

Clinical Research

Clinical characteristics of acute respiratory distress syndrome survived patients at a tertiary hospital in Jakarta

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ABSTRAK

Latar belakang: Berbagai penelitian mengenai perbedaan karakteristik antara pasien yang bertahan hidup dan meninggal karena ARDS sudah banyak dilaksanakan di seluruh dunia, akan tetapi masih sedikit penelitian yang berasal dari negara berkembang. Tujuan penelitian ini mengetahui karakteristik klinis pasien ARDS yang bertahan hidup selama perawatan di rumah sakit.

Metode: Penelitian ini menggunakan desain prospektif dan observasional yang dilaksanakan di Jakarta mulai dari Oktober 2015 hingga April 2016. Data primer didapatkan dari pasien ARDS (berdasarkan definisi Berlin) yang dirawat di IGD, ICU, HCU, ICCU, dan semua bangsal perawatan. Pasien diikuti perkembangannya sampai mereka keluar dari rumah sakit. Analisis data hanya dilakukan pada pasien yang bertahan hidup selama perawatan. Analisis deskriptif dilakukan menggunakan SPSS 21.0.

Hasil: Sebanyak 43 pasien bertahan hidup selama jangka waktu penelitian. Mayoritas pasien adalah laki-laki (53,5%), berusia kurang dari 65 tahun (69,8%), mengalami ARDS ringan (62,8%), onset dini (55,8%), dan disebabkan oleh sepsis (97,7%). Mayoritas memiliki komorbiditas (74,4%), skor APACHE II <20 (77,3%) dengan rata-rata 15,6±4,8, rata-rata albumin 2,9±0,6 dan median procalcitonin 3 (0,1-252,3).

Kesimpulan: Profil klinis pasien ARDS yang bertahan hidup dalam penelitian ini hampir sama dengan pasien pada penelitian lain yang dilaksanakan baik di negara berkembang maupun negara maju.

ABSTRACT

Background: While a good deal of research on characteristic the different characteristics between surviving and dying patient with ARDS has been conducted globally, such research is scarce in developing countries. This study aimed to obtain clinical profile of ARDS survivors during hospitalization.

Methods: This was a prospective, observational study conducted at a tertiary hospital in Jakarta from October 2015 to April 2016. Primary data was collected from ARDS patients based on Berlin Definition admitted to emergency room, ICU, HCU, ICCU, and all other wards. The patients were followed until they discharged. We only included survivors on the analysis. Descriptive analysis was done using SPSS 21.0.

Results: A total of 43 patients were survived during study period. The majority were below 65 years of age (69.8%) and were male (53.5%). ARDS was mainly mild in severity (62.8%) and early onset (55.8%). Sepsis was the most common causes of ARDS (97.7%). Most of the patients had comorbidities (74.4%). Majority of the patients had APACHE II score <20 (77.3%) with mean 15.6±4.8. The mean of albumin was 2.9±0.6 and the median of procalcitonin was 3 (0.1-252.3).

Conclusion: The clinical profile of ARDS survivors in our study were mostly similar with other studies conducted in developed and other developing countries.

Keywords: ARDS, clinical profile, survivors

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Acute respiratory distress syndrome (ARDS) is an acute inflammatory lung injury, characterized by increased pulmonary capillary endothelial cells and alveolar epithelial cells permeability leading to respiratory failure in the absence of cardiac failure.¹ ARDS may arise from sepsis and non-sepsis causes.² Despite recent advances in treatments, overall mortality rate remains high ranging from 25 to 49%.³ Death within 72 hours of admission is mainly caused by the condition that caused ARDS. Meanwhile after 72 hours of admission, nosocomial pneumonia and sepsis were the most common cause of death.^{4,5}

While a good deal of research on different characteristics between surviving patients and dying one has been conducted globally, such research is scarce in developing countries. The aim of this study was to obtain clinical profile of patients with ARDS who survived during hospitalization at a tertiary hospital in Jakarta.

METHODS

This was a prospective, observational study conducted in emergency room, intensive care unit (ICU), high care unit (HCU), intensive coronary care unit (ICCU) and all other wards at a tertiary hospital in Jakarta from October 2015 to April 2016. All patients admitted with ARDS were followed until they discharged. The inclusion criteria were as follows: (1) diagnosed as ARDS based upon Berlin definition 2011, (2) age 18 years and older. The exclusion criteria was death during hospitalization. The protocol of this study has been approved by Medical Ethics Committee of Universitas Indonesia (No. 998/UN2.F1/ETIK/2015).

Variables and measurement

The demographic characteristics included age and gender. The clinical characteristics included etiology of ARDS, ARDS severity, onset of ARDS, days from admission to ARDS onset, duration of mechanical ventilation prior to ARDS, comorbidity, Acute Physiology and Chronic Health Evaluation (APACHE) II score, length of stay, and mean arterial pressure. The laboratory result included hemoglobin (Hb), white blood cells (WBC), platelet count, aspartate transaminase (AST), alanine transaminase (ALT), albumin, random blood glucose, blood urea nitrogen

(BUN), serum creatinine, ratio of arterial oxygen partial pressure to fractional inspired oxygen ($\text{PaO}_2/\text{FiO}_2$ ratio), pH, partial pressure of carbon dioxide in arterial blood (PaCO_2), partial pressure of oxygen in arterial blood (PaO_2), Na, K, Cl, and procalcitonin.

ARDS was defined as a precipitant of lung injury or development of new or worsening respiratory symptoms within one week, in which the presence of bilateral infiltrates on a chest radiograph and pulmonary edema was not caused by cardiac problem. The severity of ARDS was categorized based on the degree of hypoxemia: mild ($\text{PaO}_2/\text{FiO}_2$ 201-300 mmHg), moderate ($\text{PaO}_2/\text{FiO}_2$ 101-200 mmHg), and severe ($\text{PaO}_2/\text{FiO}_2 \leq 100$ mmHg).⁶

The etiology of ARDS was categorized into sepsis and non-sepsis causes. Sepsis was diagnosed if there were at least two of the following symptoms: body temperature $>38^\circ\text{C}$ or $<36^\circ\text{C}$, heart rate >90 x/minute, respiratory rate >24 x/minute or $\text{PaCO}_2 < 32$ mmHg, leucocyte count $>12,000$ cells/ mm^3 or $<4,000$ cells/ mm^3 or $>10\%$ immature form, and definite source of infection.² Non-sepsis condition may arise from large burn, repeated transfusion, emboli, acute pancreatitis, severe trauma, drowning, inhalation of drug, lung contusion prior to ARDS.²

Early onset ARDS was defined as ARDS developing during the first 48 hours after hospital admission. Comorbidity was defined by documented clinical diagnosis at the end of hospitalization. Its category included diabetes mellitus, chronic kidney disease, systematous lupus erythematosus (SLE), liver cirrhosis, cerebrovascular disease (CVD), and acquired immune deficiency syndrome (AIDS). The APACHE II score is a measure of severity of disease and used to assess risk of in-hospital mortality.⁷ It was calculated on the first 24 hour of ARDS and categorized into <20 and ≥ 20 .

Statistical analysis

Data was analyzed using SPSS (SPSS Inc., Chicago, IL, USA) program version 21.0. For qualitative variables, a descriptive analysis was done and presented as frequencies (percentage). Frequency of quantitative variable was calculated and represented using mean \pm SD or median

(interquartile range/IQR) if the data was not normally distributed.

RESULTS

Demographic, clinical characteristics, and laboratory result of the patients are listed in Table 1, 2, and 3 respectively. There were 43 patients who survived of ARDS during the study. The majority were below 65 years old (69.8%) and were male (53.5%).

The clinical characteristics that have been identified among the majority are as follows: they developed mild ARDS (62.8%), the cause of ARDS was sepsis (97.7%), their onset was early (55.8%), their APACHE II score was less than 20 (77.3%), they had comorbidities (74.4%), and the length of their stay was 16 (from 2 to 65) days. Comorbidities included diabetes mellitus (23.2%), chronic kidney disease (16.2%), SLE (2.3%), liver cirrhosis (2.3%), cancer (30.2%), cerebrovascular disease (16.2%), and AIDS (2.3%).

DISCUSSION

The present study attempts to obtain clinical profile of patients who survived from ARDS during hospitalization at a tertiary hospital in Jakarta.

In the present study, the majority of ARDS survivors were below 65 years of age with the median of 61 (18-88). This result is similar with the study conducted by Sharif et al⁸ which found that 90% of the survivors were below 65 years old. It has also been shown by the study from

Tabel 1. Demographic characteristics

| Variables | Survivors (n=43) |
|-------------------|------------------|
| Age, median (IQR) | 61 (18-88) |
| Age, n (%) | |
| <65 years | |
| >65 years | 30 (69.8) |
| Gender, n (%) | |
| Male | 13 (30.2) |
| Female | 20 (46.5) |

IQR= interquartile range

Zilberberg et al⁹ that older age (>65 years) was independently associated with higher mortality rate among ARDS patients.

Female gender was associated with lower mortality rate in several studies. They attributed it to different genetic susceptibility in response to ARDS and the therapy or hormonal difference.¹⁰ However, the predilection of gender was vary among studies. In our study, the majority of survivors were male (53.5%). This result is in accordance with the results by Venet et al¹¹, Bhadade et al¹²

Tabel 2. Clinical characteristics

| Variables | Survivors (n=43) |
|--|------------------|
| Etiology of ARDS, n (%) | |
| Septic | 42 (97.7) |
| Non Septic | 1 (2.3) |
| Severity of ARDS, n (%) | |
| Mild | 27 (62.8) |
| Moderate | 11 (25.6) |
| Severe | 5 (11.6) |
| Early-onset, n (%) | |
| No | 19 (44.2) |
| Yes | 24 (55.8) |
| Days from admission to ARDS Onset, median (IQR) | 2 (0-33) |
| Days of mechanical ventilation prior to ARDS, median (IQR) | 0 (0-7) |
| Comorbidity, n (%) | 32 (74.4) |
| Diabetes mellitus | 10 (23.2) |
| Chronic kidney disease | 7 (16.2) |
| SLE | 1 (2.3) |
| Liver cirrhosis | 1 (2.3) |
| Cancer | 13 (30.2) |
| CVD | 7 (16.4) |
| AIDS | 1 (2.3) |
| APACHE II, n (%) | |
| <20 | 34 (77.3) |
| ≥20 | 10 (22.7) |
| APACHE II, mean ± SD | 15.6±4.8 |
| Duration of stay, median (IQR) | 13 (2-65) |
| Mean arterial pressure, median (IQR) | 83.3 (70-134.3) |

ARDS= acute respiratory distress syndrome; IQR= interquartile range; SLE= systemic lupus erythematosus CVD= cardiovascular disease; AIDS= acquired immune deficiency syndrome; APACHE II= acute physiology and chronic health evaluation

Table 3. Laboratory result

| Variables | Survivors (n=43) |
|--|---------------------|
| Hb (g/dl), mean ± SD | 11.2±2.36 |
| WBC (10 ³ cells/mm ³), mean ± SD | 16.6±8.3 |
| Platelet count (10 ³ cells/mm ³), mean ± SD | 234 (34.5–725) |
| AST ^a , median (IQR) | 36 (11–1,960) |
| ALT ^b , median (IQR) | 23 (9–1,336) |
| Albumin ^a , mean ± SD | 2.9±0.6 |
| Random blood glucose ^c , median (IQR) | 137.5 (81–991) |
| BUN (mg/dL), median (IQR) | 42.5 (12.2–198) |
| Serum creatinine (mg/dL), median (IQR) | 1 (0.1–7.5) |
| PaO ₂ /FiO ₂ , mean ± SD | 259.7±137.1 |
| pH, mean ± SD | 7.4±0.1 |
| PaCO ₂ (mmHg), median (IQR) | 29.4 (17.3–77.1) |
| PaO ₂ (mmHg), mean ± SD | 128.8±54 |
| HCO ₃ ^b (mmol/L), mean ± SD | 23.3±6.4 |
| Natrium (mEq/L), mean ± SD | 134.7±10.2 |
| Postassium (mEq/L), (mEq/L), median (IQR) | 3.8 (2.31–6.75) |
| Chloride (mEq/L), mean ± SD | 101.2±12.1 |
| Procalcitonin ^a (mg/mL), median (IQR) | 3 (0.1–252.3) |

^a) Data were missing for 1 patient; ^b) Data were missing for 2 patients; ^c) Data were missing for 3 patients, WBC= white blood cells; AST= aspartate transaminase; ALT= alanine transaminase; IQR= interquartile range; BUN= blood urea nitrogen, PaO₂/FiO₂; Ratio= ratio of arterial oxygen partial pressure to fractional inspired oxygen; PaO₂= partial pressure of oxygen in arterial blood; PaCO₂= partial pressure of carbon dioxide in arterial blood.

and Tseng et al¹³ which stated that most of ARDS survivors were male, with percentage 76.5%, 75.5%, and 57.5%, respectively.

Majority of survived patients in our study developed ARDS due to sepsis. This is due to the fact that although sepsis-related ARDS has higher mortality than non-sepsis related, sepsis is the major cause of ARDS.²

According to Berlin definition, the severity categories of ARDS (mild, moderate, severe) are associated with increased mortality (27%, 32%, and 45%, respectively).⁶ The majority of ARDS survivors in our study were developed mild ARDS.

The majority of patients developed early-onset ARDS which was similar with the study by Liao et al.¹⁴ According to the study, late-onset ARDS contributed to increased mortality. In addition,

the duration of mechanical ventilation before the onset of ARDS was also independent risk factors of mortality. In our study, the median of duration of mechanical ventilation prior to ARDS was similar with the result from Liao et al¹⁴ (0 (0–7) vs 0.5±0.7).

Almost all of the patients in this study had comorbidities. This finding was similar with other study by Sheu et al² and Erickson et al¹⁵ which shown that 40% of survived ARDS patients had comorbidity. This study conducted in a tertiary care centre which accepts referral patients from other hospitals in Jakarta and other provinces. That's why patients usually had complex conditions and more than one underlying diseases.

According to the study conducted by Saleh et al¹⁶ which compared mortality prediction of different scoring system, APACHE scoring system was recommended to be used rather than other systems because of its superior accuracy. In addition, the APACHE II scoring system also routinely used in our hospital. Higher APACHE II represented severity of diseases and significantly associated with mortality. In our study, 77.3% of patients who survived have APACHE II score <20. This result is consistent with the other study conducted by Sharif N et al⁸ (75%). The median of APACHE II score (15.6±4.8) was also similar with the results from Estenssoro et al⁴ (19±6.3) and Luecke et al¹⁷ (17.9±4.7).

For the laboratory result, the result we found in our study was quite similar with the study by Liao et al.¹⁴ In our study, the mean of WBC (10³/mm³) was 16.6±8.3 compared to 15.3±8.7; platelet count (10³/mm³) 234 (34.5–725) compared to 226.3±132.4; BUN (mg/dl) 42.5 (12.2–198) compared to 38.5±28.2; serum creatinine 1 (0.1–7.5) compared to 2.4±2.8.

The median of procalcitonin level was similar with study by Tang et al¹⁸ (3 (0.1–455) vs 2.59 (0.95–6.25)). High level of procalcitonin could be arised from the damage alveolar integrity. Similarity on albumin level was also found between our study and Tseng et al¹³ (2.9±0.6 vs 2.56±9.67).

Meanwhile, the mean of PaO₂/FiO₂ (259.7±137.1), pH (7.4±0.1) and the median of PaCO₂ (29.4 (17.3–

77.1) were different from the results found in the study by Estenssoro et al⁴ PaO₂/FiO₂ (149±61) pH (7.32±0.09) and PaCO₂ (42.8±13). However, other laboratory results were not included in other study.

There were several limitations in our study. The number of patients included was small due to the short duration of study. In addition, although we used the Berlin Definition in our study, we did not include complete ventilatory parameter due to the lack of data. We also did not include complete biomarker variables in our study.

In conclusion, the majority of patients who survived of ARDS during hospitalization in our hospital are as follows: below 65 years old, male, mild ARDS, caused by, early onset, diabetic comorbidities, APACHE score was <20, mean of albumin was 2.9, and median of procalcitonin was 3. The clinical profile was similar with the other studies from developed and developing countries.

Conflicts of interest

The authors affirm no conflict of interest in this study.

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