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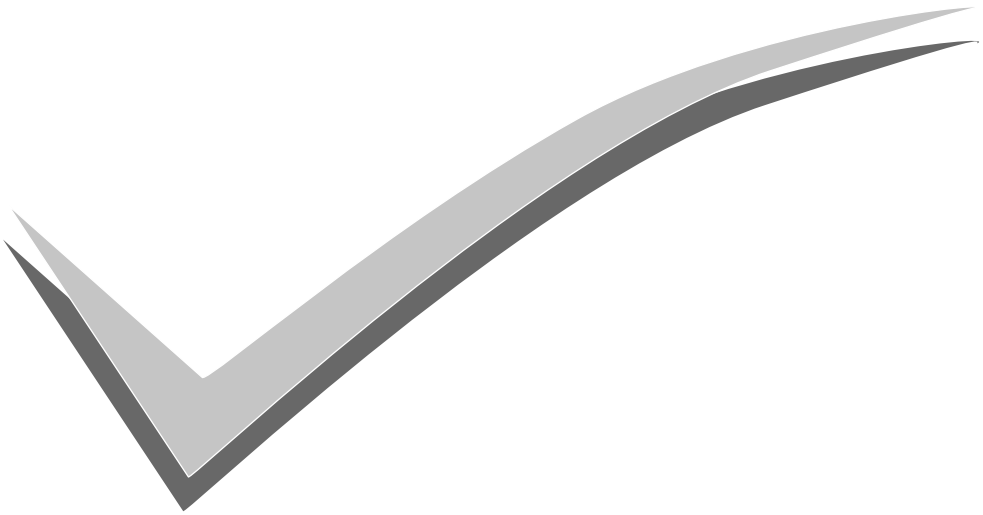

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Cephaloplastin reagent for APTT determination

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Cephaloplastin reagent for APTT determination

Role of Prothrombin time International normalized ratio and activated partial thromboplastin time in beta thalassemia major: A cross sectional study

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Abstract

Objectives: To evaluate the changes in PT/ INR and APTT in Beta thalassemia major cases.
Materials and Methods: A cross sectional study was conducted on 100 patients diagnosed with beta thalassemia major.
Results: Mean PT was noted to be 15.58s and mean APTT was 41.05s. These were elevated than controls and statistically significant. Association between serum ferritin and INR was not statistically significant. Correlation graph analysis between age and APTT was positive and significant while that for ferritin and APTT was negative.
Conclusion: Significant alterations in PT / INR and APTT exist in beta thalassemia major patients. Additional parameters and a tailored approach is suggested.

Keywords: PT, APTT, INR beta thalassemia Major.

Introduction

Thalassemia is recognized as one of the most common genetic disorder affecting the world with approximately 1-5% of the people having beta thalassemia. It is estimated that approximately 1-2 lakh individuals are born each year with severe forms of thalassemia with beta thalassemia comprising 60,000.[1]

The average life expectancy of patients with beta thalassemia has improved over the years as compared to that of in the previous millennium. This has led to the discovery of new set of problem such as increased hypercoagulable state in beta thalassemia in addition to the existing set of problems. Furthermore there is evidence of increased pro-thrombotic events, such as micro infarcts in spleen and lungs according to post mortem studies, indicating an activated coagulation pathway.[2]

Studies done between 1983 -1997 at Italy, observed that 4% of patients with thalassemia major and 9.6 percent of patients with thalassemia intermedia had a thromboembolic episode.[3]

Elevated levels of PT, APTT along with reduced levels of Protein C, Protein S and Anti-Thrombin III, have been described.[4-6]

Materials and Methods

This study was a cross sectional study done on 100 known cases of beta thalassemia major attending thalassemia day care clinics between January 2017-December 2017 at KLE'S Dr. Prabhakar Kore Hospital & M.R.C. Prior to the commencement, ethical clearance for the study was obtained from the Institute ethics committee. A total of 100 BTM cases were included in the study. The objective of this study was to evaluate the abnormalities of PT INR and APTT in transfusion dependant beta thalassemia major (BTM) in patients aged above 5 years of age. Newly diagnosed patients with beta thalassemia, haemoglobin less than 4 grams/dl, patients on warfarin or heparin, nephrotic syndrome, known cases of hemoglobinopathies other than beta thalassemia major, disseminated intravascular coagulation severe deranged liver function as assessed by history and medical records, acute thrombosis and those who lacked a minimum of 20 days gap from previous transfusion were excluded from the study. Written informed consent was obtained from the patients.

Samples for analysis were collected prior to the commencement of blood transfusion. Blood was drawn under aseptic precautions for all the tests. Two millilitre of whole blood was collected from clean venipuncture in a K2 EDTA coated vial and hemoglobin concentration, platelet count was determined using hematology auto analyser, councell 23 plus, Tulip Diagnostics.

Blood samples for determination of PT INR and APTT were collected on 3.2% Sodium Citrate vials, AcCuvet-PLUS (1:10 v/v) and platelet poor plasma was prepared for all the coagulation tests by centrifugation at 3000g for 15 min. PT was estimated by using "Uniplastin" kit supplied by Tulip Diagnostica, with an ISI of 1.1. APTT was estimated using "Liquicellin" supplied by Tulip Diagnostica. Serum ferritin estimation was done by CLIA method on Siemens Advia Centaur.

A PT of value above 13s (normal control being 13s) was taken as abnormal. APTT value of more than 30 seconds (normal control range 27s-29s) was taken as abnormal.

Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study

parameters on continuous scale between two groups. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for qualitative data analysis. Fisher exact test used when cell samples are very small.

Statistical Software

The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables. Pearson correleation coefficient (r) was used to test the correlation between age and APTT, Serum ferritin and APTT.

Results

Table 1 depicts the mean of the parameters in our study

Parameters	Mean
PT (Control 13s)	15.61 ± 1.43
INR	1.22 ± 0.24
APTT s (Control 27-29s)	40.96 ±6.54
Ferretin ng/ml	3801.92 ± 1585
Hemoglobin g/dl	8.38 ± 0.87
Platelet count lakhs/ mm^3	2.96 ±0.7

A total of 100 thalassemia major patients, above five years of age were included in the study, of which 42 had undergone splencetomy.

All the diagnosed cases were divided into three groups that is 5-10, 11-15 and 16 years and above. The age of the patients ranged from 5 years to 26 years.

In our study, the overall male: female ratio was 1.7: 1 with males more commonly affected than females.

Parents of 68% of thalassemic children gave a history of consanguineous marriage while parents of 28 percent of thalassemic children had non-consanguineous marriage, and 4% of parents of thalassemic children were not aware of their consanguineous status.

Prothrombin time (sec) distribution of patients studied according to age group studied, the range of PT ranged from 14-20s. Student's t- test was used to compare the PT among all the patients versus normal control. The *p*-value obtained was < 0.00001, which is strongly significant. However the variation of PT among the three groups was not significant as assessed by chi square test. (p = 0.107, Not Significant)

The range of APTT was between 31 to 60 seconds. The distribution of the APTT among the age groups is shown in table 2. Student's t- test was used to compare the APTT among, all the patients versus normal control. The *p*-value obtained was < 0.00001, which is strongly significant. The variation of APTT among the three groups was significant. (p value of 0.025, Fisher Exact test).

The hemoglobin level was reduced in all the patients. The highest hemoglobin observed was 10.3 g/dl in a patient aged 14 years and the lowest hemoglobin observed was 6.3 g/dl in a patient aged 8 years. The highest platelet count observed was 4.32 lakh /mm^3 in a patient aged 13 years and the lowest count observed was 1.57 lakh /mm^3 in a patient aged 10 years.

The serum ferritin ranged from 820 ng/ml in a patient aged 8 years to 8310 ng/ml in a patient aged 15 years. In our study we had 64% of the patients with ferritin value below 4000, while 36% of the patients had ferritin above 4000 nanograms/ml.

In the 56 number of the patients, the INR was less than 1.2 followed by 31 patients having the INR between 1.2 to 1.4 and 13 patients had the INR above 1.4 with the highest INR noted to be 1.60 in a patient aged 26 years.

Correlation analysis was done between age and APTT, and the results revealed that the pearson's correlation coefficient (r) was 0.217, with p value of 0.030, which was statistically significant. This implies there is a weak positive linear correlation of age with APTT. (Fig. 1)

Correlation analysis was done between serum ferritin and APTT, and the results revealed that the pearson's correlation coefficient (r) = - 0.071 and p= 0.482, which is not significant statistically. This implies that there is a weak linear negative correlation of ferritin with APTT and is not statistically significant. (Fig. 2) Depicts the correlation graph between APTT and serum.

Table 2: Describes the APTT distribution among the three age groups

APTT	Group 1	Group 2	Group 3
	5-10 yrs	11-15 yrs	16 yrs & above
31- 40s	26(47.3%)	17(73.9%)	8(36.4%)
41-50s	25(45.5%)	6(26.1%)	9(40.9%)
>51s	4(7.3%)	0(0%)	5(22.7%)
Total	55(100%)	23(100%)	22(100%)

P=0.025, Significant, Fisher Exact Test

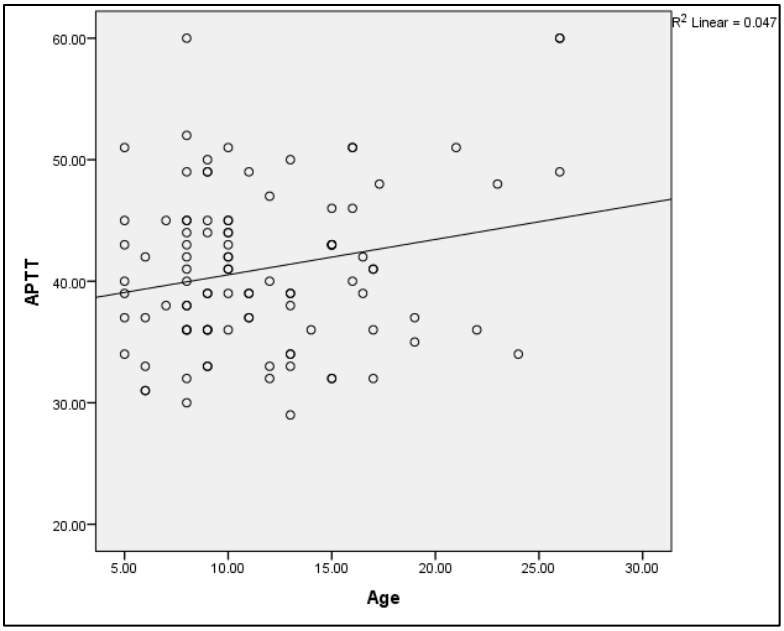

Fig. 1: Correlation graph between age and APTT

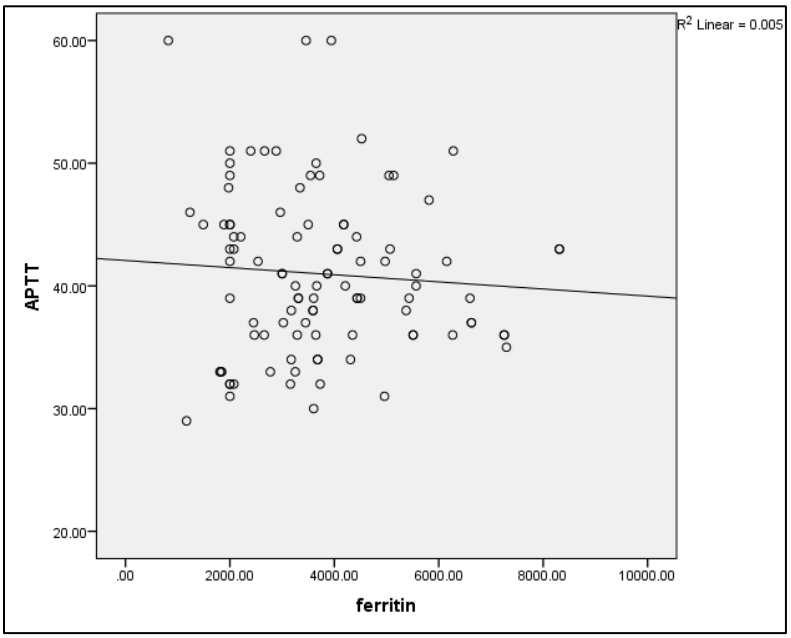

Fig. 2: Correlation graph between ferritin and APTT

Discussion

In our study the number of males were 63 and number of females were 37, with the overall male: female ratio of 1.7:1. According to the study conducted by Rahul Naithani, the male: female ratio of 1.5: 1 was observed.[7]

A positive history of consanguineous marriage among the parents of thalassemics was noted to be 68%. In a study conducted by Rakholia and Chaturvedi, the prevalence for beta thalassemia trait was noted to be 17.2 percent in and around Wardha, Maharashtra among Sindhi community.[8] As we noted a high degree of consanguinity among parents of thalassemia major marriage and genetic counselling should be strongly advised for couples willing for consanguineous marriage.

The overall mean prothrombin time was noted to be 15.61 seconds which is higher than the control and statistically significant in our study. (p = < 0.00001 student's t- test) These findings are in concordance with the study conducted by Rahul,[7] Abhishek Maithi,[9] and Safa A Faraj.[10]

The mean APTT was noted to be 40.96 seconds, which is elevated than the normal levels. This was Statistically significant (p = < 0.00001 student's t- test) and in concordance with the studies done by Rahul,[7] Abhishek Maithi,[9] and Safa A Faraj.[10]

Ferritin level of 4000 nanograms/ml is considered as the maximum level of physiological synthesis and any levels higher than this would represent the intracellular release of ferritin, either due to inflammation or malignancy [11] with this background, in our study we had 64% of the patients with ferritin value below 4000, while 36% of the patients had ferritin above 4000 nanograms/ml.

The platelet count among the three groups of thalassemics, was within the normal range. A study done by Rahul naithani[7] had a mean platelet count of 2.26+/- 1.23 lakhs/ mm^3 and another study conducted by Abhishek[9] had a platelet of 2.17+/- 1.60 lakhs/ mm^3. Thrombocytopenia may be due to the oral chelators and also hypersplenism. In our study we did not find any cases of thrombocytopenia, this may be due to poor compliance towards serum ferritin as we have noted elevated levels of serum ferritin.

We also noted that elevated ferritin levels were associated with more prolonged INR, however, this was statistically not significant. (p=0.057, not significant, Fisher's exact test) Bleeding manifestations were seen in two patients. The first patient was aged 9 year old male with repeated episodes of haemorrhagic manifestations in the form of epistaxis which were of 1-2 episodes / month. The PT was noted to be 17s and APTT to be 49s. Splenectomy was not done and elder sibling was apparently normal.

The second patient was a 14 year old male, having undergone a splenectomy at the age of 9 years. The PT and APTT was noted to be 18s and 60s, without any major bleeding manifestations except for epistaxis which was noted since the age of 4 years, with epistaxis of 2 to 3 episodes per month. The other two siblings were apparently healthy.

In a study conducted by Rai et al [12] 10% of the patients had clinical hemorrhagic manifestations. Another study conducted by Ibrahim[13] had noticed few patients to have bleeding manifestations in the form of epistaxis. Inherited deficiency as a cause for haemorrhagic tendencies is very unlikely according to a study done by Eldor.[4] One might say that the synthetic function of the liver can be reduced due to secondary hemochromatosis or other chronic liver disease. We know that the liver is responsible for the clearance of ferritin from the plasma. Hence liver damage will cause increased serum ferritin concentrations due to reduced rate of removal of ferritin from the plasma. Despite the correlation between serum ferritin and both storage iron and liver damage, much of the variation in serum ferritin remained unexplained. Accurate assessment of liver iron requires analysis of biopsy samples or MRI- T2*. Neither method was possible in this study.

The measurement of alanine aminotransferase enzyme (ALT) activity will not necessarily correlate well with ferritin release from the liver. The clearance of ferritin from the circulation is much more rapid than ALT. The biological half-life for ferritin in plasma is approximately 10 min and for alanine transaminase 6 days. Thus raised ALT levels may possibly be found some days after an episode of necrosis when ferritin levels have already fallen. Thus liver damage will cause increased serum ferritin concentrations by reducing the rate of removal of ferritin from the plasma as well as increasing the input of ferritin, as a consequence of tissue destruction. Multivariate analysis showed that units of blood and ALT activity together only accounted for about 30% of the variation in serum ferritin concentration. The maximum rate of synthesis of ferretin is noted to be 4000ng/ml. Levels above this can strongly indicate that the excess ferritin can be due to release from tissue damage or malignancy or failure to clear by the liver.

In a study conducted by Rosnah[14] in the year 2014 among Malaysians, serum albumin, a reflector of synthetic function of liver, was within normal limits, despite this there were alterations in levels of Protein C and Protein S. This implies there are few mechanism, apart from liver dysfunction which can lead to abnormal hemostatic balance.

Studies done between 1983-1997 at Italy, observed that 4% of patients with thalassemia major and 9.6 percent of patients with thalassemia intermedia had a thromboembolic episode.[15]

A MRI imaging study done between 1996-97 at Palermo, Italy on patients with thalassemia major had 28% patients with overt stroke and 37.5% of patients with beta thalassemia minor having asymptomatic brain damage. The patients also exhibited headache and seizure.[16]

In a study conducted in 2006 at Mediterranean region and Iran, the authors observed that thromboembolic event occurred 4.38 times more in thalassemia intermidia than thalassemia major. They also concluded that venous thromboembolic event was more common in thalassemia intermedia and arterial thromboembolic event was common in thalassemia major.[17]

None of our patients had any thrombotic episodes. The reason for this could be due to regular blood transfusion and younger age group.

In a study conducted by Abhishek,[9] the authors found that the coagulation profile was deranged irrespective of the frequency of blood transfusion and no significant correlation existed between PT, APTT and platelet levels and the interval between transfusion and days since last transfused.

Mussumeci S, noted that both thrombophilic and anti-thrombotic proteins were reduced as a consequence of liver damage. The net clinical outcome depends on the fine balance between the pro thrombotic and antithrombotic pathways.[18]

Study conducted by Aruna Chhikara, found that thrombin activable fibrinolysis inhibitor (TAFI) to be elevated in beta thalassemia major patients, the higher levels of which promotes a prothrombtoic episode.[19]

Our study aimed at assessing the coagulation profile of children with beta thalassemia major, using parametrs which are routinely used. Parametrs on both the procoagulant and anticoagulant pathways are better to be performed as guided by the initial results. A step wise approach or tailored approach using better indicators of coagulant and anticoagulant factors are suggested.

Conclusion

Evaluation of PT INR and APTT is a simple test for assessing the coagulation profile in thalassemic patients. Significant alterations in PT INR and APTT exist in beta thalassemia major patients who are transfusion dependant. These alterations suggests that beta thalassemia major is a high risk condition for thrombotic or hemorrhagic tendencies. The determination of the predominant pathway should be approached on an individual basis.

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Conflict of Interest: None.

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Evaluation of PT and APTT in Type 2 Diabetes Mellitus Patients

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Abstract: ***Diabetes mellitus is a group of metabolic disorders in which a person has high blood sugar, either because the body does not produce enough insulin or because cells do not respond to the insulin that is produced. There is evidence to show that patients with diabetes mellitus have changed hematological parameters. Prolonged hyperglycemia in diabetes mellitus patients exposes red blood cells to high glucose concentrations, which glycates proteins implicated in clotting mechanisms such as fibrinogen, prothrombin, and hemoglobin. 30 Blood samples of each type 2 diabetic mellitus patients and non-diabetic patients were collected during this period and their prothrombin time and Activated partial thromboplastin time was analyzed. From the present study there was a significant elevation of PT and APTT in Type 2 diabetes mellitus patients when compared to non-diabetic patients.***

Keywords: Diabetes**,** FBS-Fasting Blood Sugar**,** PT-Prothrombin Time, APTT-Activated Partial Thromboplastin Time

1. Introduction

Diabetes mellitus is a prevalent endocrine disorder with several etiologies. It is typified by chronic hyperglycemia and the ensuing disturbances in the metabolism of carbs, lipids, and proteins. The characteristic symptoms of polydipsia (increased thirst), polyuria (frequent urination), and polyphagia (increased appetite) are brought on by excessive blood glucose. About 90% of diabetic people have non-insulin type II diabetes, whereas 10% have insulin dependency. Diabetes is a serious health issue [1].

There is evidence to suggest that patients with diabetes mellitus have changed hematological parameters. Persistent hyperglycemia exposes red blood cells (RBCs) to high glucose concentrations in patients with diabetes mellitus, which causes glycation of hemoglobin, prothrombin, fibrinogen, and other proteins involved in clotting mechanisms. The clotting cascade is not fully activated and functions as a result of the glycation. The availability of intrinsic and extrinsic coagulation proteins is reduced by glycosylation, which impacts the ability to clot [2].

Hematological indices such as prothrombin time (PT) and activated partial thromboplastin time (APTT) provide information about a patient's coagulation state. These elements, which can be categorized into three pathways: intrinsic, extrinsic, and common, together are crucial for stopping bleeding disorders. There are roughly twelve clotting factors in one unit of blood. These are blood-borne proteins that are dormant but can become active in response to injury to blood vessels or tissues. The process of turning liquid blood into a semisolid gel is called blood clotting. Fibrin, a protein, is the fiber (polymer) that forms clots. Fibrinogen is the inactive precursor that gives rise to fibrin monomers. Fibrinogen, often known as Factor I, is essential to blood viscosity. Vascular damage induction is linked to hyperfibrinogenemia, or an increased concentration of fibrinogen in patents with uncontrolled NIDDM [2], [3].

In the laboratory, measurement of PT, APTT, and fibrinogen concentration are the most commonly employed laboratory tests in patients with a suspected coagulopathy. Prothrombin time is a laboratory screening test used to detect disorders involving the activity of the factors I, II, V, VII, and X of the extrinsic and common pathways. Activated partial thromboplastin time is used to screen for abnormalities of the intrinsic and common clotting systems and to monitor the anticoagulant effect of circulating heparin. It measures the activities of factors I, II, V, VIII, IX–XI, and XII of the intrinsic and common pathways. These proteins undergo modifications that encourage the emergence of a hypercoagulable and pro-thrombotic state. Due to the increased chance of an occlusive thrombus within a cerebral or coronary artery, which can result in the development of an atherosclerotic lesion, this can increase the risk of cardiovascular disease. Therefore, in patients with diabetes mellitus, PT and APTT can be utilized to evaluate the risk of clotting problems. Even though coagulation diagnostic tests are becoming increasingly complex, PT and APTT are still crucial foundational tests in clinical laboratories. To conclude the purpose of the current study was to assess the PT and APTT in Diabetic and Non Diabetic subjects [1] - [5].

2. Method

This study was conducted in Department of Pathology, Total Sixty (60) Samples, 30 diabetic samples and 30 apparently healthy non diabetic controls were selected and blood samples taken and analysed. Type 1 diabetes mellitus, Patients with thromboembolism history, Patients who were pregnant or had just undergone surgery were not allowed to participate in the trial. Specimens for PT and APTT measurement were obtained by venipuncture and samples collected into a citrated anticoagulant tube in ratio 1:9 after a

12 hour fast. Semi-Automatic Erba ECL coagulation analyser is used for the determination of PT, APTT by using Uniplastin and Liquicelin-E and Tulip Calcium Chloride kit. The reference ranges for PT and APTT in our lab are 11–14 seconds and 22–37 seconds, respectively.

3. Result

3.1 Fasting blood glucose of cases and controls

Group	*Number*	*Mean* FBS (mg/dl)
Case group	30	217.73
Control group	30	73.56

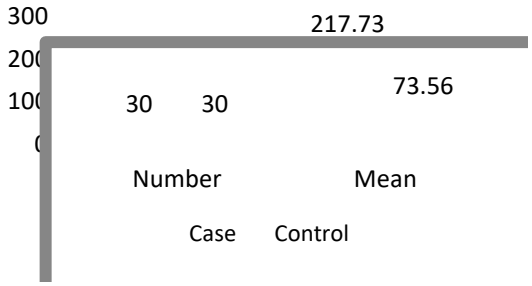

Figure 1: Fasting Blood Glucose of cases and controls

3.2 Mean Protrombin Time of Cases and Controls

Group	*Number*	*Mean* PT (Sec)
Case	30	17.78
Control	30	12.83

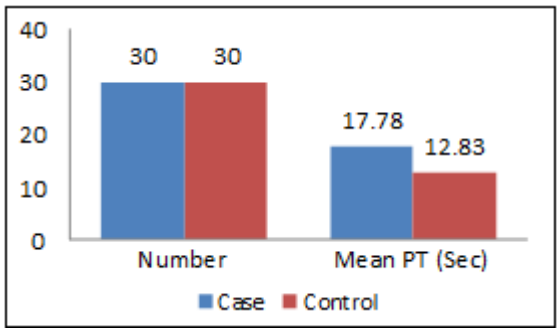

Figure 2: Mean PT of cases and controls

3.3 Mean APTT of Cases and Controls

Group	*Number*	*Mean* APTT (Sec)
Case	30	17.78
Control	30	12.83

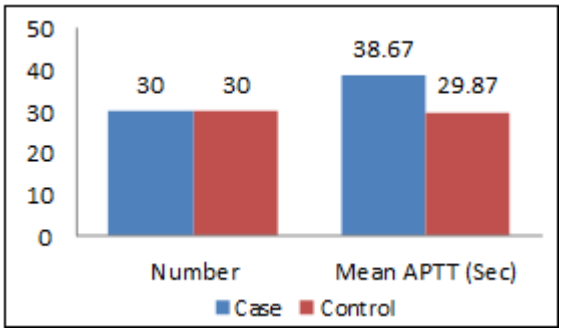

Figure 3: Mean APTT of cases and controls

4. Conclusion

This prospective study found that PT and APTT is an important factor in Diabetes Mellitus. In the present study, it was observed that the Mean level of prothrombin time in Type 2 diabetic patients was 17.78 and of control was 12.83 and the mean level of activated partial thromboplastin time in Type 2 diabetic patients was 38.67 and of control were 29.85. A significant difference was seen among cases and controls of PT and APTT. As a result, PT and APTT shortening in type II diabetic patients who are not receiving treatment may be a helpful marker for diabetic patients. In order to avoid hypercoagulation, it is crucial to monitor the PT and APTT in individuals with recent diabetes diagnosis.

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Research Article

Study of Coagulation Profile and Platelet Counts in Pre Eclamptic and Eclamptic Patients

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Abstract

Objectives: *We conducted this prospective case-control study in rural population based medical institute of central India. The aim of the study was to assess and analyze the coagulation profile (PT, aPTT, fibrinogen and fibrin degradation product [FDP] levels) and platelet counts in 3rd trimester normotensive, pre-eclamptic and eclamptic pregnant women.*

Methods: *In all subjects (cases and controls) 2 ml of blood sample was collected in EDTA and tri-sodium citrate bulbs for platelet counts and coagulation profile respectively.*

Results: *The mean PT and aPTT were significantly high in cases and mean fibrinogen level was significantly low in cases as compared to controls. FDP was significantly increased in cases as compared to non-detectable level in the controls. Thrombocytopenia was observed in 45% of cases. No any correlation between level of platelet count and abnormal coagulation test results (PT, aPTT, fibrinogen and FDP) were found.*

Conclusion: *We found in our study that platelet count and above coagulation tests should be performed in cases of pre eclampsia and eclampsia to identify severity of disease and to prevent development of complications.*

Keywords: *pre eclampsia, eclampsia, platelet count, coagulation tests.*

Introduction

Normal pregnancy is associated with impressive changes in the haemostatic mechanism to maintain placental function during pregnancy and to prevent excessive bleeding during delivery. The combined changes of increased coagulation factors and suppression of fibrinolytic activity leads to hypercoagulable state or prothrombotic state.[1,2]

During pregnancy the concentrations of coagulation factors VII, VIII, IX, X, XII and the von Willebrand factor rise significantly, accompanied by a relevant increase in the concentration of plasma fibrinogen. Plasma fibrinolytic activity is reduced during pregnancy due to liberation of plasminogen activator inhibitor from placenta.[2]

Pre-eclampsia (PE) is a disease of pregnancy resulting from a maternal physiological response to abnormal placentation. It is a multisystem disorder affecting approximately 2-7% of all pregnancies and is a significant cause of maternal and fetal morbidity and mortality. It usually occurs in the last trimester of pregnancy and more commonly in primiparous. It is characterised by widespread maternal endothelial dysfunction presenting clinically with hypertension, edema and proteinuria.

The onset of convulsion in a woman with pre-eclampsia that cannot be attributed to other causes is termed as eclampsia.

The systemic endothelial dysfunction in pre-eclampsia results in hypercoagulable state. Many haemostatic abnormalities have been reported in association with hypertensive disorder of pregnancy. Thrombocytopenia is the most common of this.[3,4] Reduced platelet counts in patients of mild and severe pregnancy induced hypertension(PIH) and very low counts in eclampsia was reported by many authors.[5] The degree of thrombocytopenia increases with the severity of disease.[4,6] The measurement of aPTT seems to be important for early detection of coagulation abnormalities in patients with severe pre-eclampsia who have normal platelet counts.[7] Low fibrinogen levels and increase in fibrin split products (D-dimer) has also been observed with increasing severity of pre-eclampsia.[8,9]

Several studies identified imbalance between coagulation and fibrinolysis in pre eclampsia which could be due to alterations of endothelial cells and fibrin deposition in microvasculature which lead to enhanced activation of the coagulation cascade and impaired fibrinolysis associated with multiple organ dysfunctions.[10-12]

Early assessment of severity of pre eclampsia and eclampsia is necessary to prevent complications and increased maternal and fetal morbidity and mortality. Therefore, the present study was done at rural population based medical institute to analyze the significance of various coagulation parameters and platelet counts in assessing severity of pre-eclampsia and eclampsia to prevent further complications.

Material and Methods

The present study was a prospective case-control study carried out in the haematology division of the Department of Pathology, in a rural population based medical institute over a period of 2 years. The study was approved by Research ethical committee of the institute. The blood samples for the study were obtained from the pregnant women in 3rd trimester of gestation admitted in obstetric wards. The patients of pre-eclampsia and eclampsia served as the cases whereas the uncomplicated normotensive age and gestation matched pregnant women served as controls.

Inclusion criteria

Pregnant women between 28 to 40 weeks of gestation with pre-eclampsia and eclampsia with having minimum criteria of -

(1) BP ≥140/90 mm Hg after 20 weeks of gestation.

(2) Proteinuria ≥ 300mg/24hrs or ≥1+ with dipstick.

Exclusion criteria

Pregnant women with known bleeding disorders, liver disease, abruptio placentae, intrauterine fetal death, trauma, any associated inflammatory disease or sepsis, any associated malignancy, in labor and on anticoagulant therapy.

All the cases were grouped into mild preeclampsia, severe pre eclampsia and eclampsia, The severity of pre eclampsia is graded into two categories. (Table 1)

Table 1: Grading of pre eclampsia

Abnormality	Mild	Severe
Diastolic Blood Pressure	<110 mm Hg	≥110 mm Hg
Systolic Blood Pressure	<160 mm Hg	≥160 mm Hg
Proteinuria	≤2+	≥3+
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper Abdominal Pain	Absent	Present
Oliguria	Absent	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
SerumTransaminase level	Minimal	Marked
Fetal Growth Retardation	Absent	Obvious
Pulmonary Edema	Absent	Present

Methods

In all the subjects, informed consent was obtained and the venous blood samples were collected as under-

(1) 2 ml EDTA (0.25mg/ml) bulb for complete blood count including platelet count.

(2) 2 ml in 3.2% tri-sodium citrate bulb maintaining ratio of blood and anticoagulant as 9:1 (1.8ml blood and 0.2 ml anticoagulant).

For platelet counts, the blood sample in EDTA bulb was run on Beckman coulter make (18 parameters) automated blood cell counter within 2 hours of collection of sample

For coagulation testes, the citrate blood sample was immediately centrifuged at 3000 rpm for 15 minutes and the supernatant plasma was transferred to a clean polystyrene tube. This plasma sample was used for studying Prothrombin time (PT), Activated partial thromboplastin time (aPTT), Fibrinogen levels and Fibrin degradation products (FDP) levels. These tests were carried out within 3 hours of collection of blood sample.

For PT & aPTT the semi-automated coagulometer, for quantitative estimation of fibrinogen the 'FIBROQUANT' test kit and for qualitative and semiquantitative estimation of FDP test 'TULIP XL FDP' kit were used.

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were considered abnormal if they were >15 seconds and >35 seconds respectively. Fibrinogen was considered low if it was <250 gm/dl and FDP was considered elevated if it was detected as ≥200ng/ml. Thrombocytopenia was defined as platelet count $<150 \times 10^9$/L.

The data thus obtained was tabulated and statistical analysis were performed by student's unpaired t-test, multiple comparison Tukey test, one way ANOVA test, Chi square test and Fisher's exact test. Statistical significance was considered at $p<0.05$.

Results

We have studied coagulation profile (PT, aPTT, Fibrinogen and FDP levels) and platelet count in total 80 cases of pre eclampsia and eclampsia in 3rd trimester of pregnancy. It included 21 (26.25%) cases of mild pre eclampsia, 28 (35%) cases of severe pre eclampsia and 31 (38.75%) cases of eclampsia. Similarly 80 normotensive age and gestation matched pregnant women in 3rd trimester were also studied as controls. The mean age of the cases was 24.68±3.67 years. Maximum 68 (85%) cases were between 20-29 years of age.

The mean gestational age observed in cases was 33.85±4.10 weeks. 61.25% of the cases were primiparous.

Table 2: Mean prothrombin time (PT) and Activated partial thromboplastin time (aPTT) in cases and controls.

Sr. No.	Diagnosis	No. of patients	PT (sec)		aPTT (sec)	
			Range	Range	Mean ±SD	Mean ±SD
1	Cases	80	10.8-24.5	25.6-70.1	34.88±6.37	14.30±1.77
	a. Mild PE	21	11.5-15.2	26.0-36.0	31.46±2.38	13.31±0.68
	b. Severe PE	28	11.7-24.5	25.6-46.1	34.77±5.48	14.55±2.31
	c. Eclampsia	31	10.8-18.0	27.8-70.1	37.29±7.88	14.76±1.50
2	Controls	80	10.2-13.9	26.9-34.0	31.11±1.55	12.71±0.83

On comparing, the mean PT and aPTT were found to be increased in cases as compared to that in the controls and this difference was found to be statistically significant. In subgroups of cases, the PT and aPTT were found to increase gradually with progression of disease from mild pre eclampsia to severe pre eclampsia to eclampsia.(Table 2)

Of the total 80 cases, abnormal prothrombin time results >15 seconds found in 25% cases and abnormal aPTT results >35 seconds in 38.75% cases of pre eclampsia and eclampsia.

Table 3: Mean fibrinogen levels and FDP levels in cases and controls

Sr. No.	Diagnosis	No. of patients	Fibrinogen (mg/dl)		FDP (ng/ml)	
			Range	Mean ±SD	Range	Mean ±SD
1	Cases	80	100-350	221.56±63.93	0-600	177.50±198.71
	a. Mild PE	21	160-350	269.05±45.60	0-200	9.52±43.64
	b. Severe PE	28	120-330	215.18±59.99	0-600	200.00±188.56
	c. Eclampsia	31	100-300	195.16±61.64	0-600	270.97±203.62
2	Controls	80	240-390	285.75±28.05	0	0

The mean fibrinogen level observed in cases of pre eclampsia and eclampsia was found to be significantly decreased than that in the controls. In subgroups of cases, there was gradual decrease of fibrinogen level with progression of disease. Compared to that in the controls, the decreased fibrinogen level in mild pre eclampsia was insignificant but in severe pre eclampsia and eclampsia this decreased fibrinogen level was statistically significant. Similarly amongst the subgroups of cases, the decrease in fibrinogen level in severe pre eclampsia and eclampsia as compared to that in mild pre eclampsia were statistically significant. (Table 3)

The mean fibrin degradation products (FDP) levels observed in cases was significantly increased compared to the non detectable level in the controls. (Table 3) It was seen in 40(50%) cases. In subgroups of cases only one (4.7%) case showed elevated FDP in mild pre eclampsia, whereas in severe pre eclampsia and eclampsia 60.71% cases and 70.96% cases respectively showed detectable FDP levels.

Table 4: Mean platelet counts in cases and controls

Sr. No.	Diagnosis	No. of patients	Platelet count (x 10^9/L)	
			Range	Mean ±SD
1	Cases	80	16-430	174.30±87.56
	a. Mild PE	21	97-386	214.9±80.87
	b. Severe PE	28	16-430	177.96±100.88
	c. Eclampsia	31	21.2-285	143.49±67.23
2	Controls	80	80-414	224.19±69.81

The mean platelet count in cases was found to be significantly lower than that in the controls. In subgroups of cases there was gradual decrease in mean platelet count with progression of disease. (Table 4)

In this study, cases and controls were also distributed according to the levels of platelet count into three categories as normal (>150 x 10^9/L), low (100-150 x 10^9/L), and very low (<100 x 10^9/L) platelet counts. The present study observed that there was increased frequency in thrombocytopenia cases with progression of disease. (Table 5)

Table 5: Distribution of cases and controls according to the level of platelet counts

Sr. No.	Diagnosis	Platelet Count (x 10^9/L)			
		>150	100-150	<100	Total
1	Cases No. (%)	44 (55)	22 (27.5)	14 (17.5)	80 (100)
	a. Mild PE	16	4	1	21
	b. Severe PE	15	7	6	28
	c. Eclampsia	13	11	7	31
2	Controls No. (%)	68 (85)	10 (12.5)	2 (2.5)	80 (100)

We also assessed, if there is any correlation between the level of platelet count with the simultaneous abnormal coagulation test results. (Table 6).

Table 6: Coagulation abnormalities of patients with pre eclampsia and eclampsia according to their platelet counts

Platelet counts	No. of cases	Prolonged PT(>15secs) No. (%)	Prolonged aPTT(>35secs) No. (%)	Low Fibrinogen (<250mg/dl) No. (%)	Elevated FDP(≥200ng/ml) No. (%)
<100	14	5(35.71)	10 (71.42)	10 (71.42)	7 (50)
100-150	22	4(18.18)	6 (27.27)	14 (63.63)	14 (63.63)
>150	44	11(25)	15 (34.09)	23 (52.27)	19 (43.18)
p value	-	0.49,NS	0.092,NS	0.38,NS	0.29,NS

Thus the abnormal coagulation test results of PT, aPTT, fibrinogen and FDP were also observed in patients with even normal platelet counts. Statistically there was no any correlation between level of platelet count and abnormal coagulation test results.

Discussion

In the present study, we compared the coagulation profile (PT, aPTT, levels of fibrinogen and FDP) and platelet counts in 80 cases of pre eclampsia and eclampsia in 3rd trimester of pregnancy with that in 80 normotensive age and gestation matched pregnant women as controls.

The mean age of the cases was 24.68±3.67 years. Maximum 68(85%) cases were between 20-29 years of age. Priyadarshini and Mohanty (2014)[13] also found maximum cases between 21-30 yrs of age, similar to the present findings. Younger age of occurrence of pre eclampsia and eclampsia testifies the early age of marriage and pregnancy in our country as compared to western countries.[13]

Different studies have reported the frequency of abnormal PT and aPTT in patients with pre eclampsia and eclampsia to be between 0% and 50%.[3,9] In our study also, the abnormal prothrombin time results were observed in 20 of the 80 (25%) cases with prothrombin time >15 seconds and abnormal aPTT results were observed in 31 of the 80 (38.75%) cases with aPTT >35 seconds in cases of pre eclampsia and eclampsia, similar to the findings of other studies.

The aPTT and PT reflects the function of endogenous and exogenous coagulation pathways respectively. Normal late pregnancy shows a physiological hypercoagulable state with decreased levels of aPTT, PT and TT and increased levels of fibrinogen compared to early pregnancy. This result may be caused by platelet consumption and aggregation followed by a secondary regeneration.[14] However with the

onset of preeclampsia, in particular severe pre eclampsia, there may develop complex disorders in exogenous and endogenous coagulation pathways which may relate to increased PT and aPTT in these conditions. As pre eclampsia and eclampsia syndrome is considered as a multisystem inflammatory disorder[14] and as the diagnostic criteria involve elevated serum transaminase levels suggesting increased certainty of pre eclampsia[15], it indicates hepatic insult in pre eclamptic syndrome. The liver damage is usually associated with increased prothrombin time level and this is likely to be the mechanism for increased prothrombin time in cases of pre eclampsia and eclampsia.

Similarly the significant prolongation of aPTT in severe pre eclampsia occurs due to activation and consumption of coagulation factors[1,16] especially factor VIII.[2]

The significant decrease in mean fibrinogen level in cases of pre eclampsia and eclampsia as compared to that in the controls have also been observed by Srivastava et al (1995)[8], Acmaz et al (2008)[3], Jahromi and Rafiee (2009)[7] and Dave et al (2014)[17], similar to the present findings.

The changing levels of fibrinogen in pre eclampsia were explained by various authors as under-

(1) Preeclampsia is a systemic inflammation and fibrinogen being an acute phase reactant, is increased in response to inflammation.[3]

(2) In healthy pregnant women, fibrinogen levels are increased by inflammation. However, since compensatory coagulation and fibrinolysis become exaggerated in preeclampsia, consumption coagulopathy occurs and fibrinogen levels are returned to normal values.[3]

(3) In pre eclampsia patients, the coagulation-fibrinolytic system is thought to be one of the most seriously affected systems by maternal inflammatory reactions and immune dysfunction.[16]

Srivastava et al (1995)[8], Jahromi and Rafiee (2009)[7] and Dave et al (2014)[17] also found significantly higher levels of FDP in cases as compared to controls, similar to the present findings.

D-dimer (FDP) is a specific degradation product resulting from the hydrolysis of the fibrin monomer and is considered to be an indirect marker for thrombosis and fibrinolytic activity. The maternal D-dimer concentration in normal pregnancy increases progressively from conception to delivery.[16] The findings of Heilmann et al (2007)[12], Han et al (2014)[16] and that of present study showed higher D-dimer concentrations in pregnant women with pre eclampsia, especially in women with severe pre eclampsia and eclampsia compared to normotensive women. D-dimer is involved in the dynamic balance between plasminogen activators [t-PA and Urokinase-type plasminogen activator (uPA)] and plasminogen activator inhibitor (PAI-1) in women with preeclampsia; therefore, D-dimer concentration can reflect the dynamic changes in both the super-hypercoagulable status and the activated fibrinolytic state in pre eclampsia patients.[16]

The gradually reduced platelet counts in patients of mild pre eclampsia to severe pre eclampsia to eclampsia were comparable to those reported in other studies. (Table 7).

Table 7: Comparison of platelet counts in different studies

Sr.No	Studies (year)	Platelet counts (x 10^9/L)			
		Control	Mild PE	Severe PE	Eclampsia
1.	Srivastava et al (1995)[8]	194.4	179.7	164.2	152.6
2.	Jambhulkar et al (2001)[18]	238	230	170	151
3.	Vrunda and Shaila (2004)[6]	220	200	140	130
4.	Present study	224.19±69.81	214.9±80.87	177.96±100.88	143.49±67.23

The mechanism of thrombocytopenia in pre eclampsia and eclampsia syndrome is variously explained as under

- It may be due to increased consumption of platelets with increased megakaryocytic activity to compensate it. Platelets adhere to areas of damaged vascular endothelium resulting in secondary destruction of platelets.[3,19]
- Platelets from severely preeclamptic patients showed less response than normal to a variety of aggregating agents suggesting that platelets may have undergone previous aggregation in the microcirculalion.[20]
- Recent studies have documented that increased plasma levels of sFlt1-soluble vascular endothelial cell growth factor (VEGF) receptor type 1, as well as endoglin, an endothelial cell-derived member of the tumor growth factor-² (TGF-²) receptor family, are present in patients intended to develop preeclampsia as early as the late first trimester. Increased levels of soluble fms-like tyrosine kinase-1(sFlt1) and endoglin mRNA is present in preeclamptic placentae,. sFlt1 binds and neutralizes VEGF and placental growth factor (PLGF), another important VEGF family member whose levels normally increase during pregnancy, whereas endoglin blocks the binding of TGF-² to endothelial cells. These types of pregnancies are also associated with qualitative alterations suggesting increased platelet turnover. There is a shortened platelet life span and increased number of megakaryocytes in the bone marrow, accompanied with an increased number of immature platelets seen in the peripheral blood. Many investigators believe that increased platelet consumption is due to disseminated intravascular coagulation while others suggest an immune mechanism.[3]

In the present study, the results of the distribution of cases and controls according to the levels of platelet count into three categories as normal (>150 x 10^9/L), low (100-150 x 10^9/L), and very low (<100 x 10^9/L) platelet counts are comparable with that of various authors showing decreasing platelet counts with increasing severity of disease.

The findings of various studies in cases and controls in respect to the normal, low and very low platelet counts are given below. (Table 8)

Table 8: Comparison between the normal, low and very low platelet counts in cases and controls in different studies

	Studies (Year)	>150 x 10^9/L (Normal)		100-150 x 10^9/L (Low)		<100 x 10^9/L (Very low)	
		Controls %	Cases %	Controls %	Cases %	Controls %	Cases %
1.	Vrunda and Shaila (2004)[6]	38	48	12	32	0	20
2.	Mohapatra et al (2007)[4]	100	53.3	0	27.7	0	18.8
3.	Present study	85	55	10	27.5	2	17.5

The findings of the present study are similar to that of Mohapatra et al (2007)[4] and Vrunda and Shaila (2004).[6]

The present study also assessed, if there is any correlation between level of platelet counts with simultaneous abnormalities of different coagulation test results. We found abnormal results of PT, aPTT, decreased fibrinogen level and increased FDP levels in very low, low and even normal range of platelet counts. However

statistically there was no any correlation between level of platelet count and abnormal coagulation tests results. (Table 6). Our results are in agreement with Jahromi and Rafiee (2009)[7] who commented that platelet count > 150 x 10^9/L can not assure the physician that no other significant coagulation abnormalities are present.

The deranged coagulation profile in patients of pre eclampsia and eclampsia ultimately affects maternal and fetal outcome.

Conclusion

We found in our study that platelet counts and various coagulation parameters (PT, aPTT, Fibrinogen, FDP) were important diagnostic tool to assess the severity of pre eclampsia and eclampsia to prevent further complications and to reduce maternal and fetal morbidity and mortality.

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Quality Control of Fresh Frozen Plasma using Fibrinogen, Factor VIII, PT and aPTT as Measure: A Retrospective Study in a Tertiary Care Hospital in South Gujarat

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Quality Control of Fresh Frozen Plasma using Fibrinogen, Factor VIII, PT and aPTT as Measure: A Retrospective Study in a Tertiary Care Hospital in South Gujarat

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ABSTRACT

Introduction: Quality control of blood and its components ensures the availability of high quality product with maximum efficacy and minimal risk to recipients. As per standard guidelines, for quality assurance of FFP, 1% of all the units prepared or 4 units per month are tested for stable coagulation factors: Factor VIII, Fibrinogen levels, PT and aPTT levels. Current research aims to study the quality control of fresh frozen plasma using fibrinogen, Factor VIII, PT and aPTT as measure in a tertiary care hospital in south Gujarat.

Meterial and Methods: The retrospective data was collected from archives of blood bank from the period of 1st January 2017 to 31st December 2020 in new civil hospital, Surat. Out of total 35116 units collected, 35013 were processed for component separation. 0.6% of Fresh Frozen plasma (212/35013) was tested for total volume, fibrinogen content, factor VIII, PT and aPTT levels for quality control with the help of semi-automated coagulometer.

Result: 93.86% of FFP samples tested had factor VIII levels above 0.7 IU/mL and 98.58% of samples had fibrinogen content >200mg/dl. 99.055 of FFP samples had INR >0.8 and 76% of FFP tested had aPTT in the normal range.

Conclusion: It is concluded that quality of FFP being prepared at present blood bank meets the standard guidelines. Regular quality evaluation and maintenance of records is essential for effective standards and keeping check on any deficiency

Keywords: Components, Volume, Plasma, Quality Analysis

INTRODUCTION

Plasma separated from whole blood, frozen within 6-8 hours of collection and stored at -30˚C or below is defined as fresh frozen plasma (FFP).[1] Usually 175- 250 mL of FFP is separated from standard donation of whole blood (450mL), containing 70-80 units/dl of factor VIII, factor IX, von Willebrand factor and other plasma clotting factors.[2] FFP is a constituent of blood needed to reconstitute the clotting properties of the patient's blood (by virtue of the properties of the various coagulation proteins) and very occasionally to restore the plasma volume of the patient. Therapeutically, transfusion of the FFP procedure is commonly used during severe bleeding episodes, or prophylactically in invasive surgery for non-bleeding patients. These coagulopathies may include liver diseases; vitamin K related coagulopathies, dilutional coagulopathy or disseminated intravascular coagulation (DIC).[3] The efficient quality management of blood component including FFP is effective in blood bank routine activity management and eventually betterment of patients. The demand for FFP is increasing in day to day practice, and its quality management is of utmost importance. Quality analysis of FFP depends on the concepts of quality control, quality assurance and quality management which aim at providing right blood to the right person at right place and time.[4] Quality control of blood and its components ensures the availability of high quality product with maximum efficacy and minimal risk to recipients. As per standard guidelines, for quality assurance of FFP,1% of all the units prepared or 4 units per month are tested for Factor VIII - ≥ 0.7 Units/mL and Fibrinogen levels 200- 400mg, Prothrombin time (PT), and Activated partial prothrombin time(Aptt).[2] These can be measured in a blood bank with the help of coagulometer by clotting assay.

Current research aims to study the quality control of fresh frozen plasma using fibrinogen, Factor VIII, PT and aPTT as measure in a tertiary care hospital in south Gujarat.

MATERIAL AND METHODS

Routine monthly quality check as per standard guidelines was carried out in the blood bank. The retrospective data was collected from archives of blood bank from the period of 1stJanuary 2017 to 31st December 2020.During this period, total of 35116 units of blood were collected from healthy, screened donors (more than 45 kg) in sterile single, double, triple or quadruple blood bags with anticoagulant CPDA 1 after taking written consent. Out of these 35116 units, 35013 units (99.70%) collected in double triple or quadruple bags were processed for separation of components in a refrigerated centrifuge (Cryofuge 6000i, Heraeus, Germany). After holding time of 2-4 hours, units were centrifuged at 4000

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rpm for 10 minutes at 4˚C for separation into Packed red blood cells (PRBCs)and fresh frozen plasma (FFP); 2 spin centrifugation at 1500 rpm for 10 minutes at 22˚C followed by 2750 rpm for 10 minutes at 22˚C for separation into FFP, PRBCs and Platelet concentrate.212 of 35013 units of Fresh Frozen plasma were tested for total volume, fibrinogen content, factor VIII, and PT and aPTT levels for quality control, by semi-automated coagulometer (Coastat-1, Tulip Diagnostics India), as per standard guidelines given in 'Technical Manual of Transfusion Medicine', by Directorate General of Health Services Ministry of Health and Family Welfare, India, 2nd edition, 2003.

RESULTS

Total of 35116 units of blood were collected from healthy, screened donors, out of which 35013 units were processed for preparation of FFP from the period of 1 January 2017 to 31 December 2020. 212 out of 35013 units (0.6%) were tested for quality analysis parameters, i.e., total volume, Factor VIII and Fibrinogen levels, PT and aPTT.

Mean volume was 224.96 ± 38.52 ml with range of 130- 368 mL which was well within the normal acceptable range.

Mean fibrinogen levels were 343.30 ± 110.79 mg/dl with a range of 155-718.9 mg/dl; the cut off criteria for quality control is ≥ 200mg/dl (Figure 1).

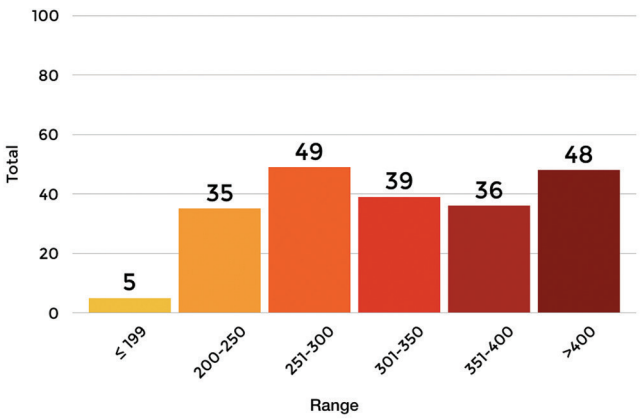

Figure-1: Bar chart showing Fibrinogen distribution in the FFP tested.

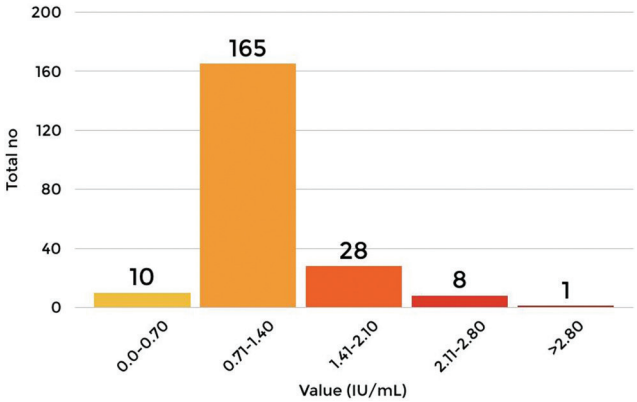

Figure-2: Bar chart showing Factor VIII distribution in the FFP tested.

Mean factor VIII levels were 1.18±0.62 IU/mL with range of 0.40 – 2.80 IU/Ml, the cut off criteria for the purpose of quality control is ≥ 0.7 U/mL (Figure 2).

Mean PT level is 13.31 +/- 1.48 seconds with range of 9-16.7 seconds. Normal range of INR is 0.8-1.1. Out of 212 FFP tested only 2 are INR <0. 8 (0.94%) and 210 out of 212 (99.05%) are in normal INR range.

Mean aPTT level is 31.30 +/- 4.39 seconds with range of 22-48.1 seconds.

199 out of 212 (93.86%) of FFP samples tested had factor VIII levels above 0.7IU/mL and 209 out of 212 (98.58%) FFP tested had fibrinogen content between>200mg/dl. 210 out of 212 FFP tested (99.05%) had normal PT INR range (Table 1).

DISCUSSION

Plasma is the aqueous component of blood in which many different cellular elements and macromolecules are suspended, but it is the proteins that have been the focus of interest for transfusion medicine, including specifically albumin, coagulation factors, and immunoglobulins.[5] Fresh frozen plasma is plasma separated from whole blood within 6-8 hours and rapidly frozen and stored at temperature below -30˚ C.

Utilization of fresh frozen plasma in clinical practice has

Parameter	Mean	Range	QC criteria	Concordance (%)
Fibrinogen (mg/dl)	343.30 ± 110.79	155-718.9	>200	98.58
Factor VIII (IU/mL)	1.18±0.62	0.40-2.80	>0.7	93.86
PT (seconds)	13.31 +/- 1.48	9-16.7	-	-
INR	1.02 +/- 0.13	0.79-1.34	>0.8	99.05

Table-1: Values of different Parameters for Quality Control of Fresh Frozen Plasma

Study	Fibrinogen (mg/dl) (Mean±SD)	Total(%) fulfilling QC cut-off for fibrinogen	Factor VIII (IU/mL) (Mean±SD)	Total(%) fulfilling QC cut-off for factor VIII
Sultan et al	247.17±49.69	100	0.84± 0.15	95
Agus N et al	-	-	1.0	75
Dogra M et al	270.66 ± 69.64	-	1.17 ±0.29	-
Bala et al	304.31±53.68	100	0.8±0.086	97.5
Present study	343.30 ± 110.79	93.86	1.18±0.62	98.58

Table-2: Values of Fibrinogen and Factor VIII in various studies for Quality Control of Fresh Frozen Plasma.

been increased in recent years: Plasma for transfusion is most often used where there is abnormal coagulation screening tests, either therapeutically in the face of bleeding, or prophylactically in non-bleeding patients prior to invasive procedures or surgery. For safe and effective preparation of blood and its components, in house quality control plays a very important role. Quality concepts comprises of a triad of quality control, quality assurance, quality management and their maintenance.[6] Quality control is the backbone of all laboratory services including blood bank. Quality testing and monitoring of blood components have led to development of safer and more potent components for transfusion practices. Factor VIII, fibrinogen levels, PT and aPTT are internal quality control parameters required for quality analysis of fresh frozen plasma as per standard guidelines.[2] The present study assessed the volume, levels of factor VIII, Fibrinogen, PT and aPTT in stored units of FFP after they were thawed for utilization. 212 of 35013units (0.006%) of FFP prepared in five years were evaluated and levels of the parameters were in concordance with standard guidelines.[2]

93.86% of units tested had factor VIII levels above 0.7 U/Ml and 98.58% units had fibrinogen levels more than 200mg/dl as per reference standards.[2] 99.05% of units tested were of normal PT INR range (Table 1).

Similar study was done by Sultan et al in which 100 units were tested for internal quality control. The mean factor VIII and fibrinogen levels were found to be 84.24± 15.01 IU/mL and 247.17±49.69 mg/dl for FFP respectively (Table 2). Almost all donors have fibrinogen ≥150 mg/dl, while only five (5%) donors had factor VIII below the desired levels.[7]

In another study done by Agus N et al, 30 units of FFP prepared within 8 hours of collection were tested for factor VIII levels (Table 2). Mean was 1.0 IU/mL with a range of 0.66- 1.47 IU/Ml.[8]

Dogra M et al also did a study on comparative analysis of activity of Factors V, VIII and level of fibrinogen in Fresh Frozen Plasma (Table 2). They studied 100 units of FFP in which levels of fibrinogen were 270.66 ±69.64 mg/dl and Factor VIII was 117.205±29.01 %.[9]

Thus, all the above mentioned studies have evaluated quality control parameters as done in the present study and results are in concordance as per standard reference parameters.

FFP is generally not used in developed countries due to the availability of recombinant or factor concentrates; however, in developing countries like India utilization of FFP is more for various inherited coagulation disorders and diseases leading to liver dysfunctions.

CONCLUSION

Internal quality control thus enhances the quality of blood products and helps in monitoring of quality standards of blood bank. Regular quality evaluation and maintenance of records helps to keep up the working standards and any deficiency can be checked and curtailed. It is concluded that quality of FFP being prepared at present blood bank meets the international standards of factor VIII > 0.7IU/mL (93.86% of units tested) and fibrinogen levels of > 200 mg/dl(98.58% of units tested). Regular update of quality assessment with respect to standard guidelines is important for effective production of blood components. A study of quality parameters as done above is essential for establishment of good transfusion practices.

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