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STUDY OF LABORATORY PARAMETERS IN HEMOPHILIA PATIENTS

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ABSTRACT

Introduction: Haemophilia is X- linked congenital bleeding disorder with a frequency of about one in 10,000 births. Haemophilia is caused by deficiency of coagulation factor VIII (haemophilia A) or factor IX (haemophilia B) related to mutations of clotting factor gene.

Objectives: To check effectiveness of various screening and confirmatory tests for diagnosis of haemophilia.

Methods: Retrospective study of laboratory diagnosis of haemophilia was conducted in our haematology section of pathology department of Tertiary Care Teaching Centre from 1 August 2014 to 30 July 2016. Patients in the age group of 0 year to 55 years with factor VIII and factor IX level below 50% of normal were included in the study. Routine haematological tests like haemoglobin and platelet count and coagulation profile of patient for prothrombin time, activated partial prothrombin time, factor VIII and factor IX level were analysed.

Results: Out of 122 cases, 97 cases were of haemophilia A while 25 cases were of haemophilia B. Haemoglobin count of patients ranged from6gm% to 14.2 gm%. Platelet count and PT (prothrombin time)of patients were within normal limits. APTT (Activated Partial Thromboplastin Time) was prolonged (41.6 sec. to 124 sec) in all patients. Factor VIII level was reduced (<50%) in all patient of haemophilia A. Factor IX level was reduced (<50%) in all patient of haemophilia B.

Conclusion: Laboratory analysis of blood for haemoglobin, platelets, PT and APTT help to suspect the diagnosis. Diagnosis of haemophilia is confirmed by factor VIII assay for haemophilia A and factor IX assay for haemophilia B. Level of factor VII and IX also decide severity of disorder.

Key Words: Haemophilia A, Haemophilia B, Factor VIII, Factor IX

INTRODUCTION

Haemophilia is X- linked congenital bleeding disorder. One in every 10,000 new-borns are suffering from haemophilia. The number of affected persons world-wide is estimated to be about 400,000.[1]

Haemophilia is caused by deficiency of coagulation factor VIII (haemophilia A) or factor IX (haemophilia B) related to mutations of clotting factor gene. Haemophilia A (80-85% of total) is more common than haemophilia B (15-20% of the total).[2]Haemophilia is rare in female. Because haemophilia is x- linked recessive disorder family history and history of consanguineous marriage is important.

Family history, hemarthrosis, hematoma and other bleeding manifestation help to support the diagnosis of haemophilia. Accurate diagnosis is important and essential for effective management. It is dependent on laboratory following strict protocols and procedures which requires knowledge and expertise in coagulation laboratory testing, use of correct equipment and reagents and quality assurance.[3]

Preparations of factor VIII are capable of correcting all coagulation abnormalities in the blood of haemophiliacs; they are equally effective in vitro and in vivo, and their administration can prevent and arrest haemorrhage in patients with haemophilia A.[4]

AIMS AND OBJECTIVES

Objectives of the Study:

1) Approach to haemophilia with detailed clinical evaluation and laboratory diagnosis.

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2) To evaluate various screening and confirmatory tests for diagnosis of haemophilia.
3) To effectively treat patient with haemophilia according to various laboratory parameter.

MATERIAL AND METHODS

Retrospective study of laboratory diagnosis of haemophilia was conducted in our haematology section of pathology department of Tertiary Care Teaching Centre for the periods of two years from 1 August 2014 to 30 July 2016. All patients referred to haematology section of pathology department in the age group of 0 year to 55 years with factor VIII and factor IX level below 50% of normal were included in the study.

Routine haematological tests like haemoglobin and platelet count were analysed. Coagulation profile of patient for prothrombin time, activated partial prothrombin time, factor VIII and factor IX level were also considered.

EDTA anti -coagulated fresh whole blood sample were obtained for Haemoglobin and Platelet count. They were done in CELL-dyn 3700 haematology analyser. Haemoglobin is measured by modified hemiglobinhydroxylamine or modified hemiglobincyanide method. Platelet count was confirmed by manual method.

Samples for coagulation tests were collected in vacuette containing 0.2 ml 3.2%sodium citrate solution and centrifuged for 15 minutes at 4000 rpm. These samples were analysed in Diagnostica Stago fully automated coagulometer. Reagents used for Prothrombin Time were NEOLASTIN CI PLUS, STA CLEANER SOLUTION, STA DESORB U.Reagents used for Activated Partial Thromboplastin Time were C.K. Prest, Cacl2 0.025 m, STACLEANER SOLUTION. Reagents used for Factor VIII were STA-Deficient Factor VIII Kit- lyophilized citrated human plasma from which factor VIII has been removed by selective immunoadsorption and for Factor IX were STA-Deficient Factor IX Kit- lyophilized citrated human plasma from which factor IX has been removed by selective immunoadsorption.

RESULTS

"Study of Laboratory Parameters in Haemophilia Patients" was a retrospective study of 122 patients of haemophilia, conducted over a period of two years.

Out of 122 cases, 97 cases were of haemophilia A while 25 cases were of haemophilia B. Haemophilia A was more common than haemophilia B. Age range of these patients very from 0-55 years. Majority of patients were below age of 20 years.

Haemoglobin count of patients with haemophilia A and B ranged from 6gm% to 14.2 gm%. Platelet count of patients with haemophilia A and B ranged from 1,50,000 /dl to 4,91,000/dl that was within normal limits. Prothrombin time was normal in all of these patients. It ranged from 10 sec. to 16.5 sec. Control for PT was 13.5 sec.

APTT was prolonged in all patients with haemophilia A and B. It ranged from 41.6 sec. to 124 sec. Normal control of APTT was 26 sec. to 40 sec. (Table 1)

Factor VIII level was reduced (<50%) in all patient of haemophilia A. Normal range for factor VIII was 50% to 150% (0.5 IU/ml to 1.5 IU/ml). According to factor VIII level, haemophilia A is divided into mild, moderate and severe. (Table 2)

Factor IX level was reduced (<50%) in all patient of haemophilia B. Normal range for factor VIII was 50% to 150% (0.5 IU/ml to 1.5 IU/ml). According to factor IX level haemophilia B is divided into mild, moderate and severe. (Table 3)

DISCUSSION

Retrograde study of haemophilia involving 122 cases was done during period of two years from 1st August 2014 to 30th July 2016 and diagnosis was made with available clinical and laboratory data. Results were analysed and discussed with previous similar studies.

In present study Haemoglobin level ranged from 6gm% to 14.2gm%. 36 cases (29%) had moderate reduction in haemoglobin (11gm%) which correlated well with study done by Steven et al[5] showing 25%of cases. This decrease in haemoglobin is explained by loss of blood due to repeated bleeding episodes.

Platelet count of all patients was ranging from 1,50,000 to 4,91,000 /cmm which correlated well with study done by Agarwal et al.[6]

Prothrombin time of all patients was between 11-16.5 second that is within normal limits. This correlated well with study done by Kitchens CS.[7]

APTT was prolonged in all cases of haemophilia A and B. In majority of patients, APTT was more than 60 seconds. These findings correlated well with study done by Kitchens CS[7] and Takim & Shrivastava.[8] Most of patients with APTT more than 80 seconds belong to severe haemophilia. This support the fact that if APTT is twice the control, chances are that patients have severe haemophilia. (Graph 1 and 2)

Factor assay was done in all cases; findings correlate with study done by Shanthala Devi et al[9] and Rodgers gm & Charles SG.[10] Most of cases of haemophilia were of severe degree. (Graph 3 and 4)

CONCLUSION

- Haemophilia A is more common than haemophilia B.
- Both haemophilia A and B are more commonly seen in male below 20 years of age.
- Laboratory analysis of blood for haemoglobin, platelets, PT and APTT help to suspect the diagnosis along with clinical findings but not confirmatory.
- Diagnosis of haemophilia is confirmed by factor VIII assay for haemophilia A and factor IX assay for haemophilia B. Level of factor VII and IX also decide severity of disorder.

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Table 1: APTT of patients with haemophilia

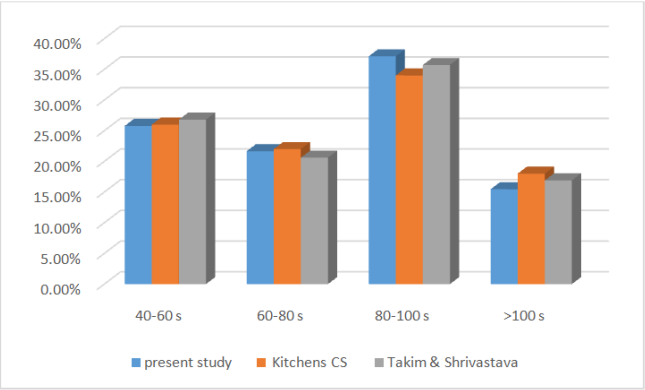
APTT in seconds	Haemophilia A		Haemophilia B	
	Number of cases	Percentage	Number of cases	Percentage
40-60	25	25.77%	4	16%
60-80	21	21.65%	7	28%
80-100	36	37.11%	10	40%
>100	15	15.46%	4	16%

Table 2: Factor VIII level and severity of patients with haemophilia A

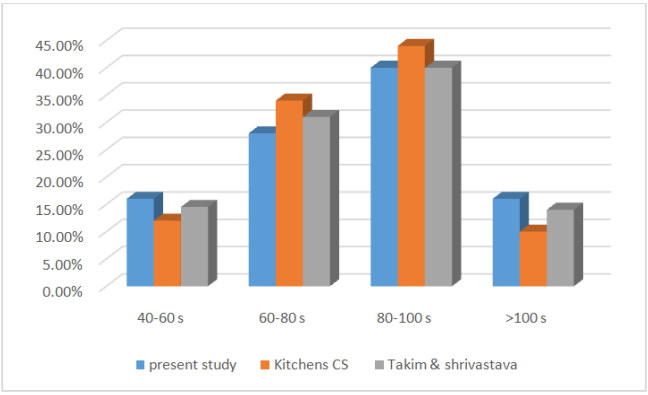
Factor level %	Severity of haemophilia	Number of cases	Percentage
5-50%	Mild	30	30.92%
1-5%	Moderate	18	18.56%
<1%	Severe	49	50.52%

Table 3: factor IX level and severity of patients with haemophilia B

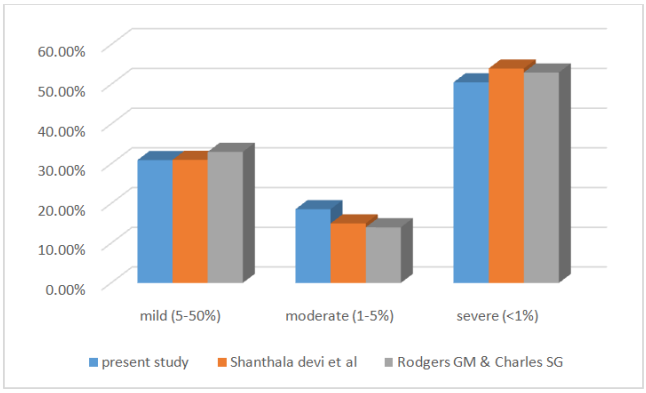
Factor level %	Severity of haemophilia	Number of cases	Percentage
5-50%	Mild	5	20%
1-5%	Moderate	6	24%
<1%	Severe	14	56%



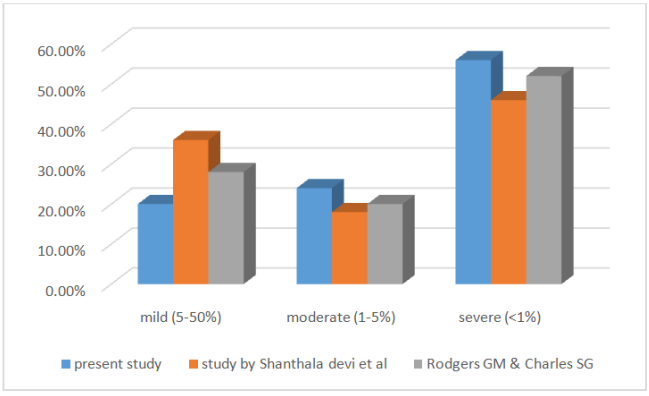
Graph 1: Comparison study between APTT in haemophilia A.



Graph 2: Comparison study between APTT in haemophilia B.



Graph 3: Comparison of severity of haemophilia A.



Graph 4: Comparison of severity of haemophilia B.