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"STUDY OF COAGULATION PROFILE IN CLINICALLY DIAGNOSED CASES OF ACUTE DISSEMINATED INTRAVASCULAR COAGULATION USING ISTH CRITERIA"

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ABSTRACT: Disseminated Intravascular Coagulation (DIC) is a pathological activation of coagulation (blood clotting) mechanisms that happens in response to a variety of diseases. It involves the generation of intravascular fibrin (small blood clots) and the consumption of pro-coagulants and platelets. It results in the disruption of normal coagulation mechanism and abnormal bleeding occurs from the skin, the gastrointestinal tract, the respiratory tract and surgical wounds. It was the prospective study of 60 patients of acute DIC, in which coagulation profile were studied from December 2010 to October 2012. 40 controls were studied. Control group include healthy voluntary blood donors. The coagulation profile was studied and DIC scoring was performed using the International Society on Thrombosis and Haemostasis [ISTH] criteria. Among the coagulation profile, the sensitivity and specificity of the parameters to diagnose and to assess the severity of DIC, in the decreasing order of frequency were of platelet count, D-dimer, PT and APTT. Fibrinogen level was not depleted below the significant level (<1 gm/l) in majority cases of DIC. According to the ISTH criteria, DIC scores among cases was ≥ 5.
KEY WORDS: DIC, coagulation profile, ISTH, Platelet count, D-dimer.

INTRODUCTION: Disseminated Intravascular Coagulation (DIC) also known as consumptive coagulopathy, is a pathological activation of coagulation mechanisms that happens in response to a variety of diseases. [1] It is a systemic intravascular activation of the coagulation system, simultaneously leading to intravascular thrombi, compromising an adequate blood supply to the organ and to bleeding as consequences of exhaustion of the platelet and coagulation factors. [2], [3] The subcommittee on DIC of the International Society on Thrombosis and Haemostasis [ISTH] has suggested the definition for DIC: "An acquired syndrome characterized by the intravascular activation of coagulation with loss of localization arising from different causes. It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction." [4] DIC is always secondary to an underlying disorder and is associated with a variety of clinical conditions. [5], [6] During this study, 60 patients with clinical diagnosis of Acute Disseminated Intravascular Coagulation (DIC) were included in the study as cases. The coagulation profile [PT, APTT, D-dimer, Fibrinogen and Platelet count] was studied and DIC scoring was performed using the International Society on Thrombosis and Haemostasis [ISTH] criteria.

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Parameter	Value	Score
Platelet count (x 10 ^{3}/µl)	> 100	0
	50 – 100	1
	< 50	2
Prothrombin time (sec) [prolongation by]	< 3	0
	> 3 but < 6	1
	> 6	2
Fibrinogen (gm/lit)	> 1gm / lit	0
	< 1gm / lit	1
D-Dimer [Normal –0.5 µg/ml]	No increase	0
	Moderate increase	2
	Marked increase	3
Table [1]. DIC Scoring System Using ISTH criteria: [7], [8]		

AIMS AND OBJECTIVES:
1. To study the clinical profile in cases of Acute disseminated intravascular coagulation.
2. To study the intrinsic and extrinsic pathways of coagulation in clinically diagnosed cases of Acute disseminated intravascular coagulation, with the help of Prothrombin time and Activated Partial Thromboplastin Time.
3. To assess the fibrinolytic activity (using D-dimer assay) in clinically diagnosed cases of Acute disseminated intravascular coagulation.
4. To correlate the degree of impairment of various coagulation test results in cases of Acute disseminated intravascular coagulation.
5. To score the cases of Acute disseminated intravascular coagulation using ISTH criteria.

INCLUSION AND EXCLUSION CRITERIA:
INCLUSION CRITERIA: All patients clinically diagnosed as Acute DIC.
EXCLUSION CRITERIA: Patients other than Acute DIC with deranged coagulation profile.

MATERIAL & METHODS: This prospective study was carried out in the department of pathology in the tertiary care institute during the period from December 2010 to October 2012. Cases were evaluated by routine haematological investigations and special tests like coagulation profile (PT, APTT, D-dimer and Fibrinogen assay). PT, APTT, and Fibrinogen tests were done on "Diagnostica stago coagulometer" as per manufacturer's instructions and guidelines. D-dimer assay was performed using D-di test (Latex agglutination test).

RESULT: During this study, the study population was 100. Of which 60 patients with clinical diagnosis of Acute Disseminated Intravascular Coagulation (DIC) were included in the study as cases and remaining 40 were included as control group. Control group includes the healthy voluntary blood donors. Among these 100 study population, 51(51%) were male and 49 (49%) were female with M:F ratio 1.04:1. Out of the 60 cases, 30 (50%) were male and 30 (50%) were female with M: F ratio 1:1. Age group in cases [n=60] ranging from 03 days to 65 years with mean age 32 years.

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Among the 60 cases, there were various underlying conditions associated with Acute DIC. These are shown in Table [2].

Underlying conditions	No. of cases	Percentage (%)
Septicemia	21	35.00 %
Obstetric calamities	20	33.33 %
Liver diseases	06	10 %
Leukemia	05	8.33 %
Snake bite	04	6.67 %
Trauma	04	6.67 %
Total	60	100 %

Table [2]. Underlying conditions associated with Acute DIC among cases (n=60)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	20.7	1.64	43		108	41000
Max	38	4.08	63.4		433	99500
Mean	27.45	2.67	50.92	4 to 8	244	76309
Median	27.7	2.71	50.6		234	77200
SD	5.21	0.69	5.47		86.15	18554

Table [3]. Coagulation parameters of septicemic patients (n=21)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	23.4	2.15	44.3		89	36,000
Max	80	6.2	95.7	4 to 8 in 18 cases	353	99200
Mean	34.34	3.08	55.07	&	187	73595
Median	27.85	2.63	49.75	> 8 in 02 cases.	163	75,800
SD	14.06	0.94	12.43		85.48	18026

Table [4]. Coagulation parameters of patients with Obstetrical calamities (n=20)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	22	1.99	56.8		84	58000
Max	70.3	5.44	98.5	4 to 8 in 03cases	268	98200
Mean	39.62	3.8	71.43	&	155	77983
Median	35.8	3.77	65.9	> 8 in 03 cases	151.5	82500
SD	16.59	1.22	16.41		70.01	16450

Table [5]. Coagulation parameters of patients with Liver diseases (n=6)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	18	1.55	43.5		79.8	14000
Max	44	3.99	62.8	4 to 8 in 03 cases	147	68000
Mean	28.82	2.6	51.82	&	104	38000
Median	24	2.22	46.8	> 8 in 02 cases	98	37000
SD	11.33	1.05	8.96		25.9	23717

Table [6]. Coagulation parameters of patients with Leukemia (n=5)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	22.8	2.07	43.9	4 to 8 in 1 case	124	80300
Max	38.2	4.08	65		390	98600
Mean	29.8	2.97	53.75		215	87350
Median	29.1	2.61	53.05	> 8 in 3 cases	174	85250
SD	6.4	0.93	9.21		118	8066

Table [7]. Coagulation parameters of patients with Snake bite (n=04)

Parameter	PT (sec)	INR	APTT (sec)	D-dimer (µg/ml)	Fibrinogen (mg/dl)	Platelet count (/mm3)
Min	25.2	2.38	47.1	4 to 8 in 03 cases	189	60000
Max	29.2	2.87	54		318	97500
Mean	27.02	2.60	49.62		251	85675
Median	26.85	2.46	48.7	> 8 in 01 case	250	92600
SD	1.89	0.26	3.06		62	17295

Table [8]. Coagulation parameters of patients with Trauma (n=04)

Using the ISTH criteria, these 60 patients of acute DIC with different underlying conditions were assessed for DIC score. DIC score was found to be > 5 (i.e. 5 - 8) in every case. Thus, this DIC score indicate that, laboratory evidences were consistent with DIC.

Out of the 60 cases, DIC score was found to be ≥ 5 (i.e. 5 - 6) in 21 septicemic patients, > 5 (i.e. 6 - 7) in 20 patients with obstetric calamities, > 5 (i.e. 6 - 7) in the 06 patients with liver disease, > 5 (i.e. 5 - 9) in the 05 patients with leukemia, ≥ 5 (i.e. 5 - 6) among the 04 patients of snake bite and 5 in the 04 cases of traumatic history. Thus, DIC score was maximum among the patients with leukemia followed by obstetrical calamities and liver diseases. The highest DIC score was associated with the poor prognosis of the patients.

DISCUSSION: Disseminated intravascular coagulation is an acquired disorder that occurs in a wide variety of clinical conditions. It is characterized by the widespread activation of coagulation, which results in the intravascular formation of fibrin and ultimately thrombotic occlusion of small and midsize vessels.

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During the present study, out of 60 cases, septicemia accounting for 21 cases (35%) was the most common condition associated with DIC. Septicemia was followed by obstetrical calamities, which accounts for 20 cases (33.33%).

Neame P B et al. [9] (1974-1977) found 31 patients of septicemia and all were suffering from DIC. Lee J.H. et al. [10] (2000-2005) also found septicemia (as a single entity) was the predominant underlying condition leading to DIC.

Study	Year	No. of cases	Underlying condition (n=no of cases & %)						
			Septicemia	Obstetric	Liver disease	Leukemia	Malignancy	Snake bite	Trauma
Neame PB et al.[9]	1974-1977	31	31	--	--	--	--	--	--
Lee J.H. et al.[10]	2000-2005	131 100%	42 32.06%	04 3.05%	18 13.74%	--	20 15. 27%	--	04 3.05%
Satoshi G. et al.[11]	2008	329 100%	98 29.79%	04 1.22%	04 1.22%	--	05 1.52%	--	149 45.29%
Kaneko T. & Wada H.[7]	2011	1027 100%	244 23.76%	--	101 9.83%	247 24.05%	402 39.14%	--	--
Present study	2010-2012	60 100%	21 35%	20 33.33%	06 10%	05 8.33%	--	04 6.67%	04 6.67%

Table [9]. Comparison of studies according to underlying conditions associated with DIC

Study	Year	No. of cases	PT (% of cases)	APTT (% of cases)	D-dimer (% of cases)	Fibrin-ogen (% of cases)	Platelet count (% of cases)
Colman et al. [12]	1972	48	90	--	--	71	93
Al-Mondhiry et al. [13]	1975	89	87	62	--	66	100
Lewis et al. [14]	1977	215	72	65	--	55	96
Siegel et al. [15]	1978	118	98	93	--	23	88
Saxena R. et al.[16]	2004	29	83	83	100	--	--
Present study	2010-2012	60	100	100	100	33	100

Table [10]. Comparison of studies according to Percentage of laboratory abnormalities in patients with DIC

The coagulation parameters of cases and controls were compared statistically using 'student T test.' The P value was obtained and it showed highly significant P value (0.007) in terms of platelet count, P value (0.003) in terms of D-dimer. P values in terms of PT (0.04) and APTT (0.02) were also statistically significant. Thus, coagulation parameters in cases are consistent with clinical findings of DIC. The parameters like platelet count and D-dimer assay are the highly sensitive as well as specific marker for DIC. The parameters like PT and APTT showed linear correlation with DIC. The

fibrinogen levels were variable and statistically were not highly significant as that of platelet count and D-dimer assay.

Although various laboratory assays have been used to diagnose Acute DIC, there is no single laboratory test currently available for accurate and precise diagnosis of acute DIC.

ISTH guidelines help to predict the severity and clinical outcome in DIC cases. DIC scoring using ISTH criteria, can diagnose the early DIC, which is beneficial for treating physician or surgeon to take prompt action in order to save the life of the patient.

CONCLUSION: DIC cases almost invariably associated with thrombocytopenia (moderate to severe) and increased D-dimer levels. Fibrinogen level was variable in Acute DIC cases so it is inconsistent parameter to assess Acute DIC.

Although various laboratory assays have been used to diagnose Acute DIC, there is no single laboratory test currently available for accurate and precise diagnosis of acute DIC. ISTH guidelines help to predict the severity and clinical outcome in DIC cases.

DIC scoring using ISTH criteria, can diagnose the early DIC, which is beneficial for treating physician or surgeon to take prompt action in order to save the life of the patient.

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