Disseminated Intravascular Coagulopathy (DIC) Score in Critically Ill Patients and its Impact on Prognosis

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Abstract

Objectives: To study the correlation between the incidence of Disseminated Intravascular Coagulopathy (DIC) in critically ill patients with Acute Physiology and Chronic Health Evaluation II (APACHE II) score ≥25 and the incidence and outcome of Multi-Organ Dysfunction Syndrome (MODS), and to investigate the relation between DIC and increasing mortality.

Design: A prospective, randomized, cohort, non-controlled, single center study.

Setting: Medical and Surgical Intensive Care Units (ICU’s) of Critical Care Department in Kasr-Alainy Hospital of Cairo University.

Patients: Fifty critically ill patients with APACHE II score ≥25, not including those with disseminated malignancies, chronic liver cell, renal failure or chronic hematological disorders.

Intervention: All included patients were subjected to informed consent, detailed history taking, careful physical examination, Laboratory investigations; including: Routine lab tests, Serum Fibrinogen and quantitative D-dimer levels.

Measurements: For all included patients with APACHE II score ≥25 on admission, DIC and Sequential Organ Failure Assessment (SOFA) scores were calculated at baseline (on ICU admission) and subsequently thereafter every 48 hours until ICU discharge or death or up to a total of 28 days. Clinical outcome (duration of stay in the ICU, need for mechanical ventilation, need for inotropic/vasopressor therapy, need for Renal replacement therapy (RRT), and final outcome of survival/mortality rates) were recorded.

Results: Through comparison between patients who improved or survived and patients who died at day 28; there was a significant variance between both groups in terms of SOFA score at day 2, day 4 and upon discharge (5.61±2.004 vs 7.69±2.901, p-value 0.01, 4.28±1.526 vs 8.97±3.578, p-value <0.001 and 3.17±1.543 vs 11.69±3.514, p-value <0.001 respectively). DIC score at day 2, day 4 and upon discharge (2.83±0.985 vs 3.59±0.946, p-value 0.01, 2.67±0.907 vs 3.91±1.174, p-value <0.001, and 2.33±1.085 vs 4.34±1.004, p-value <0.001 respectively), we found good correlation between DIC scores & SOFA scores at day 0,2,4 and at discharge (p-values: <0.001, <0.001, <0.001 & <0.001 respectively). There was good correlation between DIC scores at day 4 & at discharge & patient's outcome (p-value <0.001 & <0.001 respectively).

Conclusion: There was a strong correlation between SOFA and DIC scores in critically ill patients with APACHE II score ≥25 as regards MODS and mortality.

Key Words: Critically ill patients – Quantitative D-dimer level – Disseminated intravascular coagulopathy – Multi-Organ dysfunction syndrome – Apache II score – SOFA score – DIC score – Clinical outcome.

Introduction

ACUTE illness and injury are leading causes of death and morbidity worldwide [1]. In general, the earlier an accurate diagnosis is made and appropriate treatment started, the greater the chance of survival, reduced complications, better quality of life, and reduced health care costs. Therefore, the need to identify scores that aid clinicians in diagnosis, prognosis, and disease monitoring is driving the clinical scientific research [2].

Mortality risk prediction in patients admitted to ICU is commonly used in clinical research and practice. It helps to improve accuracy when evaluating management policies, refine indications for admission to ICU and facilitate comparison of actual and predicted mortality in different series [3].

Accurate prediction of prognosis for patients in intensive care unit (ICU) is important to allow appropriate treatment decisions by patients, relatives, and medical attendants [4].
The most commonly available tools for prediction of prognosis in ICU are the APACHE II (Acute Physiology and Chronic Health Evaluation II) score \[5\], and the SOFA (Sequential Organ Failure Assessment) score \[6\], which predict morbidity and mortality of critically ill patients.

These scoring systems are based on several physiological indices and chemical analyses. Over the years, several problems, pitfalls, and limitations of these scoring systems have been identified. Furthermore, they are very cumbersome and time consuming to apply, as they are based on several biochemical measurements and several physiological indices \[4\].

Although numerous scoring systems have been evaluated to predict morbidity and mortality of critically ill patients in the intensive care setting, yet none of them have proven entirely useful. Examples of such scoring systems include; SAPS (Simplified Acute Physiology Score), MPM (Mortality Prediction Models), MODS (Multiple Organ Dysfunction Score) and LODS (Logistic Organ Dysfunction Score). Interest has been developed in the use of DIC (Disseminated Intravascular Coagulopathy) score as a prognostic marker for critically ill patients in intensive care unit (ICU). DIC score is a diagnostic approach that depends on a set of criteria developed for the diagnosis of DIC \[7\].

**Aim of the study**:

- Evaluating the prognostic role of DIC score in critically ill patients with APACHE II score \(\geq 25\).
- Investigating the relation between DIC and increasing mortality in critically ill patients with APACHE II score \(\geq 25\).
- Studying the correlation between the occurrence of Disseminated Intravascular Coagulopathy (DIC) in critically ill patients (with Acute Physiology and chronic health evaluation (APACHE) score \(\geq 25\)) with the incidence and the outcome of Multi-Organ Dysfunction Syndrome (MODS) defined by Sequential Organ Failure Assessment (SOFA) score.

**Material and Methods**

Out of more than 200 critically ill patients admitted to the ICU of Critical Care Department in Cairo University due to a variety of etiologies during the period from July 2011 to January 2012; Only 50 patients were enrolled into our prospective, randomized clinical trial that was conducted at a Multidisciplinary Intensive Care Unit (ICU) with permission from the Institutional Ethical Committee.

**Inclusion criteria**:

- Our study was conducted on patients with the following criteria:
  - Age group (\(\geq 15\) and \(<80\) years).
  - Informed consent given by the patient or first degree relative.
  - Critically ill patients with high APACHE II Score on admission or within 24 hours of ICU admission \(\geq 25\).

**Exclusion criteria**:

- Extremes of age (\(<15\) and \(>80\) years).
- Disseminated malignancies
- Chronic liver cell failure classified as Child-Pugh class C.
- Chronic renal failure on regular dialysis.
- Chronic haematological disorders (e.g. leukemia, lymphoma, myelo-proliferative diseases, and purpura).
- Patients known to have coagulation defects or receiving anticoagulation therapy.
- Concomitant treatment with carcinostatics or irradiation.
- Post-cardiopulmonary resuscitation status.
- APACHE II score on admission or within 24 hours of admission <25.
- More than 24 hours after meeting inclusion criteria.
- Patients discharged from ICU against medical advice.
- Unknown outcome or loss of patient follows-up due to transfer to other hospitals.

Patients who were described as being critically ill immediately on admission, or within 24 hours of admission fulfilling the inclusion criteria and did not met any of the exclusion criteria were selected randomly and prospectively included into the study on the day of ICU admission and they were followed-up for a maximum period of 28 days or till the day of discharge or death.

**All included critically ill patients of our study were subjected to**:

- Signed Consent form the patient or 1st degree relative.
- Medical ethics committee approval.
- Detailed history taking.
- Careful physical examination: Including:
  a- Conscious level: Using Glasgow Coma score (GCS) which was evaluated at the day of admission and then followed daily.
  b- Vital signs which were evaluated at the day of admission and then followed daily, including:
    • Mean arterial blood pressure (MAP).
    • Heart rate.
    • Temperature.
    • Respiratory rate.
    • 24 hour-urine output monitoring through a urinary catheter.
    • Central venous pressure monitoring through a central line or a pulmonary artery catheter insertion.
    • Oxygen saturation monitoring through a pulse oximeter.
  c- Systemic examination.
- Laboratory investigations: Including
  Routine Laboratory investigations: Withdrawn on the day of admission and subsequently thereafter every 48 hours until ICU discharge or demise or up to a total of 28 days.
  Special laboratory investigations: These special laboratory investigations are specific to the study and they were done on day of admission and repeated every 48 hours till discharge or demise or up to a total of 28 days, and including:
  • Quantitative Fibrinogen level.
  • Quantitative D-dimer and Fibrin degradation products (FDP’s) assay.
- Clinical evaluation:
  The following data were evaluated and recorded up to a follow-up period of 28 days:
  • Length of ICU stay.
  • Need for mechanical ventilation & its duration.
  • Need for vasopressor or inotropic support & its duration.
  • Need for renal replacement therapy (haemodialysis).
  • Final outcome.
Survivors:
  • Patients recovered and discharged from ICU after improvement of their general condition.
  • Patients still morbid and stayed in ICU more than 28 days.
Non-survivors:
  • Patients who died within 28 days of ICU stay.
- Application of APACHE II, SOFA and DIC scoring Systems:
  APACHE II score [5] was evaluated in the first 24 hours of admission in patients with score ≥25 who didn’t get any of the exclusion criteria.
  For these patients, SOFA [6] and DIC [7] scores were evaluated on day of admission and serially every 48 hours until ICU discharge or demise or up to a total of 28 days (Tables 1-4).

Table (1): A) Acute physiology points of APACHE II score (APS) [5].

<table>
<thead>
<tr>
<th>Physiology variables</th>
<th>High abnormal range</th>
<th>Low abnormal range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+4</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>+2</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>+3</td>
<td>+4</td>
</tr>
<tr>
<td>Temperature (rectal)</td>
<td>≥41</td>
<td>39-40.9</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>≥160</td>
<td>130-159</td>
</tr>
<tr>
<td>Heart rate</td>
<td>≥180</td>
<td>140-179</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>≥50</td>
<td>35-49</td>
</tr>
<tr>
<td>Oxygenation (mmHg)</td>
<td>A-aDO2 or PaO2</td>
<td></td>
</tr>
<tr>
<td>a. FiO2&gt; 0.5 record A-aDO2</td>
<td>≥500</td>
<td>350-499</td>
</tr>
<tr>
<td>b. FiO2 &lt;0.5 record only PaO2</td>
<td>200-349</td>
<td></td>
</tr>
<tr>
<td>Arterial pH</td>
<td>≥7.7</td>
<td>7.6-7.69</td>
</tr>
<tr>
<td>Serum Sodium</td>
<td>≥180</td>
<td>160-179</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>≥23.5</td>
<td>23.4-24</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>≥260</td>
<td>50-59.9</td>
</tr>
<tr>
<td>White cell count (in 1000s/cmm)</td>
<td>≥240</td>
<td>20-39.9</td>
</tr>
<tr>
<td>Serum HCO3 (if PH is not available)</td>
<td>≥52</td>
<td>41-51.9</td>
</tr>
<tr>
<td>Glasgow Coma sale (204) = 15-actual GCS</td>
<td>653</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: A) Acute physiology points of APACHE II score (APS) [5].

Total APS-Sum of 12 individual variable points
**Disseminated Intravascular Coagulopathy (DIC) Score**

**Chronic health points:**

If the pt has a history of severe organ insufficiency or immuno-compromized assign points as follows:

- For nonoperative or emergency postoperative patients: 5 points.
- For elective postoperative patients: 2 points.

**APACHE II Score equals the Summation of A, B and C points:**

- **a- APS Points.**
- **b- Age points.**
- **c- Chronic Health points.**

**Follow-up:**

All patients were followed-up clinically and laboratory for a total of 28 days (4 weeks) from day of admission or till the day of discharge or demise.

**Correlation of scoring systems:**

We correlate between DIC score for critically ill patients with high APACHE II Score ≥25 and the incidence and the outcome of MODS as defined by SOFA score.

**Table (2): Age points of APACHE II score.**

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤44</td>
<td>0</td>
</tr>
<tr>
<td>45-54</td>
<td>2</td>
</tr>
<tr>
<td>55-64</td>
<td>3</td>
</tr>
<tr>
<td>65-74</td>
<td>5</td>
</tr>
<tr>
<td>≥75</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table (3): DIC score [7].**

<table>
<thead>
<tr>
<th>Risk assessment</th>
<th>Does the patient have an underlying disorder (e.g. sepsis, trauma, obstetric emergency) compatible with DIC?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory tests</td>
<td>Platelets' count, D-dimer and FDPs level</td>
</tr>
<tr>
<td>Scoring</td>
<td></td>
</tr>
<tr>
<td>Platelets' count</td>
<td>&gt;100=0 points, ≤100=1 point, ≤50=2 points</td>
</tr>
<tr>
<td>Elevated fibrin marker (D-dimer level): No elevation: (&lt; 1 mg/ml)=0 points, Moderate increase: (1-5 mg/ml)=2 points, Strong increase: (&gt;5 mg/ml)=3 points</td>
<td></td>
</tr>
<tr>
<td>Prolonged PT:</td>
<td>&lt;3 sec=0 points, &gt;3 &lt;6=1 point, &gt;6=2 points</td>
</tr>
<tr>
<td>Fibrinogen level</td>
<td>&gt;1 gm/l=0 points, ≤1 gm/l=1 point</td>
</tr>
</tbody>
</table>

**Table (4): SOFA Score [6].**

<table>
<thead>
<tr>
<th>SOFA score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration: PaO2/FiO2 (mmHg)</td>
<td>&lt;400</td>
<td>&lt;300</td>
<td>&lt;200</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Coagulation: Platelets (X 103/mm3)</td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Cardiovascular: Hypotension MAP &lt;70 mmHg</td>
<td>Dopamine &lt;5 mg/kg/min or dobutamine (any dose)</td>
<td>Dopamine &gt;5 mg/kg/min Or Epinephrine &lt;0.1 mg/kg/min Or Norepinephrine &lt;0.1 mg/kg/min</td>
<td>Dopamine &gt;15 mg/kg/min Or Epinephrine &lt;0.1 mg/kg/min Or Norepinephrine &lt;0.1 mg/kg/min</td>
<td></td>
</tr>
<tr>
<td>Central nervous system: Glasgow Coma score</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
</tr>
<tr>
<td>Renal: Creatinine (mg/dl) or urine output</td>
<td>1.2-1.9</td>
<td>2.0-3.4</td>
<td>3.5-4.9 or &lt;500 ml/day</td>
<td>&gt;5.0 or &lt;200 ml/day</td>
</tr>
</tbody>
</table>

**Statistical methods:**

- All obtained data were analyzed statistically by SPSS (Statistical Package for Social Science) program.
- Statistical significance will be analyzed by using analysis of variance (ANOVA).
- All values will be expressed as ranges and means ± SD (Standard Deviation) for numerical data or numbers and percentages for categorical data.
- Prevalence rate will be determined from the number of identified cases at the time of the study divided by all patients examined.
- \( p \)-value \( \leq 0.05 \) will be considered statistically significant.

- Chi square will be used as a test of significance for the qualitative data. The relationship between the studied parameters will be assayed by correlation.

- Pearson’s correlation coefficient will be applied. The cut-off points will be used as <0.3 for weak correlation, 0.3-0.7 for moderate correlation, and > 0.7 for strong correlation.

**Results**

It is a prospective non-controlled cohort study including fifty critically ill patients who were admitted to the Critical Care department Cairo University, from July 2011 to January 2012.

- **Demographic analysis:**

A total number of 50 patients were involved in our study. They included 22 males (44%) and 28 females (56%) (Fig. 1) with mean age 63.8 ± 12.7 years. Average length of stay was 12±8.9 days.

There was variable contribution of different age groups in our study. Age group (71-80 years old) constituted 36% of patients, while patients younger than 40 years old constituted 4% of all patients.

- **APACHE II score:**

Seventy Six percent of patients had APACHE II score 25-29, 14% of patients had APACHE II score 30-34 and 10% of patients had APACHE II score >34. It was noted that no patients with APACHE II score >34 survived in our study (Fig. 3).

- **SOFA score:**

SOFA score was implemented to assess incidence of organ dysfunction and determine severity of organ dysfunction in the critically-ill patients enrolled in our study. The figure below showed average values and standard deviation of SOFA scores (Fig. 4).
DIC score:

DIC score range, from score 0 to score 6, was tabulated and plotted for day zero, day 2, day 4 and at death or upon discharge to follow-up DIC score trend (Table 5).

Table 5: DIC score range in the study patients.

<table>
<thead>
<tr>
<th>DIC Score pts at Day</th>
<th>No. of pts at Day 0</th>
<th>No. of pts at Day 2</th>
<th>No. of pts at Day 4</th>
<th>No. of pts on Discharge or at Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>7</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>21</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>13</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>7</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Length of ICU stay:

Most of patients stayed for 2 weeks (78%) and only 8% of patients stayed for more than 28 days (proposed duration of the study).

Organ dysfunction:

In our study, 10% of patients had one organ affected, 48% had two organs affected, 34% had three organs affected and 8% had four organs affected in first 48 hours of admission to the intensive care unit.

Organ dysfunction varied in our study where CNS failure encountered in 94% of our patients, hemodynamic instability in 62%, renal failure in 54%, ARDS in 50% and liver cell failure in 38% of our patients.

Need for artificial support:

Need for artificial support varied in our study where need for mechanical ventilation was detected in 84% of our patients, need for hemodynamic support trough vasopressors was detected in 64% and need for RRT was needed in 22% of our patients.

Outcome of study population:

In the current study only 18 patients survived the ICU course (36%), yet 32 patients died (64%).

The current study patient’s characteristics were summarized in the following table and shown as mean, standard deviation, and values range (Table 6).

Table (6): Study population characteristics as mean, standard deviation and values range.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>63.8±12.7</td>
<td>17–80</td>
</tr>
<tr>
<td>GCS</td>
<td>9.7±3.7</td>
<td>3–15</td>
</tr>
<tr>
<td>Acid Base Status (Base deficit)</td>
<td>6.72±4.4</td>
<td>1–22</td>
</tr>
<tr>
<td>APACHEII Score</td>
<td>28.2±4</td>
<td>25–39</td>
</tr>
<tr>
<td>SOFA Score at day 0</td>
<td>6.3±2.6</td>
<td>2–13</td>
</tr>
<tr>
<td>SOFA Score at day 2</td>
<td>6.9±2.8</td>
<td>1–14</td>
</tr>
<tr>
<td>SOFA Score at day 4</td>
<td>7.3±3.8</td>
<td>0–15</td>
</tr>
<tr>
<td>SOFA Score on Discharge</td>
<td>8.6±5.1</td>
<td>0–19</td>
</tr>
<tr>
<td>DIC Score at day 0</td>
<td>3.1±1.1</td>
<td>0–5</td>
</tr>
<tr>
<td>DIC Score at day 2</td>
<td>3.3±1</td>
<td>1–5</td>
</tr>
<tr>
<td>DIC Score at day 4</td>
<td>3.5±1.2</td>
<td>0–6</td>
</tr>
<tr>
<td>No. of Organs affected in First 48 hr</td>
<td>2.4±0.8</td>
<td>1–4</td>
</tr>
<tr>
<td>Length of ICU stay (days)</td>
<td>12±8.9</td>
<td>2–40</td>
</tr>
</tbody>
</table>

Through comparison between patients who improved or survived and patients who died at day 28; there was a significant variance between both groups in terms of SOFA score at day 2, day 4 and upon discharge (5.61±2.004 vs 7.69±2.901, p-value 0.01, 4.28±1.526 vs 8.97±3.578, p-value <0.001, and 3.17±1.543 vs 11.69±3.514, p-value <0.001 respectively), DIC score at day 2, day 4 and upon discharge (2.83±0.985 vs 3.59±0.946, p-value 0.01, 2.67±0.907 vs 3.91±1.174, p-value <0.001, and 2.33±1.085 vs 4.34±1.004, p-value <0.001 respectively).

When compared to the mortality group, the survivor group showed statistically significant lower incidence of liver cell failure (16.7% vs 50%, p: 0.019), CNS failure (83.3% vs 100%, p: 0.04), hemodynamic instability (35.3% vs 78.1%, p: 0.002), need for vasopressor (33.3% vs 81.3%, p: 0.001), need for MV (61.1% vs 100%, p: <0.001) and the need for RRT (5.6% vs 31.3%, p: 0.035) (Table 7).

There was no significant difference between both groups in terms of age. There was no significant difference between patients group who improved or survived and the other patient group who died on admission, patients who died had higher APACHE II scores upon admission than those who improved but this was not statistically significant, (p-value 0.057) (Table 7).

SOFA scores increased for patients who died and decreased for patients who improved or survived, (p-value 0.996, 0.01, <0.001, and <0.001 for SOFA at day 0,2,4 and upon discharge respectively) (Table 7).

DIC scores increased for patients who died and decreased for patients who survived, (p-value
There was a good correlation between number of organ dysfunction at day 2 and outcome. As number of organ dysfunction increases, death rate increases. (1.83 ± 0.514 vs 2.72 ± 0.729, p-value <0.001) (Table 7).

Table (7): Comparison between study patients who improved or survived and those who died at day 28.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Improved</th>
<th>Died</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>64.67±15.243</td>
<td>63.31±11.243</td>
<td>.721</td>
</tr>
<tr>
<td>GCS</td>
<td>11.06±2.461</td>
<td>8.97±4.036</td>
<td>.052</td>
</tr>
<tr>
<td>Acid Base Status</td>
<td>5.33±2.351</td>
<td>7.47±5.042</td>
<td>.097</td>
</tr>
<tr>
<td>(Base deficit)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHEII Score</td>
<td>26.72±1.809</td>
<td>29.00±4.656</td>
<td>.053</td>
</tr>
<tr>
<td>SOFA Score at day 0</td>
<td>6.28±2.270</td>
<td>6.28±2.808</td>
<td>.996</td>
</tr>
<tr>
<td>SOFA Score at day 2</td>
<td>5.61±2.004</td>
<td>7.69±2.901</td>
<td>.010</td>
</tr>
<tr>
<td>SOFA Score at day 4</td>
<td>4.28±1.526</td>
<td>8.97±3.578</td>
<td>.0001</td>
</tr>
<tr>
<td>SOFA Score on Discharge</td>
<td>3.17±1.543</td>
<td>11.69±3.514</td>
<td>.000</td>
</tr>
<tr>
<td>DIC Score at day 0</td>
<td>3.11±1.132</td>
<td>3.13±1.129</td>
<td>.967</td>
</tr>
<tr>
<td>DIC Score at day 2</td>
<td>2.83±0.985</td>
<td>3.59±0.946</td>
<td>.010</td>
</tr>
<tr>
<td>DIC Score at day 4</td>
<td>2.67±0.907</td>
<td>3.91±1.174</td>
<td>.000</td>
</tr>
<tr>
<td>DIC Score on Discharge</td>
<td>2.33±1.085</td>
<td>4.34±1.004</td>
<td>.000</td>
</tr>
<tr>
<td>No. of Organ Failure in First 48 hrs</td>
<td>1.83±0.514</td>
<td>2.72±0.729</td>
<td>.000</td>
</tr>
<tr>
<td>Length of ICU stay (days)</td>
<td>10.61±5.135</td>
<td>12.84±10.377</td>
<td>.398</td>
</tr>
</tbody>
</table>

- Correlations:

The below figure shows correlation between DIC score at day 0 and SOFA score at day 0, (p-value <0.001) (Fig. 5).

The below figure shows correlation between DIC score at day 2 and SOFA score at day 2, (p-value <0.001) (Fig. 6).

The following figure shows correlation between DIC score at day 4 and SOFA score at day 4, (p-value <0.001) (Fig. 7).

There was good correlation between DIC score at discharge and SOFA Score at discharge, (p-value <0.001) (Fig. 8).

Receiver operating characteristic (ROC) curves analyses:

There is a significant correlation between SOFA scores at day 4 and patient’s outcome, (p-value <0.001) (Fig. 9).

When receiver operating characteristic (ROC) curve was used to determine SOFA score on day 4 as a determinant of outcome, the area under the curve was 89.3% and the best cut-off value was 5.5 with sensitivity 81.3% & specificity 77.8% (Fig. 9).

There is a significant correlation between SOFA scores at discharge and patients’ outcome, (p-value <0.001) (Fig. 10).

When receiver operating characteristic (ROC) curve was used to determine SOFA score upon discharge as a determinant of outcome, the area under the curve was 99.6% and the best cut-off value was 5.5 with sensitivity 96.9% and specificity 100% (Fig. 10).

There is a significant correlation between DIC scores at day 4 and patients’ outcome, (p-value <0.001) (Fig. 11).

When receiver operating characteristic (ROC) curve was used to determine DIC score on day 4 as a determinant of outcome, the area under the curve was 80.9% and the best cut-off value was 2.5 with a sensitivity 96.9% and a specificity 38.9% which was changed to a sensitivity of 62.5% and a specificity of 83.3% with cut-off value of 3.5 (Fig. 12).

There is a significant correlation between DIC scores at discharge and patients’ outcome, (p-value <0.001) (Fig. 13).

When receiver operating characteristic (ROC) curve was used to determine DIC score upon discharge as a determinant of outcome, the area under the curve was 90.6% and the best cut-off value was 2.5 with a sensitivity 96.9% and a specificity 66.7% which was changed to a sensitivity of 81.3% and a specificity of 88.9% with cut-off value of 3.5 (Fig. 13).

In our study, 32 out of 50 critically ill patients died while 18 patients survived with an average mortality rate of 64%. Of those patients who survived, 88.8% have an APACHE II score <30 and most of them stayed for less than 2 weeks duration in the ICU. While of those patients who died, 31.25% have an APACHE II score >30 and most of them didn’t stay in the ICU for more than 2 weeks.
Our study also showed that:

- Increasing value of SOFA score during follow-up of critically ill patients in our study is associated with poor prognosis; all patients who died had SOFA score value on admission lower than that before death.
- Decreasing value of SOFA score during follow-up of critically ill patients in our study is associated with better prognosis; all patients who survived have SOFA score value on admission higher than that before discharge.
- About 71.4% of included critically ill patient with DIC score $\geq 5$ on day 0 (i.e diagnosed as overt DIC since admission) died.
- About 46.87% of included critically ill patients who died in our study have DIC score $\geq 5$ either on admission or during follow-up.
- Increasing value of DIC score during follow-up of critically ill patients in our study is associated with poor prognosis; about 96.8% of our study patients who died have DIC score value on admission lower than that before death.
- Decreasing or constant value of DIC score during follow-up of critically ill patients in our study is associated with better prognosis; about 94.4% of our study patients who survived have DIC score value on admission higher than or equal to that before discharge.
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Sensitivity

120.0
100.0
80.0
60.0
40.0
20.0
0.0
-20.0

Fig. (11): Relation between DIC score at day 4 and outcome.

Discussion

Acute illness and injury are leading causes of death and morbidity worldwide [1]. In general, the earlier an accurate diagnosis is made and appropriate treatment started, the greater the chance of survival, reduced complications, better quality of life, and reduced health care costs [2].

Mortality risk prediction in patients admitted to ICU is commonly used in clinical research and practice. It helps to improve accuracy when evaluating management policies, refine indications for admission to ICU and facilitate comparison of actual and predicted mortality in different series [3].

The most commonly available tools for prediction of prognosis in ICU are APACHE II (Acute Physiology and Chronic Health Evaluation) score and SOFA (Sequential Organ Failure Assessment) score which predict morbidity and mortality of critically ill patients [5,6].

These scoring systems are based on several physiological indices and chemical analyses. Over the years, several problems, pitfalls, and limitations of these scoring systems have been identified. Furthermore, they are very cumbersome and time consuming to apply, as they are based on several biochemical measurements and several physiological indices [4].

Although numerous scoring systems have been evaluated to predict morbidity and mortality of critically ill patients in the intensive care setting, yet none of them have proven entirely useful. Interest has been developed in the use of DIC (Disseminated Intravascular Coagulopathy) score as a prognostic marker for critically ill patients in intensive care unit (ICU) [7].

Our study used a simple scoring system that was developed by the International Society of Thrombosis and Hemostatis (ISTH) as a diagnostic approach with good sensitivity and high specificity depending on a set of criteria for the diagnosis of DIC including the presence of an underlying disorder, platelets count, prothrombin time, quantitative D-dimer and fibrinogen levels. A score of 5 points or greater indicates overt DIC, while a score of less than 5 points does not rule out DIC but may indicate non-overt DIC [8].

Therefore, the objectives of our study were:

- Studying the correlation between the incidence of Disseminated Intravascular Coagulopathy (DIC) in critically ill patients (with Acute Physi-
iology and chronic health evaluation (APACHE II score ≥ 25) to catch patients with severe illness on admission with the incidence and the outcome of Multi-Organ Dysfunction Syndrome (MODS) defined by Sequential Organ Failure Assessment (SOFA) score.

Our research was conducted as a prospective, randomized study on only 50 critically ill patients because we had a wide scale of exclusion criteria and we included only patients with APACHE II score of 25 and higher, from July 2011 to January 2012, with five different causes for ICU admission including: trauma, post-operative care, respiratory failure, sepsis and circulatory shock.

The included critically ill patients were examined carefully and subjected to the measurement of SOFA and DIC scores on day of admission and serially every 48 hours until ICU discharge or death or up to a total of 28 days.

The following ICU outcome variables were recorded for all studies patients:

- Duration of stay in the ICU.
- Number and type of Organ dysfunction/failure.
- Need for mechanical ventilation.
- Need for inotropic/vasopressor support.
- Need for renal replacement therapy (RRT).
- Final outcome of survival/mortality rates.

Since the prediction of outcome is one of the major problems associated with critical illness. Recently, investigations have been performed on the potential evaluation of DIC score for prognosis of a variety of critical illness conditions.

Through comparison between two groups of patients; patients who improved or survived and patients who died within 28 days of ICU admission.

Patients who died had higher APACHE II score upon admission than those who improved but this was not statistically significant (p-value 0.057). Many studies demonstrated that the correlation between APACHE II score and clinical outcome. Van der Merwe et al. [9] conducted a prospective study on 304 critically ill patients and concluded that the use of the APACHE II model to accurately describe the risk of ICU death is validated and patients with severe sepsis and/or CAP had a significantly higher mortality [9]. Lee H, et al. [10] conducted a prospective single-center study on 131 critically ill patients and validated the use of APACHE II score as a severity scoring system that allows reliable prediction of outcome in intensive care patients. Mohammad et al., [11] conducted a descriptive analytical study on 204 hospitalized patients with multiple diagnostic diseases admitted to ICU. This study showed that APACHE-II score can truly predict mortality rate in patients in ICU [11]. In contrast to our study, Arnold et al., [12] published a study in the journal of parenteral and enteral nutrition showing the lack of predictive value and accuracy of APACHE II score in hypoalbuminemic severely ill patients. This study stated that the mortality rate in the severely hypoalbuminemic patients with serum albumin level <2.5gm/dl was fivefold higher than that would be predicted by their APACHE II score, but this study didn’t explain why low serum albumin, despite not being one of the APACHE II score parameters, underestimate mortality predicted by APACHE II score.

In the present work, when compared to the mortality group, the survived group showed statistically significant lower incidence of: Liver Cell Failure (p-value: 0.019), CNS Failure (p-value: 0.04), Hemodynamic Instability (p: 0.002), Need for vasopressor (p-value: 0.001), Need for Mechanical ventilation (p-value: <0.001), and the need for Renal Replacement Therapy (p-value: 0.035). Also, there was a strong correlation between the number of organ dysfunction in first 48 hours and clinical outcome. As number of organ dysfunction increases, mortality rate increases (p-value <0.001).

Lee et al., [13] conducted a study to correlate between Acute LCF and mortality and found a high mortality rate in patients with acute LCF. Sprung C, et al., [14] showed in his study that alterations in mental status are common in septic patients, and are associated with significantly higher mortality. Philippa et al., [15] conducted a study to correlate between shock and clinical outcome which revealed that shocked patients had higher mortality rate. Pedro et al., [16] conducted a cohort, multiple-center, observational study on seventeen Portuguese intensive care units (ICUs) on 897 patients with community-acquired septic shock, the study revealed suggestive data that norepinephrine administration could be associated with worse outcome. The norepinephrine group had a higher hospital mortality (52% vs. 38.5%, p-value=0.002) and this means that administration of norepinephrine was associated with an increased risk of death. Acute Physiology Score II and norepinephrine administration were independent risk factors for ICU mortality in patients with septic shock. Kendirli et al., [17] conducted a retrospective study on 407 mechanically ventilated patients in the ICU, the study revealed that mechanical ventilation can be lifesaving, but more than 50% of complications in
conditions that require intensive care are related to ventilatory support particularly if it is prolonged. Heinz et al., [18] conducted a prospective, cohort, multi-center study on 17,126 patients, admitted to 30 different ICUs in Austria, who underwent renal replacement therapy because of acute renal failure (renal replacement therapy patients). These patients had significantly higher hospital mortality (p-value <0.001). Shapiro, et al., [19] conducted a cohort prospective study on 3,102 patients with suspected infections. This study revealed that each additional organ dysfunction increased the adjusted 1-year mortality hazard by 82%.

In our study, DIC score was higher in patients who died when compared to those who survived or improved on admission, yet with no statistical significance (p-value 0.967). However, there was a statistically significant higher DIC score in patients who died when compared to those who survived or improved at day 2, 4 and upon discharge or at death (p-value: <0.01, <0.001, and <0.001 respectively). Battah A, et al., [20] conducted a study on fifty patients who had been admitted to the ICU of Critical Care Medicine Department at kasr Alainy hospital of Cairo University in Egypt during 2007 with the diagnosis of severe sepsis or septic shock to predict the outcome using the simple evolving DIC score (only using PT and platelet count). In concordant with our study, Battah A, et al., [20] showed that the simple evolving DIC score calculated in the first 48hrs from two readily available global coagulation markers, platelet count and Prothrombin time, was an accurate predictor of clinical course and outcome in patients with sepsis. In contrast to our study, Battah et al., [20] included only patients with sepsis and excluded any patient with septic shock. While our study included all critically ill, traumatic, post-operative, septic, shocked patients and those with respiratory failure, with APACHE II score >25, not only septic patients, in addition our study included patients with septic shock. Battah et al., [20] also used SOFA and DIC scores only on admission and after 48 hours of admission, in addition to the use of only two of the four essential parameters needed to calculate ISTH score for DIC (platelets count and prothrombin time), together with the lack of DIC score value >5 as a diagnostic value for the presence of disseminated intravascular coagulopathy in critically ill patients. While our study used SOFA and DIC scores not only on admission but also every 48 hours at day 0, day 2 and day 4 during ICU stay and upon discharge or at death, in addition to the use of all of the four essential parameters needed to calculate ISTH score for DIC (including; platelets’ count, prothrombin time, serum fibrinogen and D-dimer levels), together with the use of DIC score value >5 as a diagnostic value for the presence of disseminated intravascular coagulopathy in critically ill patients.

SOFA score was higher in the study patients who died when compared to those who survived or improved on admission, yet with no statistical significance (p-value 0.996). However, there was a statistically significant higher DIC score in patients who died when compared to those who survived or improved at day 2, 4 and upon discharge or at death (p-value: 0.01, <0.001, and <0.001 respectively). There was a significant correlation between SOFA score at day 4 and upon discharge or at death and clinical outcome of the study patients (p-value <0.001). The area under the ROC curve was 89.3% and 99.6% respectively and the best cut-off value was 5.5 with a sensitivity of 81.3% and 96.9% respectively.

In concordance with our study, Okabayashi et al., [21] conducted a study on 1789 patients admitted to the ICU of the department of Anaesthesiology at Mie University School of Medicine in Japan from January 1998 to December 2001 showing that the SOFA score is very useful for predicting the outcome of DIC patients in the ICU. Argyriou et al., [22] conducted a prospective study on 200 patients admitted to CCU from April 2010 to May 2011 showing that APACHE II and SOFA scores on admission are independent predictors of mortality in patients hospitalized in ICU. Both scores demonstrate excellent performance in discriminating high-risk patients and thus are useful tools to predict clinical outcome in CCUs. Minne L, et al., [23] published a systematic review studies. Eighteen articles differed widely in the SOFA derivatives used and in their methods of evaluation. The combination of SOFA derivatives with APACHE II/III and SAPS II models clearly improved prognostic performance of either model alone. Huang et al., [24] conducted a retrospective study on 726 patients with acute myocardial infarction at the division of cardiology of internal medicine department at Taipei general hospital of National Yang-Ming hospital of Taiwan showing that SOFA score provides potentially valuable prognostic information on clinical outcome. Oliviera et al., [25] conducted a retrospective study on 673 women with severe maternal mortality showing that total maximum SOFA score proved to be an effective tool for evaluating severity and estimating prognosis in cases of severe maternal mortality. However, Huang et al., [24] and Oliviera et al., [25] conducted their studies on a selective type of patients (e.g. acute
myocardial infarction, obstetric emergencies), while our study was performed on critically ill patients with various etiologies for ICU admission including trauma, post-operative, sepsis, respiratory failure and shock. Shrestha et al., [26] conducted a prospective study on one hundred and seventeen critically ill patients, the study compared APACHE II score and SOFA score in prediction of mortality in ICU showing that there is a strong and good correlation between APACHE III and initial SOFA score. Moreover, initial SOFA score had better calibration and performed better to predict patients who died within 28 days of ICU admission, for the prediction of their adverse outcomes and rapid risk stratification that might allow clinicians to make more rational therapeutic decisions.

Our study stated that the change in DIC score from admission to 48hr later was an accurate predictor of clinical course and may reflect improving or worsening of the underlying disease (p<0.001). Even when the absolute values of PT and/or platelet count were within normal range but moving in the direction that could suggest an underlying coagulopathy. This may highlight the value of change over time rather than single admission score. These results agree with the results of the study of Dhainaut et al., [29] who noted that worsening coagulopathy predicts a worse outcome in patients with severe sepsis. Unlike our study, Dhainaut J, et al., [29] didn't use the ISTH scoring system in his study to diagnose patients with DIC.

There was a significant correlation between DIC score on admission, at day 2, at day 4 and upon discharge or at death with SOFA score at on admission, at day 2, at day 4 and upon discharge or at death for the study patients (p-value <0.001). So, it can be concluded from our study that there is a strong correlation between DIC score and SOFA score regarding the final outcome, mortality rate and prognosis of critically ill patients with APACHE II score >25. In concordant with our study, Hiromoto et al., [30] published a retrospective study on 254 patients with severe trauma admitted to ICU. This study showed that DIC and SOFA scores on day 0 were independent factors that predicted the continuous progression of the DIC from the early to late phase of trauma. Trauma itself, but not sepsis, contributes to the continuous progression of DIC from the early to late phase of trauma. In contrast to our study, Hiromoto M, et al., [30] used DIC and SOFA scores only on day 0, while our study compared DIC and SOFA score on day 0,2,4 and upon discharge or at death. Also Hiromoto et al., [30] conducted his study on a selective type of patients with severe trauma, in addition to the difference in the sample size.

Finally, all of the three scores intended to prognosticate patients’ outcome showed variable data. As regards the conflicting data in these scores as discussed before. So we recommend combining the three scores, APACHE II score, SOFA score and DIC score, together in order to improve the prognostic capability of these scores.

Conclusion:
DIC score could be used as a potentially useful marker for the evaluation of critically ill patients when admitted to the ICU and for the prediction of their adverse outcomes and rapid risk stratification that might allow clinicians to make more rational therapeutic decisions.
Therefore, DIC score could be used as a predictive test that is easy to perform and interpret for early prognosis and prediction of adverse outcome of critically ill patients at their admission to the ICU, this early risk stratification is of particular significance in the intensive care environment to ensure that the hospital resources are used efficiently and appropriately.

Limitations:

- Unfortunately, our study was conducted on fifty patients only, being a self-funding research. In addition, our study included follow-up of serial DIC score for all studied patients every 48 hours on admission, at day 2, at day 4 and upon discharge or at death.

- The high selectivity of our study patients as mentioned before also limit the number of patients as the exclusion criteria were variable.

- Finally, concerning some statistically insignificant results observed in our study, it will be better to be re-evaluated again in future studies on a larger number of patients to give more accurate statistical results.

Disclaimer:

The current study is self funding one and there were no conflicting interests during our work.

References


