AVERAGE LEVEL OF FACTOR VIII A IN HEALTHY BLOOD DONORS OF PESHAWAR

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ABSTRACT

Objective: The aim of this study is to determine average level of factor VIII in local healthy blood donors of Peshawar.

Material and Method: It was a descriptive cross sectional study conducted in the blood bank of Hayatabad Medical Complex Peshawar. In this study total number of one hundred and thirty nine (Male n=121, Female n=18) healthy volunteer blood donors coming for blood donation were included and those donors who have any history of bleeding/ family bleeding history were excluded. At the time of blood donation 3 ml blood were collected in citrated anticoagulant tube (Blue Top) from donors and immediately sent to hematology laboratory for determination of factor VIII levels. All donors Factor VIII levels were measured byStago STA Compact Haemostasis analyzer. All data was documented and analysis was performed by SPSS-20. Mean $\pm$ SD was analyzed for age and factor VIII level. Analyzed data was presented in tables and graphs.

Results: Out of these 139 blood donors 78 (56.1%) were found to have Factor VIII levels between 0.5- 1.0 IU/ml and 61(43.9%) had Factor VIII levels between 1.0- 1.5 IU/ml with mean levels of 1.0 $\pm$ 0.498 standard deviation. Factor VIII level was more in females as compared to male. The factor VIII levels were higher in old age group (>50 years).

Conclusions: Factor VIII levels wereperformed in all the blood donors to select FFPs with high levels of Factor VIII given to the hemophiliac patients to attain maximum replacement deficient individuals. This will avoid volume overload due to excess FFP transfusion by giving a product of high yield rather than low factor VIII yield.

Key Words: Factor VIII, Hemophilia, Blood donors, Freshfrozen plasma.

INTRODUCTION

FACTOR VIII (F-VIII) IS blood clotting factor also known as anti-hemophilic factor (AHF)[1]. Factor VIII is encoded by the FVIII gene on the long arm of the X chromosome. Mutations in this gene results in hemophilia A as a result of low or absent factor VIII.[2] Hemophilia has sex-linked transmission and carries a 50% risk of transmitting the disease to male offspring of the female carriers. Hemophilia A is the most common hereditary bleeding disorder, present in about 1 in 5,000-10,000male births.[3] Children present with bleeding tendency after injury or spontaneously depending upon the severity of the disease. The bleeding is common in the joints although other sites can also be affected but knee, elbow and ankle joints are more frequently involved. If not treated adequately the affected child developarthropathies and lifelong disabilities.[4]

Hemophilia was first described in the early 19th century and required comprehensive care, counseling, and support to hemophilic patients because their families had always suffered physical, psychological and financial difficulties. In early 90´s hemophilics were treated with whole blood or fresh plasma. Hemophilia care has improved dramatically as compared to a few generations ago.[5] In developed countries effective and safe factor VIII concentrates and recombinant Factor VIII are widely available for adequate treatment and prophylaxis of bleeding and for prevention and management of chronic complications. Achieving the highest quality of life with factor VIII replacement are now the main goals of hemophilia management.[6]

In developing countries like Pakistan where there is high prevalence of inherited bleeding disorders financially it becomes difficult for families to get proper hemophilia treatment as the cost of factor concentrates is very high.[7] Fresh frozen plasma is the most commonly used product due to financial constraints. Financially it becomes difficult for families to get proper hemophilia treatment and patients get suboptimal doses of blood components mostly fresh frozen plasma and cryoprecipitate.[8]

The ideal treatment for hemophilia is replacement therapy of the missing factor as soon as the bleeding episode is recognized.[9] Fresh frozen plasma and cryoprecipitate are the common modalities used in the treatment of hemophilia. The blood transfusion services now provide FFP and cryoprecipitate for the treatment of hemophilic patients and it is becoming essential to know more about the mean level of factor VIII in our local population.[10] Factor VIII is typically the

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only plasma protein whose levels are quality controlled in the specification of the product, as required by AABB, UK and EU guidelines; this level needs to be met for a proportion of units (typically 0.75 iu /ml).[11] It is likely that there is heterogeneity in levels, reflecting biological variation in factor levels among individual donors and physiologically, factors such as estrogens, pregnancy, exercise, and epinephrine can raise factor VIII.[12]

The treatment of hemophilia requires detail knowledge of the normal blood concentrations of factor VIII. If the normal range varies from 0.5-1.50 iu /ml and if the concentration is inherited and constant in an individual then the selection of high value donor would improve the general treatment of hemophilia patients.[13]

This study will provide strong grounds for hematologists to decide about the provision of correct doses of fresh frozen plasmas to hemophilia patients. Also this study will provide us with local mean level of factor VIII in our population.

MATERIAL AND METHODS

It was a descriptive cross sectional study conducted in blood bank of Hayatabad Medical Complex Peshawar. In this study total number of one hundred and thirty nine (Male n=121, Female n=18) healthy volunteer blood donors were enrolled.All healthy blood donors (presenting to blood bank) meeting the inclusion criteria and having no history of clotting disorder in themselves and family, no history of any infectious disease and no history of blood donation in the last 56 days will be included in the study and those donors who have any history of bleeding/ family bleeding history were excluded. At the of blood donation 3 ml blood were collected in citrated anticoagulant tube (Blue Top) from donors and immediately sent to hematology laboratory, to determine factor VIII assay. All donors Factor VIII levels were measured by Stago STA Compact Hemostasis Analyzer. All data was stored and analyzed in SPSS-20. Mean + SD was calculated for numerical variables like age and factor VIII level. Mean factor VIII level was stratified among age and gender to see the effect modifications. All results were presented in the form of tables and graphs.

RESULTS

Total numbers of 139 healthy blood donors were enrolled in this study. Majority of blood donors,43(30.9%), age was ranged between 20 to 40 years, while only 2(1.4%) blood donors were in the age range of 60-70 years, with mean age of 31 years. (Table No 1)

Out of these 139 blood donors 121 (87.1%) were male while18 (12.9%) were female.(Table no2) Out of these 139 blood donors 78 (56.1%) were found to have Factor VIII levels between 0.5- 1.0 IU/ml and 61(43.9%) had Factor VIII levels between >1.0- 1.5 IU/ml with mean levels of 1.0 ± 0.498 standard deviation. Maximum number of blood donors had Factor VIII levels between 0.5- 1.0 IU/ml.(Table no 3) The higher FVIII levels (> 1.0- 1.5 IU/ ml) are found in upper age group from 50 years to 70 years.(Table No 4)

In 70 males the factor VIII levels was 0.5- 1.0 IU/ ml, the percentage was 57.85%. Whereas factor VIII level of 0.5 – 1.0 IU/ml was found in 8 females (44%). 55.55% females had 1.0- 1.5 IU/ ml levels of factor VIII, whereas it was found in 42.1% male blood donors. A Factor VIII level was more in females as compared to males. (Table No 5)

DISCUSSION

The mean activity of factor VIII in the healthy blood donors in this study was 1.0 iu/ ml with standard deviation ± 0.498 this correlates with the study conducted by Grazzini et al in which mean factor VIII levels were 0.99 iu/ml in random whole-blood plasma produced by the 10 Italian regions.[14] The study conducted in Nigeria demonstrated the mean factor VIII was 1.90 iu/ml. The normal factor VIII levels in Nigerian population was 0.65-5.55iu/ml with the mean value of 1,90iu/ml.[15]

Table No 1: Age of the Blood Donors

Age of blood donors	Frequency	Percent (%)
19-20 years	43	30.9
21-30 years	38	27.3
31-40 years	26	18.7
41-50 years	18	12.9
51-60 years	12	8.6
61-70 years	02	1.4
Total	139	100.0

Mean age was 31 years with ±1.353 standard deviation.

Table No 2: Sex of the Blood Donors

Sex of the Donor	Frequency	Percent(%)
Male	121	87.1
Female	18	12.9
Total	139	100.0

Male to female ratio was 7.7:1

Table No 3: Factor Viii Levels of Blood Donors

Factor VIII Levels	Frequency	Percent(%)
0.5- 1.0	78	56.1
1.0- 1.5	61	43.9
Total	139	100.0

Mean level of factor VIII in blood donors was 1.0 iu/ml with ± 0.498 standard deviation.

Table No 4: Age of the Blood Donors and Factor Viii Levels

Age of the Donor	Factor Viii Levels of the Blood Donors		Total
	0.5 – 1.0 iu/ml	>1.0 – 1.5 iu/ml	
19 -20 years	25	18	43
21 - 30 years	23	15	38
31 - 40 years	17	9	26
41 -50 years	9	9	18
51 -60 years	4	6	12
61 -70 years	0	2	2
TOTAL	78	61	139

Chi-square test was used and P value was 0.03

Table No 5: Gender Wise Factor Viii Levels of the Blood Donors

Sex of the Blood Donors	Factor Viii Levels of the Blood Donors		Total
	0.5 – 1.0 iu/ml	>1.0 – 1.5 iu/ml	
MALE	70	51	121
FEMALE	8	10	18
TOTAL	79	60	139

In this study the levels of factor VIII in females was significantly higher as compared to the levels in male subjects. Overall 42% male had higher levels of factor VIII while 56 % females had higherlevels, this difference was significant (P 0.05). This correlates with the study conducted by Essien EM in Africa which demonstrated that mean factor VIII activity in females was significantly higher than the male subjects.[16] The study conducted by Lowe et al. and Malda M. demonstrated that mean factor VIII levels in young females were higher than males of the same age group.[17] A study by Morange and Kovare also showed that FVIII level in males are lowers than females in both generation.[18] Whereas in the study by Jeremic M. the effect of sex was not significant.[19]

In this study the older age group had significantly higher levels of factor VIII than younger age group. Blood donors in upper age group (50-70years) had levels more than1.0 iu/ml whereas age < 50 years donors had levels below 1.0 iu/ml. The relationship between the levels of factor VIII and age was significant (P= 0.03). The noticeable positive correlation of FVIII plasma levels with the blood donor's age is consistent with a large number of publications. It is well recognized that plasma FVIII levels increase progressively with age. The factor VIII activity in older age group in this study was higher than the young blood donors which correlates with the findings in the study by Jeremic M which show an increased factor VIII levels in older age group.[19] In an another study conducted by Essien EM in Africa no FVIII level differences were noted in different age groups.[15] The study conducted by Lowe and Malda also demonstrated particularly in male donor plasma an increase in FVIII levels with increasing age (P < 0·05).[20]

In this study there is significant variation in factor VIII levels in different geographic groups (P 0.001). Majority of donors from FATA had levels more than 1.0 iu/ml whereas most of the donors of Afghan origin had levels lower than 1.0 iu/ml. In other studies the variation in factor VIII levels has been found in several countries and among widely different geographic groups. Previous population studies conducted by Conlan et al and Miller et al have demonstrated that plasma FVIII levels are influenced by ethnicity and geographic variations, with significantly higher levels in African- Americans compared to Caucasians. The study by Jenkins also showed ethnical and geographical variations in factor VIII levels.[21,22]

CONCLUSSION

It is concluded from the results of our study that the mean and SD values of factor VIII were 1.0 iu/ml with ±349 standard deviation. The mean level of factor VIII was higher in females than males. The levels were higher in older age group than younger age group. The study show geographic variation in the factor VIII levels.

REFERENCES

1. Nichols, Timothy C. et al. "Protein Replacement Therapy and Gene Transfer in Canine Models of Hemophilia A, Hemophilia B, von Willebrand Disease, and Factor VII Deficiency." ILAR journal / National Research Council, Institute of Laboratory Animal Resources 50.2 (2009): 144–167.
2. QIAO, SHU-KAI et al. "Compound Heterozygous Hemophilia A in a Female Patient and the Identification of a Novel Missense Mutation, p.Met1093Ile."

Molecular Medicine Reports 9.2 (2014): 466–470.

3. Orlova, N. A. et al. "Blood Clotting Factor VIII: From Evolution to Therapy." ActaNaturae 5.2 (2013): 19–39.

4. Mansouritorghabeh, Hassan. "Clinical and Laboratory Approaches to Hemophilia A." Iranian Journal of Medical Sciences 40.3 (2015): 194–205.

5. "Abstracts from the 38th Annual Meeting of the Society of General Internal Medicine." Journal of General Internal Medicine 30.Suppl 2 (2015): 45–551.

6. DARGAUD, Y. et al. "Achievements, Challenges and Unmet Needs for Haemophilia Patients with Inhibitors: Report from a Symposium in Paris, France on 20 November 2014." Haemophilia : the official journal of the World Federation of Hemophilia 22.Suppl 1 (2016): 1–24.

7. Ghosh, Kanjaksha, and KinjalkaGhosh. "Management of Haemophilia in Developing Countries: Challenges and Options." Indian Journal of Hematology & Blood Transfusion 32.3 (2016): 347–355.

8. Abstracts from the 37th Annual Meeting of the Society of General Internal Medicine." Journal of General Internal Medicine 29.Suppl 1 (2014): 1–545.

9. Kempton, Christine L., and Gilbert C. White. "How we treat a hemophilia A patient with a factor VIII inhibitor." Blood 113.1 (2009): 11-17. Web.

10. Cicchetti, Americo et al. "Health Technology Assessment of Pathogen Reduction Technologies Applied to Plasma for Clinical Use." Blood Transfusion 14.4 (2016): 287–386.

11. Sultan, Sadia et al. "Internal Quality Control of Blood Products: An Experience from a Tertiary Care Hospital Blood Bank from Southern Pakistan." Journal of Laboratory Physicians 10.1 (2018): 64–67

12. Gibson, D.A. et al. "Estrogen-Dependent Regulation of Human Uterine Natural Killer Cells Promotes Vascular Remodelling via Secretion of CCL2." Human Reproduction (Oxford, England) 30.6 (2015): 1290–1301

13. Rocino, Angiola et al. "Principles of Treatment and Update of Recommendations for the Management of Haemophilia and Congenital Bleeding Disorders in Italy." Blood Transfusion 12.4 (2014): 575–598.

14. GiulianoGrazzin. Quality control of recovered plasma for fractionation: an extensive Italian study. Transfusion; July 2008; 48(7): 1459- 68.

15. Essien EM, Ayeni O. Factor VIII Coagulant Activity in an African Population in Relation to a Recognized Standard. Br J Haematol. March 2008; 39(2): 225-31.

16. Madla W, Alt T, Jungk H, Bux J. Fresh frozen plasma quality: relation to age and gender of blood donors. VoxSanguinis; February 2012; 102(2):116–124.

17. P. E. Morange et al. Biological and genetic factors influencingplasma factor VIII levels in a healthy family population: resultsfrom the Stanislas cohort. Br J Haematol. Jan 2005; 128(1): 91- 99.

18. Kovar, C Marsik-Strasser, C Joukhadar, T Schickbauer, P Kyrle, OWagner and G Endler. Prediction of long-term survival andcoagulation factor VIII levels: interactions with gender in a largehospital-based cohort. Critical care. March 2009; 13(1): 35.

19. Jeremic M, Weisert O, Geddi- Dehl T. W. Factor VIII levels in 1016 blood donors. Effect of age, sex and ABO blood groups; Scandinavian J. clin. lab. invest; 1976; 34; 461-66.

20. Madla W, Alt T, Jungk H, Bux J. Fresh frozen plasma quality relation to age and gender of blood donors. VoxSanguinis February 2012; 102(2):116–124.

21. Conlan, M.G. Folsom, A.R. Finch, A. Davis, C.E. Sorlie, P. Marcucci, G. & Wu, K.K. (1993) Associations of factor VIII and von Willebrand factor with age, race, sex, and risk factors for atherosclerosis. The Atherosclerosis Risk in Communities (ARIC) Study. Thrombosis and Haemostasis, 70: 380–385.

22. Miller, C.H. Dilley, A. Richardson, L, Hooper, W.C. &Evatt, B.L. (2001) Population differences in von Willebrand factor levels affect the diagnosis of von-Willebrand disease in African–American women. American Journal of Hematology. 67: 125–129.