Original Article

Factors associated with mortality outcomes of patients with disseminated intravascular coagulation resulting from septicemia: a single center

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Abstract:

Background: *Disseminated intravascular coagulation (DIC) acquired from sepsis is a life-threatening condition which results in high mortality rates. The basic knowledge of epidemiology and the related factors causing morbidity and mortality can help physicians to recognize symptoms as well as provide proper management to decrease death rates.* ***Objective:*** *The aim of the study was to determine prevalence of DIC among patients with septicemia and factors associated with mortality outcomes.* ***Materials and Methods:*** *The medical records of 205 septic patients from 2011 to 2015 at HRH Princess Maha Chakri Sirindhorn Medical Center were gathered, reviewed, and analyzed as a retrospective study.* ***Results:*** *According to information obtained from 205 medical records, the median age of the patients was 68 years (range, 20-104). One-hundred and four patients were female (50.7%) and 101 patients (49.3%) were males. The blood cultures were positive for bacteria in 68.80% of cases. Urinary tract infection was the most common followed in rank by those of the respiratory tract, intra-abdominal area, skin and central nervous system. Thirty-nine of the 205 patients (19.0%) developed DIC. Multivariate analyses revealed significant associations with mortality within 28 days of hospital admission for patients presenting stage 4 chronic kidney disease (CKD) ($p = 0.002$), simple DIC score ≥ 2 at; diagnosis ($p = 0.019$) and 28 days of hospitalization ($p < 0.001$). Seventeen patients of the 39 (43.6%) diagnosed with DIC expired.* ***Conclusion:*** *A high mortality rate was observed among patients who developed sepsis with concurrent DIC. Patients presenting CKD stage 4, high level of simple DIC score at admission or 28 days of hospitalization were associated with higher mortality outcomes.*

Keywords : ● *Disseminated intravascular coagulation (DIC)* ● *Septicemia* ● *Red blood cell transfusion* ● *Cryoprecipitate transfusion* ● *DIC score*

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นิพนธ์ต้นฉบับ

ปัจจัยที่มีผลต่อการเสียชีวิตในผู้ป่วยที่มีภาวะลิ่มเลือดแพร่กระจายในหลอดเลือดที่เกิดจากการติดเชื้อในกระแสเลือดในศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี

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บทคัดย่อ

ความเป็นมา *ภาวะลิ่มเลือดแพร่กระจายในหลอดเลือดในผู้ป่วยที่ติดเชื้อในกระแสเลือดเป็นภาวะที่พบได้ค่อนข้างบ่อย ผู้ป่วยเหล่านี้มีโอกาสเสียชีวิตสูง จึงมีความสำคัญในการศึกษาถึงปัจจัยที่มีผลต่อการเสียชีวิตของผู้ป่วย* ***วัตถุประสงค์*** *ศึกษาความชุกของภาวะลิ่มเลือดแพร่กระจายในหลอดเลือดที่เกิดจากการติดเชื้อในกระแสเลือด และศึกษาปัจจัยที่มีผลต่อการรอดชีวิตของผู้ป่วยที่มีภาวะนี้* ***วิธีการ*** *เป็นการวิจัยแบบศึกษาแบบไปข้างหลังโดยการทบทวนเวชระเบียนผู้ป่วยที่ได้รับการวินิจฉัยภาวะลิ่มเลือดแพร่กระจายในหลอดเลือดที่เกิดจากการติดเชื้อในกระแสเลือดที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี ตั้งแต่ 1 ตุลาคม 2554 ถึง 30 กันยายน 2558* ***ผลการศึกษา*** *พบว่ามีผู้ป่วยที่ได้รับการวินิจฉัยภาวะติดเชื้อในกระแสเลือดทั้งหมด 205 ราย มีอายุเฉลี่ย 68 ปี (ช่วง 20-104 ปี) เพศหญิง 104 คน (50.7%) เพศชาย 101 ราย (49.3%) มีผู้ป่วยร้อยละ 68.8 ที่มีผลเพาะเชื้อในเลือดเป็นบวก สำหรับตำแหน่งที่ติดเชื้อ พบว่าส่วนใหญ่มีการติดเชื้อในทางเดินปัสสาวะจำนวน 83 ราย (40.5%) รองลงมาได้แก่ ติดเชื้อทางเดินหายใจจำนวน 62 ราย (30.2%) ติดเชื้อในช่องท้องจำนวน 30 ราย (14.5%) ติดเชื้อในระบบประสาทจำนวน 4 ราย (2%) และติดเชื้อบริเวณผิวหนังจำนวน 12 ราย (5.9%) ตามลำดับ พบว่ามีผู้ป่วย 39 ราย (19.02%) จากผู้ป่วยทั้งหมด 205 ราย มีภาวะลิ่มเลือดแพร่กระจายในหลอดเลือด สำหรับปัจจัยที่มีผลต่อการเสียชีวิตที่วันที่ 28 ของการนอนโรงพยาบาลได้แก่ ผู้ป่วยที่มีโรคประจำตัวเป็นไตวายเรื้อรังระยะที่ 4 โดยมีค่านัยสำคัญทางสถิติที่ 0.002 ผู้ป่วยที่มีคะแนน simple DIC score มากกว่าเท่ากับ 2 เมื่อนอนโรงพยาบาล และวันที่ 28 ของการนอนโรงพยาบาล โดยมีค่านัยสำคัญทางสถิติอยู่ที่ 0.019 และน้อยกว่า 0.001 ตามลำดับ จากจำนวนผู้ป่วยที่ได้รับการวินิจฉัยลิ่มเลือดแพร่กระจายในหลอดเลือดทั้งหมด 39 คน พบว่ามีผู้ป่วยเสียชีวิตทั้งหมด 17 คน คิดเป็นร้อยละ 43.59* ***สรุป*** *ภาวะลิ่มเลือดแพร่กระจายในหลอดเลือดที่เกิดจากการติดเชื้อมีอัตราการเสียชีวิตสูง ปัจจัยที่มีผลต่อการเสียของผู้ป่วยได้แก่ ไตวายเรื้อรังระยะที่ 4 และมีคะแนน simple DIC มากกว่าเท่ากับ 2 เมื่อนอนโรงพยาบาล และวันที่ 28 ของการนอนโรงพยาบาล*

คำสำคัญ : ● *Disseminated intravascular coagulation (DIC)* ● *Septicemia* ● *Red blood cell transfusion* ● *Cryoprecipitate transfusion* ● *DIC score*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2561;28:431-42.

Introduction

Disseminated intravascular coagulation (DIC) is a serious condition and a common problem among patients with septicemia. The mortality rate of DIC patients is very high. Thereafter, factors associated with survival among patients with consumptive coagulopathy pro-blems are important for prognosis and treatment. DIC is a syndrome that occurs from increased activation of coagulation systems and could generate excess thrombin. The activated fibrinogen, factor V and factor VII can cause thrombosis in small vessels. Moreover, activated fibrinolysis destroys coagulation factors, including platelets. Finally, bleeding complications can occur[1-3]. Most of these conditions are found among patients suffering from bacterial infections[4,5]. A recent study from Mayne ES, et al., showed that DIC resulting from infection was found in 84% of cases. The most common pathogen was co-infection between HIV and *Mycobacterium tuberculosis*.[6] The rising mortality rate in DIC with subsequent organ failure is more than that observed in DIC with acute leukemia[7].

Mahanupap P. and coworkers reported that 74% of the 165 Thai patients with a diagnosis of DIC, obtained from an infection[8]. Moreover, shock and acute renal failure were factors associated with high mortality rates in DIC[8]. Studies from others researchers have shown that patients with DIC acquired from serious infections could affect mortality rates at approximately 40-44%[9-11]. In addition, many studies have been conducted to identify parameters that determine the outcomes of patients with high DIC scores to predict poor outcomes[8,12]. Fibrin degradation products (FDP) and Acute Physiology and Chronic Health Evaluation (APACHE II) scores are associated with coagulation abnormalities and higher mortality rate[13]. As a result, clinicians use DIC scores combined with organ system failure scores to define parameters to predict the outcome of infectious patients[14].

The International Society on Thrombosis and Haemostasis (ISTH)(1) DIC score can be used to separate patients in two groups; overt and non-overt DIC. D-dimer and fibrinogen levels are used in calculating the DIC score. The score for test results of platelet counts are 0 for a platelet count $\geq$ 100 $x10^9$/L, 1 point when $<$ 100 $x10^9$/L, and 2 points for platelet counts $<$ 50 $x10^9$/L. For elevated fibrin markers such as D-dimer, and fibrin degradation products, scores are categorized as 0 for increased levels, 2 points for a moderate increase and 3 points for a significant increase. Prolonged PT is categorized as 0 for $<$ 3 sec, 1 point for between 3-6 seconds and 2 points for $>$ 6 seconds. Fibrinogen level is categorized as 0 for more than 1 g/dL and 1 point for $<$ 1 g/L. Calculated scores when $\geq$ 5 are compatible with overt DIC and need repeated scores daily. Scores $<$ 5 points, are suggestive of non-overt DIC and needs to be repeated in 1-2 days. Generally, D-dimer and fibrinogen are not routinely measured in general hospitals. Because of this, a simple DIC score (non calculated D-dimer and fibrinogen) can be calculated with not only prothrombin time but also platelet count and can be evaluated within 48 hours after admission. This simple DIC score can assist in predicting the outcomes[15] and can be used in general practice. Therefore, our study aimed to define the correlation between simple DIC score and the survival of patients. Moreover, APACHE II and organ system failure scoring are calculated among patients in the intensive care unit (ICU). However, not all patients with septicemia are treated in the ICU and as a result, this score was not calculated in our study.

The primary objective the study was to determine the prevalence of DIC among patients with septicemia, admitted at the HRH Princess Maha Chakri Sirindhorn Medical Center. For overall survival, determining the parameters affecting survival rates was considered a secondary objective.

Materials and Methods

A retrospective study was conducted from 2011-2015. The medical records of patients with septicemia were reviewed. Two hundred and five patients were included in this study. The inclusion criteria included patients

aged greater than 18 years and having a diagnosis of septicemia. The exclusion criteria were patients with DIC from other reasons. This study was approved by the ethics committee at Srinakharinwirot University.

The laboratory markers and clinical history of a disease recognized to cause DIC were used to diagnose DIC in our study. Laboratory markers consistent with DIC included prolongation of PT and aPTT, low level platelet count, and fragmented red blood cells in peripheral blood smear[16-18]. The simple DIC scores[15] included 1 point for each of the following: a) an absolute platelet count <100 x10^9/L; b) a prothrombin time > 15.0 sec; c) a 20% decrease in platelets and d) a > 0.3-sec increase in prothrombin time. This simple DIC score was used to separate the patients in two groups. The first group had scores ≥ 2, and second group < 2 points.

The Systemic Inflammatory Response Score (SIRS) was calculated using white blood cell count (WBC), body temperature (BT), respiratory rate (RR), and heart rate (HR). A value of 1 point was assigned for BT ≥ 38°C or < 36°C. One point was given when the HR was more than 90 beats per min, 1 point when the RR was more than 20 times per min and 1 point when the WBC count was > 12 x10^9/L or < 4 x10^9/L or bands > 10%[19]. SIRS score was used to divide patients in two groups. The first group had scores ≥ 3 for severe infection and less than 3 for a lower virulence of infection.

Data that were collected includes; age, gender, underlying disease (diabetes mellitus, hypertension, gout etc.), primary site of the septicemia, type of organism, complete blood count (CBC), prothrombin time (PT) with INR, activated partial thromboplastin time (aPTT), simple DIC score, and SIRS score.

Statistical Analysis

The results of this study were analyzed as descriptive statistics including percentage, mean and median. The Chi-square test was used to analyze the differentiation between both categories. Continuous factors used were taken from the one-way ANOVA test. All data, as mention above, were analyzed using SPSS software, version 20.0.0.0 and p-values less than 0.05 were defined as statistically significant. The survival analyses were calculated using the Kaplan-Meyer curve.

Results

Data were collected from 205 patients with a diagnosis of DIC resulting from septicemia. The baseline characteristics are shown in Table 1.

Table 1 Baseline characteristics of patients with septicemia (n = 205)

Characteristics	No. of patients	Rate (%)
Gender		
Male	101	49.3
Female	104	50.7
Underlying disease		
DM	89	43.4
HT	139	67.8
DLP	98	47.8
Heart	33	16.1
Liver	28	13.7
CKD stage 1	53	25.9
CKD stage 2	88	42.9
CKD stage 3	8	3.9
CKD stage4	29	14.1
CKD stage 5	27	13.2
Cancer	18	8.8
Thalassemia	15	7.3
SIR score 3	130	63.4
SIR score 4	75	36.6
Positive hemoculture	141	68.8
Types of infection		
UTI	83	40.5
Intra-abdominal	30	14.6
infection	62	30.2
Pneumonia	150	73.2
Primary bacteremia	4	2
CNS infection	12	5.9
Skin infection		

DM, diabetic mellitus; HT, hypertension;
DLP, dyslipidemia; CKD, chronic kidney disease;
SIR, systemic inflammatory response;
UTI, urinary tract infection; CNS, central nervous system

SIRS scores of 3 and 4 were present in 130 (63.4%) and 75 (36.6%) patients, respectively. One-hundred one (68.8%) septicemia patients showed positive blood cultures. The sites of infection included the urinary tract, respiratory tract, intra-abdominal area, skin and central nervous system were 83 (40.5%), 62 (30.2%), 30 (14.5%), 12 (5.9%) and 4 (2%), respectively. The data are shown in Table 1. The mean estimated glomerular filtration rate (eGFR) was 65.84% (median 76; range 4-186).

The factor associated with the mortality of patients with septicemia as taken by univariate ($p < 0.001$, HR 4.97, 95%CI: 2.60-9.49) and multivariate analyses ($p < 0.001$, HR 3.89, 95%CI: 2.0-7.57) was CKD stage 4 (Table 2). Patients with CKD stage 1 showed higher survival rates than those in any alternative stage of CKD.

Thirty-nine of the 205 patients (19.0%) developed DIC. The percentage of simple DIC scores ≥ 2 and simple DIC score < 2 were 10.73 and 8.29, respectively (Table 2).

Table 2 Univariate analysis of factors associated with mortality outcomes in patients with septicemia (n = 205)

Factors	No. of patients (%)	Mortality outcome			
		No. of patients (%)	HR	95%CI	*p* value
Gender					
Male	101 (49.3)	19 (18.8)	0.95	0.51-1.78	0.88
Female	104 (50.7)	20 (19.2)			
Diabetic mellitus					
Yes	89 (43.4)	16 (18)	0.88	0.47-1.67	0.70
No	116 (56.6)	23 (19.8)			
Hypertension					
Yes	139 (67.8)	27 (19.4)	1.05	0.53-2.1	0.9
No	66 (32.2)	12 (18.2)			
Dyslipidemia					
Yes	98 (47.8)	17 (17.3)	0.82	0.43-1.54	0.53
No	107 (52.2)	22 (20.6)			
Heart disease					
Yes	33 (16.1)	8 (24.2)	1.38	0.63-2.99	0.42
No	172 (83.9)	31 (18)			
Liver disease					
Yes	28 (13.7)	2 (7.1)	0.32	0.08-1.34	0.12
No	177 (86.3)	37 (20.9)			
CKD stage 1					
Yes	53 (25.9)	3 (5.7)	0.22	0.07-0.7	0.01
No	152 (74.1)	36 (23.7)			
CKD stage 2					
Yes	88 (42.9)	12 (13.6)	0.57	0.28-1.10	0.09
No	117 (57.1)	27 (23.1)			
CKD stage 3					
Yes	8 (3.9)	3 (37.5)	2.22	0.68-7.22	0.18
No	197 (96.1)	36 (18.3)			
CKD stage 4					
Yes	29 (14.1)	15 (51.7)	4.97	2.60-9.49	< 0.001
No	176 (85.9)	24 (13.6)			

Table 2 Univariate analysis of factors associated with mortality outcomes in patients with septicemia (n = 205) (continue)

Factors	No. of patients (%)	Mortality outcome			
		No. of patients (%)	HR	95%CI	*p* value
CKD stage 5					
Yes	27 (13.2)	6 (22.2)	1.23	0.52-2.95	0.64
No	178 (86.8)	33 (18.5)			
Cancer disease					
Yes	18 (8.8)	2 (11.1)	0.55	0.13-2.29	0.41
No	178 (91.2)	37 (19.8)			
Thalassemia disease					
Yes	15 (7.3)	4 (26.7)	1.52	0.54-4.27	0.43
No	190 (92.7)	35 (18.4)			
SIR score					
3	130 (63.4)	25 (19.2)	0.95	0.49-1.82	0.87
4	75 (36.6)	14 (18.7)			
Positive hemoculture					
Yes	141 (68.8)	25 (17.7)	0.79	0.41-1.52	0.47
No	64 (31.2)	14 (21.9)			
Urinary tract infection					
Yes	83 (40.5)	12 (14.5)	0.62	0.31-1.22	0.16
No	122 (59.5)	27 (22.1)			
Intra-abdominal infection					
Yes	30 (14.6)	2 (6.7)	0.28	0.07-1.18	0.08
No	175 (85.4)	37 (21.1)			
Pneumonia					
Yes	62 (30.2)	17 (27.4)	1.88	1-3.55	0.05
No	143 (69.8)	22 (15.4)			
Primary Bacteremia					
Yes	150 (73.2)	26 (17.3)	0.71	0.36-1.37	0.30
No	55 (26.8)	13 (23.6)			
CNS infection					
Yes	4 (2)	1 (25)	1.51	0.21-11.03	0.68
No	201 (98)	38 (18.9)			
Skin infection					
Yes	12 (5.9)	2 (16.7)	0.83	0.20-3.45	0.80
No	193 (94.1)	37 (19.2)			

CKD, chronic kidney disease; CNS, central nervous system; PRC, packed red cell; FFP, fresh frozen plasma

Sites of infection were the only differences noted between simple DIC < 2, simple DIC ≥ 2 and non-DIC. The data are shown in Table 3.

Comparisons of hemostatic laboratory assays among the simple DIC groups were found to be significant among those with lower platelet counts, prolonged PT and aPTT in the simple DIC group ≥ 2. The group of simple DIC < 2 had significantly lower platelet counts than those in the non-DIC group. However, no differences were found between the PT and aPTT in both groups. Data are shown in Table 4.

The 28-day mortality rate of DIC patients was 43.59% as shown in Figure 1. The average mean survival time was 19.18 days (SE 1.69) and ranged from 15.86-22.5 days. The analysis of simple DIC scores to predict the severity and prognostics of DIC showed higher mortality rates in the group with simple DIC score ≥ 2 at admission, 48 hours and 28 days of hospitalization. The data are shown in Table 5.

Factors associated with the 28-day mortality in the DIC group included CKD stage 4 (p = 0.004, HR 4.21, 95%CI: 1.57-11.26), simple DIC score ≥ 2 at admission (p = 0.04, HR = 2.84, 95%CI: 1.05-7.70) and 28 days of hospitalization (p = 0.02, HR 6.15, 95%CI: 1.36-27.93), received packed red cell (p = 0.001, HR 5.85, 95%CI: 2.03-16.86) and cryoprecipitate transfusions (p = 0.03, HR 3.05, 95%CI: 1.12-8.31). These results are shown in Table 5. Patients with stage 4 of CKD (p = 0.002,

Table 3 Baseline characteristics of patients with DIC in comparison with non-DIC (n = 205)

	simpleDIC ≥ 2 (n = 18))	**simpleDIC DIC < 2 (n = 21))**	**Non-DIC (n = 166)**	***p* value**
Age, median (range)	64.5 (40-88)	64 (20-91)	69 (24-104)	0.82
Male/female, n	11:7	13:8	77:89	0.23
DM (n = 89)	6	8	75	0.55
HT (n = 139)	10	11	118	0.08
DLP (n = 98)	7	8	83	0.43
Heart (n = 33)	3	2	28	0.69
Liver (n = 28)	5	3	20	0.18
CKD				
CKD stage 1 (n = 53)	1	4	48	0.08
CKD stage 2 (n = 88)	8	10	70	0.89
CKD stage 3 (n = 8)	1	0	7	0.60
CKD stage 4 (n = 29)	6	3	20	0.05
CKD stage 5 (n = 27)	2	4	21	0.70
Cancer (n=18)	3	3	12	0.26
Thalassemia (n=15)	1	3	11	0.43
SIR 3 point (n=130)	13	15	102	0.23
SIR 4 point (n=75)	5	6	64	0.33
Positive hemoculture (n = 141)	14	17	110	0.27
UTI (n = 83)	7	5	71	0.25
Intraabdominal infection (n=30)	3	2	25	0.78
Pneumonia (n = 62)	4	5	53	0.55
Primary bacteremia (n = 150)	13	17	120	0.70
CNS (n = 4)	1	2	1	0.01
Skin (n = 12)	1	0	11	0.48

DM, diabetic mellitus; HT, hypertension; DLP, dyslipidemia; CKD, chronic kidney disease;
SIR, systemic inflammatory response; UTI, urinary tract infection; CNS, central nervous system

Table 4 Baseline hemostatic markers in study patient groups classified by DIC status

	DIC ≥ 2 (n = 18)	*p* value**	DIC < 2 (n = 21)	*p* value***	Non-DIC (n = 166)
Platelet ($x10^9$/L)	46.5 (7-97)	0.01	94 (50-136)	< 0.001	244.5 (115-803)
PT (sec)	20 (16-31)	< 0.001	13 (11-25)	0.66	13 (10-32)
aPTT (sec)	42 (29-81)	< 0.001	30 (22-44)	0.39	30 (16-80)

*Median (range); **p-value between simple DIC score ≥ 2 and DIC score < 2; ***p-value between simple DIC score < 2 and non-DIC. The statistics were analyzed by one-way ANOVA test.

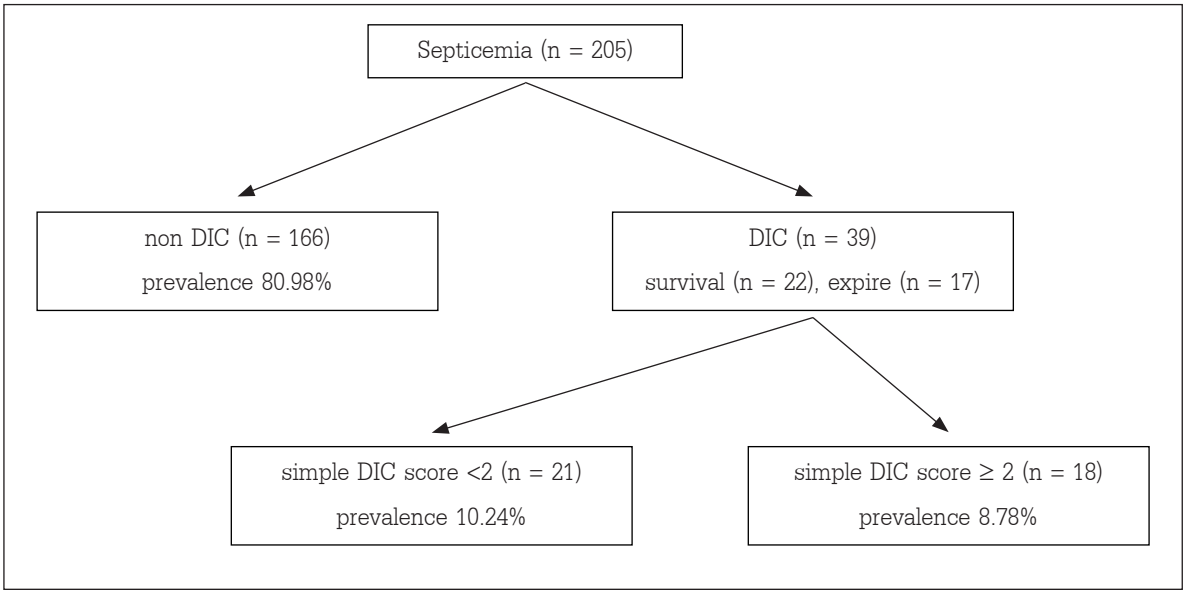

Figure 1 Outcomes of the study patient groups as classified by DIC status on admission

Table 5 Univariate analysis of factors associated with mortality outcomes of DIC in patients with septicemia (n = 39)

Factors	No. of patients (%)	Mortality outcome			
		No. of patients (%)	HR	95%CI	*p* value
Gender					
Male	24 (61.5)	8 (33.3)	0.42	0.16-1.1	0.08
Female	15 (38.5)	9 (60)			
Diabetic mellitus					
Yes	14 (35.9)	7 (50)	1.11	0.42-2.92	0.83
No	25 (64.1)	10 (40)			
Hypertension					
Yes	21 (53.8)	12 (57.1)	2.17	0.76-6.2	0.15
No	18 (46.2)	5 (27.8)			
Dyslipidemia					
Yes	15 (38.5)	7 (46.7)	0.97	0.37-2.55	0.95
No	24 (61.5)	10 (41.7)			
Heart disease					
Yes	5 (12.8)	3 (60)	2.29	0.65-8.04	0.2
No	34 (87.2)	14 (41.2)			
Liver disease					
Yes	8 (20.5)	1 (12.5)	0.2	0.03-1.52	0.12
No	31 (79.5)	16 (51.6)			

Table 5 Univariate analysis of factors associated with mortality outcomes of DIC in patients with septicemia (n = 39) (continue)

Factors	No. of patients (%)	Mortality outcome			
		No. of patients (%)	HR	95%CI	*p* value
CKD stage 1					
Yes	5 (12.8)	1 (20)	0.38	0.05-2.88	0.35
No	34 (87.2)	16 (47.1)			
CKD stage 2					
Yes	18 (46.2)	6 (33.3)	0.47	0.18-1.29	0.14
No	21 (53.8)	11 (52.4)			
CKD stage 3					
Yes	1 (2.6)	1 (100)	2.44	0.32-18.71	0.39
No	38 (97.4)	16 (42.1)			
CKD stage 4					
Yes	9 (23.1)	7 (77.8)	4.21	1.57-11.26	0.004
No	30 (76.9)	10 (33.3)			
CKD stage 5					
Yes	6 (15.4)	2 (33.3)	0.74	0.17-3.24	0.69
No	33 (84.6)	15 (45.5)			
Cancer disease					
Yes	6 (15.4)	0 (0)	0.04	0.0-6.27	0.21
No	33 (84.6)	17 (51.5)			
Thalassemia disease					
Yes	4 (10.3)	2 (50)	1.4	0.32-6.08	0.66
No	35 (89.7)	15 (42.9)			
SIR score					
3	28 (71.8)	13 (46.4)	0.75	0.24-2.30	0.61
4	11 (28.2)	4 (36.4)			
Positive hemoculture					
Yes	31 (79.5)	13 (41.9)	0.73	0.24-2.24	0.58
No	8 (20.5)	4 (50)			
Urinary tract infection					
Yes	12 (30.8)	5 (41.7)	0.88	0.31-2.5	0.81
No	27 (69.2)	12 (44.4)			
Intra-abdominal infection					
Yes	5 (12.8)	1 (20)	0.32	0.04-2.43	0.27
No	34 (87.2)	16 (47.1)			
Pneumonia					
Yes	9 (23.1)	5 (55.6)	1.48	0.52-4.20	0.47
No	30 (76.9)	12 (40)			
Primary Bacteremia					
Yes	30 (76.9)	13 (43.3)	0.87	0.29-2.70	0.81
No	9 (23.1)	4 (44.4)			

Table 5 Univariate analysis of factors associated with mortality outcomes of DIC in patients with septicemia (n = 39) (continue)

Factors	No. of patients (%)	Mortality outcome			
		No. of patients (%)	HR	95%CI	*p* value
CNS infection					
Yes	3 (7.7)	1 (33.3)	0.82	0.11-6.19	0.85
No	36 (92.3)	16 (44.4)			
Skin infection					
Yes	1 (2.6)	1 (100)	3.78	0.48-29.86	0.21
No	38 (97.4)	16 (42.1)			
PRC transfusion					
Yes	16 (41)	12 (75)	5.85	2.03-16.86	0.001
No	23 (59)	5 (21.7)			
FFP transfusion					
Yes	14 (35.9)	9 (64.3)	2.56	0.98-6.65	0.05
No	25 (64.1)	8 (32)			
Cryoprecipitate transfusion					
Yes	8 (20.5)	6 (75)	3.05	1.12-8.31	0.03
No	31 (79.5)	11 (35.5)			
Platelet transfusion					
Yes	9 (23.1)	3 (33.3)	0.64	0.19-2.24	0.49
No	30 (76.9)	14 (46.7)			
Simple DIC score at admission					
≥ 2	18 (46.2)	11 (61.1)	2.84	1.05-7.70	0.04
< 2	21 (53.8)	6 (28.6)			
Simple DIC score at 48 hours					
≥ 2	24 (61.5)	12 (50)	1.69	0.60-4.80	0.33
< 2	15 (38.5)	5 (33.3)			
Simple DIC score day 28					
≥ 2	19 (48.7)	11 (57.9)	6.15	1.36-27.93	0.02
< 2	16 (41)	2 (12.5)			

CKD, chronic kidney disease; CNS, central nervous system; PRC, packed red cell; FFP, fresh frozen plasma

HR 63.38, 95%CI: 4.73-850.13), simple DIC score ≥ 2 at admission (p = 0.019, HR 15.14, 95%CI: 1.56-146.93) and 28 days of hospitalization (p < 0.001, HR 151.04, 95%CI: 9.13-2,499.65) were found to be significantly associated with mortality using multivariate analysis as shown in Table 6.

Discussion

The study found that urinary tract infections were predominant among the causes of sepsis in the study. This differed from a study conducted by Iba T, et al.[20] finding respiratory tract infections as the common causes of sepsis. Thirty-nine of the 205 patients (19.0%) developed DIC–and the high mortality of 43.59 at 28 days was similar to that reported in related studies[9-11,20].

Regarding hemostasis, the analysis compared between simple DIC scores at ≥ 2 and < 2. The platelet counts for the simple DIC score ≥ 2 were significantly lower. The prolongation of PT and aPTT regarding simple DIC score ≥ 2 was significant. When comparing between the groups of simple DIC < 2 and nonDIC simple DIC < 2 had significantly lower platelet counts. However,

Table 6 Multivariate analysis of factors associated with mortality outcomes of DIC patients with septicemia (n = 39)

Factors	HR	95%CI	*p*-value
Simple DIC score ≥ 2 at day 28	151.04	9.13-2,499.65	< 0.001
CKD stage 4	63.38	4.73-850.13	0.002
Simple DIC score ≥ 2 at admission	15.14	1.56-146.93	0.019

no differences were observed in the PT and aPTT between both groups.

Using simple DIC scores to evaluate the severity of DIC at admission, 48 hours, and 28 days of hospitalization revealed a high mortality rate among patients in the simple DIC ≥ 2 group. The high mortality rate in admission and 48 hours among those with simple DIC scores ≥ 2 were similar to Kinasewitz GT et al.[15] (Survival rates for simple DIC < 2 were at 86%. The 28-days mortality rate in simple DIC ≥ 2 was at 54.5% and lower than stated by Kinasewitz GT et al.[14] (mortality rate 85%). Similarly, Iba T et al.[20] found decreased levels of platelet count, increased PT ratio and lower antithrombin levels related to 28-day mortality.

High mortality rates of CKD stages 4 and 5 including hemodialysis patient were found in 22-41% of the 30-day mortality rate[21-24]. The reported CKD stage 4 in our study was related to high mortality similar to related studies[21-24]. However, CKD stage 5 was not found to be a significant factor related to mortality and may be due to the small population in this group. Survival analysis using simple DIC score showed a significant difference in the simple DIC score < 2 group.

Limitations of this study included that it lacked the clinical presentations of DIC such as bleeding, thrombosis or both. No data about the volume of packed red cells, fresh frozen plasma and cryoprecipitate transfusions and no data concerning Hb levels between treatments were collected. Also, fibrinogen levels were not measured. Further studies, using larger populations of patients who fall in this category should be conducted over an extended period of time. Subsequent studies may find measured bleeding, thrombosis, or both values could be beneficial in predicting outcomes.

Summary

CKD stage 4, simple DIC score ≥ 2 at admission and 28 days of hospitalization were found to be significant factors associated with mortality among patients with DIC patients resulting from sepsis.

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