail B, Hamilton PJ. Volunteer blood donors who fail the copper sulfate screening test. What does failure mean, and what should be done? Transfusion. 1988; 28(5):467-69.

19. Jeremiah ZA, Koate BB. Anaemia, iron deficiency and iron deficiency anaemia among blood donors in Port Harcourt, Nigeria. Blood Transfus. 2010;8(2):113-7.

20. Yousefinejad V, Darvishi N, Arabzadeh M, Soori M, Magsudlu M, Shafiayan M. The evaluation of iron deficiency and anemia in male blood donors with other related factors. Asian J Transfus Sci. 2010;4(2):123-7.

21. O'Meara A, Infanti L, Stebler C, Ruesch M, Sigle JP, Stern M, Buser A. The value of routinen ferritin measurement in blood donors. Transfusion. 2011;51(10):2183-8.

22. Ghosh K. Iron deficiency in healthy blood donors exposes vulnerability of the nation to iron deficiency. Indian J Med Res. 2006;124(6):611-2.

23. Souza CA. Iron deficiency and protection of blood donors. Sao Paulo Med J 2001;119(4):131.

24. Norashikin J, Roshan TM, Rosline H, Zaidah AW, Suhair AA, Rapiaah M. A study of serum ferritin levels among male blood donors in hospital universiti sains Malaysia. Southeast Asian J Trop Med Public Health. 2006;37(2):370-3.

25. Pittori C, Buser A, Gasser UE, Sigle J, Job S, Rüesch M, et al. A pilot Iron Substitution Programme in female blood donors with iron deficiency without anaemia. Targeted iron substitution prevents the development of anaemia and enhances donation return in premenopausal female blood donors with iron deficiency. Vox Sang. 2010;100(3):303-11.

26. Ali M, Lafferty J. The clinical significance of hemoglobinopathies in the Hamilton region: a twenty-year review. Clin Invest Med. 1992;15(5):401-5.

27. Leoneli GG, Imperial RE, Marchi-Salvador DP, Naoum PC, Bonini-Domingos CR. Hemoglobinas anormais e dificuldade diagnóstica. Rev Bras Hematol Hemoter. 2000;22(3):396-403.

28. Wagner SC, Silvestri MC, Bittar CM, Friedrisch JR, Silla LM. Prevalência de talassemias e hemoglobinas variantes em pacientes com anemia não ferropênica. Rev Bras Hematol Hemoter. 2005;27(1):37-42.

29. Gasperini D, Cao A, Paderi L, Barella S, Paglietti E, Perseu L, et al. Normal individuals with high HbA2 levels. Br J Haematol. 1993;84(1):166-8.

CENTRAL MARKETING OFFICE

Terumo Penpol Limited
New No. 71, Gandhi Court,
4th Main Road, Gandhi Nagar,
Adyar, Chennai-600020
Tel – 044-4205 4528/38
0471-3015649/47
tplmarketing@terumopenpol.com
pmt@terumopenpol.com

www.terumopenpol.com
http://www.terumo.co.jp/English/location/japan.html

TERUMO PENPOL®