Blood Component Utilization for Disseminated Intravascular Coagulation (DIC) Cases with Respect to Underlying Condition

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Received: 14 February 2015 / Accepted: 6 April 2015 / Published online: 25 April 2015
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Abstract To understand transfusion requirement in DIC with respect to (wrt) underlying cause. Patients' details were analyzed using parameters like yearly requirement, hemoglobin (Hb) and blood components utilization wrt age, sex and cause of DIC. Total 1931 DIC cases from 167 hospitals received 21,153 blood units including whole blood, red cell concentrate fresh frozen plasma, random donor platelets, single donor platelets and cryoprecipitate from year 2001 to 2013. Significant risk of DIC was for females compared to males ($p < 0.0001$). Whole blood utilization was 25.5 % in 2001 which reduced to 1.2 % in 2013. Mean $\pm$ SD Hb concentration was 8.6 ± 3.0 in females and 9.8 ± 3.2 g/dL in males. The lowest mean Hb was 7 g/dL in female DIC cases having malignancy. Septicemia was the major cause of DIC followed by obstetric complications. The highest requirement was for trauma associated with septicemia, requiring 35 units/case. Combination of two or more underlying causes for DIC increased the blood component requirement.

Keywords Disseminated intravascular coagulation (DIC) · Blood components · Septicemia · Trauma · Obstetric complications · Liver disorders

Introduction

Disseminate intravascular coagulation (DIC) is thrombo-hemorrhagic disorder caused by variety of underlying conditions [1]. The clinical conditions that induce DIC include septicemia and other infections; obstetric complications; severe trauma; liver disorder; post surgery complications; malignancy etc.

The corner stone of DIC treatment is treatment of underlying condition [2]. Risk of bleeding is generally due to low platelet count and reduced levels of coagulation proteins. Hence transfusion of components like red cell concentrates (RCC), random donor platelets (RDP), single donor platelets (SDP), fresh frozen plasma (FFP) and cryoprecipitate (Cryppt) is recommended [3]. We have analyzed 13 years data of our blood center retrospectively to assess the utilization of blood components for DIC cases due to various underlying clinical conditions.

Materials and Methods

We have a stand alone blood bank and regional blood transfusion centre supplying whole blood and components to more than 500 hospitals including government, trust and private hospitals, general hospitals, maternity homes, children hospitals, nursing homes, intensive care units etc. Our blood bank has customized integrated blood bank management software. We also have a practice of entering patients' details available in the requisition forms and also the blood components issue information in the Microsoft Excel data sheet. DIC data from January 2001 to 31st December 2013 were analyzed retrospectively. Year wise analysis was carried out to understand the trend of component utilization during the period of study. Most of the

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clinicians provided hemoglobin (Hb) values but did not give results of any other laboratory test in the requisition form. The parameters used for analysis were age, sex, Hb, cause of DIC and number of units of whole blood, RCC, RDP, SDP, FFP and/or Cryppt used. Calculations were done to assess the number of blood units used per case.

Statistical evaluation was done using Mean, standard deviation (SD), t test for comparison of individual means and Chi square (χ^2) tests [4]. Statistical significance was considered by p value.

Results

During last 13 years 176,800 patients received whole blood and components consisting 88,726 females (50.2 %) and 88,074 (49.8) males. Out of 1831 patients 1191 (65 %) were transfused all types of products like whole blood, red cells, FFP, cryoprecipitate and platelets while remaining patients received only FFP, cryoprecipitate and platelets. Total 1057 (1.2 %) females and 874 (1.0 %) males received transfusion support for DIC. The incidence of DIC among all patients was 1.1 %. There were 1931 DIC cases from 167 hospitals requiring 21,153 units of whole blood and components. The average per year was 148 with 54.7 % females and 45.3 % males having DIC. χ^2 test revealed significant risk of DIC in females compared to males ($p < 0.0001$).

Table 1 shows that during 2001–2013 whole blood use decreased and components increased. Combined χ^2 test

comparing whole blood use versus other components with respect to years showed significant ($p < 0.0001$) reduction in the use of whole blood during last 13 years. FFP was the most frequently (58.8 %) ordered component followed by RCC (13.5 %) and platelets (13.3 %). Cryoprecipitate utilization was 9.4 %.

Table 2 shows number of blood units used for male and female patients. The requirement for blood in DIC was comparable in both the sexes ($p > 0.5$). The “t” test showed significantly low Hb in females compared to males ($p < 0.005$).

Table 3 shows age wise requirement of blood components per case. The highest percentage of cases (39.6 %) was in the ≤ 1 year category followed by 19–40 years. Infants required minimum units/case while maximum units/case, were needed for 41–60 years age group. Mean Hb values were comparable in all age groups except ≤ 1 year category in which significantly higher mean Hb was observed by t test ($p < 0.005$).

Hb analysis was carried out comparing patients receiving red cell products in addition to FFP, cryoprecipitate and platelets and those receiving only FFP, cryoprecipitate and platelets. The mean $\pm$ SD Hb values were 8.6 ± 2.8 and 10.5 ± 3.4 respectively in these two groups. The difference was statistically significant ($p < 0.005$). As seen in Table 4, mean Hb values ranged from 7.7 to 8.8 g/dL in more than 1 year old age group. Among various underlying conditions obstetric cases showed the lowest Hb of 7.7 g/dL while highest Hb concentration was observed in surgery cases (8.8 g/dL), the difference between these two

Table 1 Yearwise requirement of blood for DIC

Year	WB (%)	RCC	FFP	RDP	SDP	Crypt	Total cases	Total components	Blood units/case
2001	82 (25.5)	43	129	24	0	43	31	321	10
2002	75 (12.9)	28	354	107	15	0	92	579	6
2003	230 (17.8)	65	781	192	3	20	122	1291	11
2004	227 (11.8)	164	1304	194	17	22	176	1928	11
2005	202 (8.9)	211	1432	223	50	149	179	2267	13
2006	173 (7.5)	264	1504	226	90	61	165	2318	14
2007	139 (8.6)	217	890	218	38	105	152	1607	11
2008	107 (5.2)	350	1022	253	30	281	154	2043	13
2009	66 (4.0)	247	905	155	41	253	145	1667	11.5
2010	39 (2.0)	307	888	242	22	405	181	1903	10.5
2011	89 (4.0)	383	1236	239	26	252	224	2225	10
2012	38 (2.1)	340	1028	202	26	197	180	1831	10
2013	14 (1.2)	245	544	147	31	192	130	1173	9
Total	1481 (7.0)	2864	12,017	2422	389	1980	1931	21,153	11

Whole blood versus other components $\Sigma\chi^2 = 737.14$ for 12 df, $p < 0.0001$

DIC disseminated intravascular coagulation, WB whole blood, FFP fresh frozen plasma, RDP random donor platelets, RCC red cell concentrate, SDP single donor platelets, Cryppt cryoprecipitate

Table 2 Sex wise requirement of blood in DIC

Sex	Mean $\pm$ SD Hb (g/dL)	WB	RCC	FFP	RDP	SDP	Crypt	Cases	Total components	Blood units/case
Female	8.6 $\pm$ 3.0	952	1517	6725	1216	267	1259	1054	11,936	11
Male	9.8 $\pm$ 3.2	529	1347	5292	1206	122	721	877	9217	10.5
Total	9.2 $\pm$ 3.2	1481	2864	12,017	2422	389	1980	1931	21,153	11

Comparison between male and female Hb levels by t test shows significant difference ($p < 0.005$)

SD standard deviation, DIC disseminated intravascular coagulation, WB whole blood, FFP fresh frozen plasma, RDP random donor platelets, RCC red cell concentrate, SDP single donor platelets, Crypt cryoprecipitate

Table 3 Age wise requirement of blood in DIC

Age in year	Mean $\pm$ SD Hb (g/dL)	WB	RCC	FFP	RDP	SDP	Crypt	Total cases	Total components	Blood units/case
≤ 1	10.9 $\pm$ 3.6	162	550	2783	1018	11	64	764	4588	6
2–18	8.5 $\pm$ 3.0	33	172	624	177	26	122	147	1154	8
19–40	8.2 $\pm$ 2.6	1019	1403	5837	849	254	1362	737	10,724	15
41–60	8.6 $\pm$ 2.2	198	462	1889	262	73	249	180	3133	17
>60	8.8 $\pm$ 2.2	69	277	860	116	49	183	103	1554	15

Comparison of Hb levels by t test between infants up to 1 year age and remaining age groups shows significant difference ($p < 0.005$)

SD standard deviation, DIC disseminated intravascular coagulation, WB whole blood, FFP fresh frozen plasma, RDP random donor platelets, RCC red cell concentrate, SDP single donor platelets Crypt cryoprecipitate

Table 4 Hb levels with respect to underlying conditions

Cause	Hb (g/dL) Mean $\pm$ standard deviation (SD)			
	Infants	Age ≥ 1 year	Male	Female
Septicemia	11.5 $\pm$ 3.4	8.5 $\pm$ 2.4	10.6 $\pm$ 3.3	10.0 $\pm$ 3.5
Obstetric complications	–	7.7 $\pm$ 2.5	–	7.7 $\pm$ 2.5
Infections	9.2 $\pm$ 3.6	8.7 $\pm$ 2.4	9.6 $\pm$ 2.4	8.0 $\pm$ 2.5
Liver/pancreatic disorder	13.9	8.7 $\pm$ 2.4	9.0 $\pm$ 2.5	8.5 $\pm$ 2.2
Surgery	12.4 $\pm$ 3.2	8.8 $\pm$ 2.4	10.2 $\pm$ 3.4	9.2 $\pm$ 3.0
Injury/Trauma	9.2	8.5 $\pm$ 2.4	8.3 $\pm$ 2.1	8.5 $\pm$ 2.6
Malignancy	–	8.2 $\pm$ 2.3	9.0 $\pm$ 2.1	7.0 $\pm$ 3.2

categories was statistically significant ($p < 0.005$). In male DIC patients lowest mean Hb value of 8.3 g/dL was observed in trauma cases. In septicemia category males had 10.6 g/dL and females 10 g/dL Hb concentration respectively. 46.6 % patients in this category were newborn infants having higher Hb. In female DIC cases low mean Hb values of 7 and 7.7 g/dL were observed in malignancy and obstetric DIC respectively.

Table 5 gives the blood requirement in DIC units with respect to associated cause. Out of 608 cases of septicemia, 283 (46.6 %) were neonates developing DIC within a week after birth. 4.3 % septicemia cases were associated with obstetric complications like intrauterine fetal death (IUFD). There are 399 cases having obstetric complications. Besides IUFD and abortion, other causes were placental abruption or placenta previa, ectopic pregnancy (eight

cases) etc. Majority of the cases had post partum hemorrhage (PPH). Hepatitis was associated with 63 (13.8 %) pregnancy DIC cases. Malaria, Dengue or other infections were associated in 17 cases. In 190 cases DIC was associated with various infections which included Dengue (64 cases), malaria due to *Plasmodium falciparum* and/or *Plasmodium vivax* (59 cases), tuberculosis, pneumonia or other respiratory disorders, typhoid etc. Among 146 cases of Liver disorder/pancreatitis, majority was of hepatitis and cirrhosis of liver. Pancreatitis was diagnosed in eight cases. DIC was present in 103 surgery cases. Majority of the surgeries were carried out for gastrointestinal or cardiac complications. Injury/trauma caused DIC in 80 cases. Majority of them had polytrauma due to road travel accident or fall from height involving head injury; crush injury and/or fractures. One case each was of Burns and bullet

Table 5 Blood utilization with respect to cause of DIC

Cause	Total cases		Associated cause															
	n	%	Units/case		Septicemia		Obstetric cause		Infections		Liver disorders		Surgery		Injury/Trauma		Malignancy	
			n	Units/case	n	Units/case	n	Units/case	n	Units/case	n	Units/case	n	Units/case	n	Units/case	n	Units/case
Septicemia	608	31.5	10	–	–	26	21	14	16	6	28.5	18	15	6	35	1	25	
Obstetric complications	399	20.7	14	26	21	–	–	17	20	63	19	17	17	–	–	–	–	
Infections	190	9.8	15	14	16	17	20	–	–	6	17.5	2	23	–	–	–	–	
Liver/pancreatic disorder	146	7.6	18	6	28.5	63	19	6	17.5	–	–	–	–	–	–	–	–	
Surgery	103	5.3	14	18	15	17	17	2	23	–	–	–	–	–	–	–	–	
Injury/Trauma	80	4.1	24	6	35	–	–	–	–	–	–	–	–	–	–	–	–	
Malignancy	28	1.5	18	1	25	–	–	–	–	–	–	–	–	–	–	–	–	
Other causes	87	4.5	13	8	12	6	17	–	–	–	–	–	–	–	–	–	–	
number of cases, DIC disseminated intravascular coagulation																		

n number of cases, *DIC* disseminated intravascular coagulation

injury while three cases were of poisoning. Total 1897 blood units including 565 (29.8 %) RCC, 970 (51.1 %) FFP 255 (13.4 %) cryoprecipitate and 107 (5.6 %) platelets were transfused to these patients. The underlying condition in 28 cases was malignancy. Seven cases were of hematological malignancy like acute or chronic leukemia. Remaining cases were of carcinoma of stomach, esophagus, pancreas, tongue, prostate, ovary, lung, breast etc.

Miscellaneous category in Table 5 includes different causes like Kidney failure (twenty cases), snake bite (ten cases), cardiovascular problems (five cases), hematological disorders like sickle cell anemia, aplastic anemia, hemorrhagic conditions like thrombotic thrombocytopenic purpura, autoimmune conditions like Guillain–Barre Syndrom, Systemic lupus erythematosus, autoimmune hemolytic anemia etc. There were three cases of DIC with multi organ failure. In about 15 % DIC cases information about the underlying cause was not provided by the clinician.

Table 5 also gives the data of total blood units issued per case in DIC related to different causes. Average requirement for septicemia was 10 units/case but when it was associated with trauma 35 units/case were required, while 28.5 units/case were needed when Liver disorder was associated with septicemia. Malignancy associated with septicemia required 25 units/case. The average requirement for injury/trauma cases was 24 units/case. For remaining conditions the requirement varied from 13 to 18 units/case.

Discussion

Ours is a stand alone blood bank supplying blood to needy patients to more than 500 Government, municipal, private and trust hospitals. DIC cases were referred to us from 167 hospitals therefore follow up for information about morbidity and mortality was not possible. This retrospective study was mainly carried out to understand the blood components requirement in DIC due to various underlying conditions.

DIC is a complication of a variety of diseases which cause pathologic activation of the extrinsic and/or intrinsic blood coagulation pathways. Many conditions like sepsis, obstetric complication or trauma are known to activate coagulation cascade. As per the British committee for standards in haematology (BCSH), though low platelet count and decreased coagulation factor levels increase the risk of bleeding, the corner stone of treatment is the treatment of underlying condition [2]. Therefore the transfusion management in DIC depends on the cause. In the present study platelet count and coagulation factor data of DIC patients were not available hence we cannot comment on this point.

Recent literature recommends evidence-based transfusion triggers [5]. We analyzed Hb data to find out if Hb as a transfusion trigger was associated with underlying conditions. Excluding the neonatal cases that have normally high Hb, it was observed that the mean Hb ranged from 7.7 to 8.8 g/dL in different underlying conditions. Lowest Hb of 7.7 was associated with obstetric patients. Female DIC cases of malignancy had 7 g/dL Hb. Since DIC is a bleeding disorder probably Hb is not important as transfusion trigger.

The incidence of DIC in our centre was 1.09 % while Matsuda has reported it to be 1.04 % [6], which is comparable to our study. In the year 2001 there were only 31 cases of DIC requiring 321 units of blood of which 25.5 % were whole blood units. This shows lack of awareness about the transfusion management in DIC. Situation was different after 13 years. In 2013 only 1.2 % units were utilized as whole blood. The average number of cases per year was 148 and average blood units transfused were 11 per case. Maximum consumption was of FFP compared to other blood components. Cryoprecipitate which is rich in fibrinogen and factor VIII was initially rarely ordered but later on the use increased.

In our study 764 infants having DIC on average required 6 units per case. The average Hb concentration ranged from 9.2 to 13.9 g/dL in different underlying conditions in these infants. In majority of them DIC was triggered due to sepsis or infections. FFP was the most frequently ordered component. Views differ about the amount and ratio of different types of components to be used in DIC [2, 3, 7]. Generally 10–15 mL per kg FFP and 5–10 mL per kg Cryoprecipitate is recommended. The BSCH 2003 guidelines have recommended 10–15 mL per kg platelets [7].

Sepsis and infections are the most common causes of acute DIC and can be associated with a variety of viral, fungal and bacterial infections, particularly meningococemia and other Gram-negative bacteria. In the present study septicemia was the most predominant underlying cause for DIC observed in 31.5 % cases and infections (total 190 cases) mainly included dengue and malaria. In macrophages and monocytes, bacterial endotoxins stimulate release of tissue factors and pro-inflammatory mediators. Systemic inflammation during sepsis leads to the generation of cytokines which are usually responsible for coagulation and fibrinolytic activation. Both coagulation activation as well as down-regulation of fibrinolysis is principally regulated by tumor necrosis factor (TNF)- α , interleukin (IL)-1, and IL-6 [8]. Blood coagulation activation is frequently found in malaria patients and DIC is responsible for very severe disease with high mortality in such cases [9].

DIC is commonly associated with obstetric hemorrhage and causes profuse bleeding due to inadequate clot

formation. Thachil and Toh [10] have listed commonly described causes of DIC in obstetrics as amniotic fluid embolism, IUFD, HELLP, eclampsia, placental abruption, placenta previa, septic abortion, PPH and acute fatty liver. In our study there were 399 DIC cases due to obstetric complications like PPH, IUFD, abortion, placental abruption, placenta previa, ectopic pregnancy (eight cases) etc. Septicemia, Hepatitis, Malaria, dengue or other infections were associated DIC in pregnancy. In cases having active bleeding and platelet count $< 50 \times 10^9/L$, platelets and/or coagulation factors are administered [10, 11]. If FFP transfusion is not possible due to fluid over load then cryoprecipitate should be given [2].

Abnormalities in both number and function of platelets are common in liver disease [12]. Liver is the site of synthesis of most of the coagulation factors therefore liver damage is commonly associated with impairment of coagulation. In the present study there were 138 DIC cases of liver disease requiring about 18 units per case including RCC/FFP/platelets/crypt. Majority of the patients had hepatitis or liver cirrhosis.

DIC has been reported after different types of surgeries like cardiac, orthopedic, spinal, liver, malignant tumors etc. [13–16]. Our study reports 103 surgery cases majority of them were for cardiac or gastrointestinal complications. Traumatic coagulopathy has DIC with fibrinolysis as predominant initial pathogenesis. High levels of inflammatory cytokines and severe tissue injuries activate the tissue factor dependent coagulation pathway. Secondary coagulopathy is a result of dilutional and consumptive loss of coagulation factors. Treatment involves the surgical repair of the trauma and the rapid and sufficient replacement of platelet concentrate, FFP and depleted coagulation factors. The common practice of blood component therapy is RBC, FFP and platelets transfusion in 1:1:1 ratio [17]. Total 1897 blood units including 565 (29.8 %) red cell products, 970 (51.1 %) FFP, 255 (13.4 %) cryoprecipitate and 107 (5.6 %) platelets were transfused to 80 trauma patients with DIC. Thus a particular ratio was not maintained. Several clinicians had sent requisition of blood to our blood bank. Therefore the transfusion protocols differed. Many studies have recommended large transfusions of RBC, FFP and platelets to critically injured patient to prevent and treat coagulopathy [18, 19].

DIC could be associated with different types of cancers [20]. Bleeding occurs in approximately 10 % of patients with cancer [21]. In the present study seven patients had hematological malignancy like acute or chronic leukemia. Remaining cases were of carcinoma of stomach, esophagus, pancreas, tongue, prostate, ovary, lung, breast etc. Studies have shown that gastric cancer is the most frequently associated cause of DIC [22]. Different causes for 87 miscellaneous cases were kidney failure, snake bite,

hematological or hemorrhagic disorders, autoimmune diseases etc. Our blood bank is in the urban area therefore it is surprising that we had ten cases snake bite. According to Orak et al. enzymes in snake venom may induce DIC [23].

Present study has the limitation that we did not have data of different laboratory parameters in DIC cases or factors like activated protein C or coagulation factor concentrates or blood thinners given by the clinician and the information on morbidity and mortality.

Conclusion

- In our study incidence of DIC 1.09 %.
- Significant risk of DIC was for females compared to males.
- Septicemia is the major cause for DIC followed by obstetric complications.
- Majority of patients received FFP and the highest requirement of blood was for trauma associated with septicemia.
- Combination of two or more underlying causes for DIC increased the blood component requirement.
- The lowest mean Hb was 7 g/dL in female DIC cases having malignancy.

Acknowledgments This work is supported by Surat Raktadan Kendra & Research Centre Management.

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