Case Report

Respiratory Parameter Has A Great Impact in Determining Sepsis Conditionin COVID-19 Patients at Saiful Anwar Hospital Malang: Case Report

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Abstract

To describe Sequential Organ Failure Assessment (SOFA) Score parameters which have a great impact in the condition of sepsis in Corona Virus Disease-19 (COVID-19) patients and comorbidities that aggravate the patient's condition, we conducted a prospective cohort study in adult patients with sepsis and confirmed COVID-19 cases. We conducted a prospective cohort study in confirmed COVID-19 patients with sepsis who were admitted at Saiful Anwar Hospital Malang at March 10th – April 21st 2020. Diagnosis of sepsis is based on the Surviving Sepsis Campaign–III criteria. We found 6 COVID-19 confirmed patients with sepsis. There is an increased respiratory parameter in SOFA Score in these patients. Therefore, respiratory parameter of the SOFA score has a great impact in determining sepsis condition among confirmed COVID-19 patients.

Keywords : COVID-19, Sepsis, SOFA Score

BACKGROUND

COVID-19 carries an enormous health impact around the world. Most patients have mild disease, however 5% of patients experience severe symptoms which results in a case fatality ratio of 1.4%.[1,2] Sepsis is an organ dysfunction syndrome due to disregulation of host responses to infection with a mortality rate of 20–50%.[3] Thus, it is necessary to determinethis condition in COVID-19 patients.

We conducted a prospective cohort study in confirmed COVID-19 patients with sepsis who were admitted at Saiful Anwar Hospital Malang at March 10th – April 21st 2020. This study was limited to adult patients who fulfilled the sepsis criteria based on the Survival Sepsis Campaign–III. We defined organ dysfunction as a total SOFA Score ≥2. Assasement of SOFA Score performed when patient come in Isolation Emergency Room. The real time-Polymerase Chain Reaction (rt–PCR) examination for COVID-19 was carried out by "Balai Besar Laboratorium Kesehatan" (BBLK) Surabaya and Jakarta, which are standardized laboratories. The purpose of this paper is to describe about SOFA Score parameters which have a great impact in the condition of sepsis in Corona Virus Disease-19 (COVID-19) patients and comorbidities that aggravate the patient's condition.

CASE REPORT

Six confirmed COVID-19 patients with sepsis were obtained, with following demographics: 2 male and 4 female and age range 22-61 years (mean 49 years).The average patient coming from Malang (4/6).

Patients are in close contact history (3/6) and travel to visit the area affected by COVID-19 (3/6).Typical COVID-19 symptoms including shortness of breath (6/6), cough (5/6), and fever (5/6); atypical symptom includes diarrhea (2/6). Sepsis assessment is based on the SOFA Score, which includes respiratory parameter (PF Ratio), hematology (platelets), liver function (total bilirubin), cardiovascular (Mean Arterial Pressure; MAP), awareness (Glasgow Coma Scale; GCS) and renal function (Creatinin Clearance (CrCl) and/or urine output). Based on respiratory parameter, 3 patients (50%) had a PF ratio of < 200 (SOFA Score 3) and 3 patients (50%) had a PF ratio of <100 (SOFA Score 4). In hematology parameter, 2 patients (33,3%) had a platelets level of <150,000 (SOFA Score 1). Liver function abnormality was found in 1 patient (16,7%) with bilirubin level of 1.2–1.9 (SOFA Score 1). Cardiovascular parameter abnormalities were found in 2 patients (33,3%) with MAP ≤70 mmHg and norepinephrine support ≤0.1 (SOFA Score 3). All patients presented with GCS of 15 (SOFA Score 0). On renal function parameter, 1 patient had a CrCl level of 1.2–1.9 (SOFA Score 1). Lactic acid examination was only performed in 4 patients with result of >2 (Mean 3.43). Unfortunately, not all patients were checked for lactic acid levels, which is an important parameter in sepsis.

Besides sepsis, there are also various kinds of comorbidities that can aggravate the patient's condition including Diabetes Mellitus (2/6), Hypertension (4/6),

TABLE 1
Characteristic Sample and SOFA Score

Parameter		Female-1	Male-1	Female-2	Female-3	Male-2	Female-4	Mean
Age		50	22	47	61	59	57	49
Respiration	PaO2/FiO2	55.8 (4)	97.8 (4)	176 (3)	66.3 (4)	187.9 (3)	126.31 (3)	118.35
Coagulation	Platelet	129.000 (1)	254.000 (0)	292.000 (0)	273.000 (0)	147.000 (1)	193.000 (0)	182.500
Liver	Bilirubin	0.37 (0)	1.09, 1.56 (1)	0.34 (0)	0.39 (0)	0.72 (0)	0.75 (0)	0.61
	OT/PT	30/50	156/329	24/13	38/15	115/109	106/80	
Cardiovascular	MAP	75 (0)	96.7 (0)	93.3*NE (2)	75*NE (2)	81.3 (0)	77.6 (0)	83.15
Awareness	GCS	15 (0)	15 (0)	15 (0)	15 (0)	15 (0)	15 (0)	15
Renal	Creatinin; urine output	1.03 (0)	0.76 (0)	0.97 (0)	0.66 (0)	1.84 (1)	0.53 (0)	0.96
Total SOFA Score		(5)	(5)	(5)	(6)	(5)	(3)	4,8**

Note: OT/PT: oxaloacetic transaminase/ pyruvic transaminase; MAP: Mean Arterial Pressure; GCS: Glasgow Coma Scale
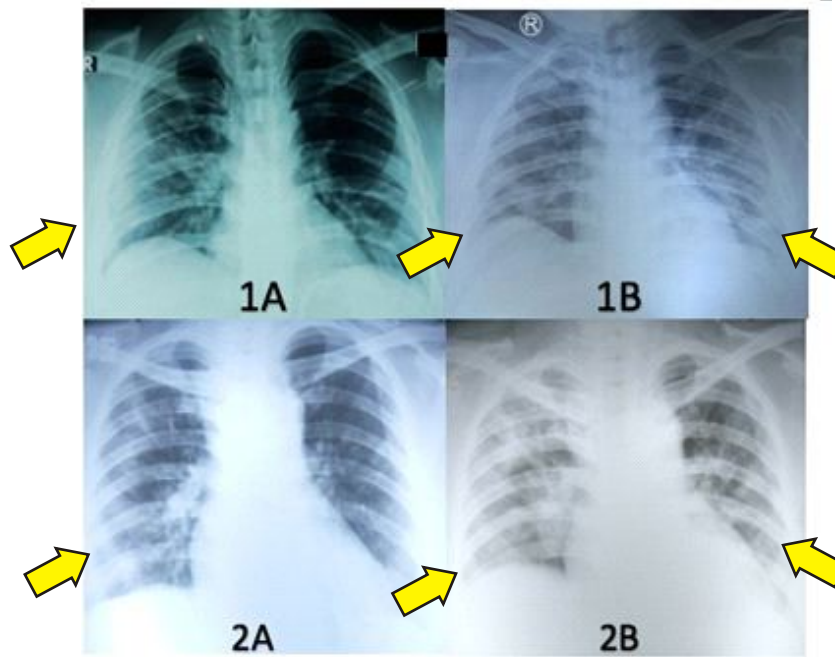
Figure 1. Comparison of CXR2 patients COVID-19 on days 1 (1A), 8 (1B)and days 1 (2A), 2 (2B); Worsening bilateral infiltrates predominantly in basal area typical of COVID-19.

Heart Failure (3/6) and obesity (1/6). After the patient received intensive care, it was found out that 1/6 patients died due to sepsis and ARDS, while 5/6 patients could survive from COVID-19.

Chest x-ray (CXR) findings including peripheral bilateral infiltrations with air bronchogram, predominantly in the basal area typical of viral pneumonia. CXR examinations were done since the first day of admission and were evaluated in a regular period. Although initial evaluation CXR showed increase of infiltrates, these findings were later improved as clinical symptoms improved.

Sepsis management is carried out by providing supportive therapies, including oxygenation, fluid resuscitation and administration of antibiotics and/or neuroamidase inhibitors. Patients with low PF ratios were given oxygen therapy using oxygen masks (RBM, NRBM, Jackson reese breathing circuit) 10-15 liter/min with target saturation maintained above 93%, which were then titrated according to clinical symptoms. All patients were given crystalloids as resuscitation fluid, and 2 patients (33,3%) were given norepinephrine as vasopressor until target MAP >65 mmHg was achieved. Patients were given antibiotics based on local antibiogram, including broad-spectrum antibiotics and/or respiratory floroquinolones. Immediate administration of neuroamidase inhibitors (hydroxycloroquine andolsetamivir) was given to inhibit development of SARS-CoV-2. One patient subsequently died due to sepsis and ARDS after receiving intensive care, while 5 patients was recovered.

DISCUSSION

We reported COVID-19 patients who fulfilled the clinical criteria for sepsis, with shortness of breath, cough, and fever as the most common clinical symptoms. These symptoms are consistent with the typical clinical symptoms seen in COVID-19 patients. Less common, atypical symptoms of COVID-19 including diarrhea, which can be seen in 1 patient in this study.[2,4]

CXR finding of COVID-19 includes multilocalized, bilateral or unilateral consolidations. Pleural effusion is rare. CXR may also normal in COVID-19. In our study, CXR findings were bilateral peripheral infiltrate, predominantly in basal area, which worsens in several days; However, these findings were improved as the patients' condition improved.[5,6]

Sepsis is defined as life-threatening organ dysfunction caused by dysregulation of host's response to infection. Organ dysfunction can be identified as acute change in the total SOFA Score ≥2 points, which reflects overall risk of death.Patients with septic shock can be identified by clinical construct of sepsis with persistent hypotension that requires vasopressors to maintain MAP ≥65 mmHg and lactate level above 2 mmol/L (18 mg/dL) despite adequate volume resuscitation.[3,7]

The prevalence of hypoxic (type 1) respiratory failure in COVID-19 patients is about 19%; Thus, oxygen therapy is of a great importance in these patients. The recommendation states that supplemental oxygen be initiated when SpO2 <90% with initial administration of 5 l/min oxygen via nasal cannula titrated to achieve

target saturation of >90% but no more than 96%. Considering the associated harm and cost of oxygen use, the panel strongly recommends toavoid lower SpO2 (<90%), and thus recommends that the reasonable range of SpO2 to be 92–96%.[2,3] We applied these recommendations to our patients, and the patients' clinical condition were shown to improve after 12 days with subsequent oxygen therapy.

Fluid resuscitation is also a paramount of sepsis management, especially in the presence of septic shock; aggressive fluid resuscitationusing crystalloids should be initiated and vasopressor (preferred norepinephrine) given should there were no improvement in MAP.[2] Anerobic metabolism and decreased tissue perfusion would give rise to increased level of lactic acid in sepsis patients, which is indeed seen in our patients (mean level 3,43). Further fluid needs should be given based on clinical response and target perfusion evaluation, including MAP >65 mmHg, urine production >0.5 ml/kg/hour, disappearance of mottled skin, improvement capillary refill time, recovery of consciousness and decreased lactic acid level.[2,8] More importantly, in patients with COVID-19 accompanied by shock, it is recommended to use dynamic parameters such as body temperature, capillary refill time, and/or lactate measurements to assess fluid response. All of patient are get fluid resuscitation using crystalloids (NS 0,9%) fluid, only 2 patients were added with vasopressor (norepinephrine) thus shock condition resolved immediately.

COVID-19 patients treated in RSSA with sepsis have several comorbidities, including DM, HT, Heart Failure and Obesity. The most common comorbidities in COVID-19 patients are hypertension (30%), diabetes (19%), and coronary heart disease (8%). Other reports show that the most common comorbidities in patients with COVID-19 who become acute respiratory distress syndrome are hypertension (27%), diabetes (19%), and cardiovascular disease (6%).[9]

Most of the existing research shows that diabetes mellitus as a typical comorbidity is associated with more severe disease, acute respiratory distress syndrome and increased mortality. Diabetes is a chronic inflammatory condition characterized by various metabolic and vascular abnormalities that can affect the host response to pathogens. Hyperglycemia and insulin resistance increase the synthesis of glycosylated end products and pro-inflammatory cytokines, oxidative stress, in addition to stimulating the production of adhesion molecules that mediate tissue inflammation. This inflammatory process can develop the underlying mechanisms that lead to a higher propensity to infections, with a worse outcome in patients with diabetes.[10,11]

The relationship between COVID-19 and hypertension cannot be concluded. However, the fact that hypertension, and other forms of cardiovascular disease are often found in COVID-19 patients, who are treated with angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB), and SARS-CoV-2, bind with ACE2 in the lungs for cell infiltration. ACE inhibitors and ARBs increase ACE2, which theoretically increases the binding of SARS-Cov-2 to the lungs and their pathophysiological effects that lead to more severe damage. However, ACE2 has actually been designed to protect from lung damage in experimental studies. ACE2 forms angiotensin 1–7 from angiotensin II, and thereby reduces the inflammatory action of angiotensin II, and increases the potential anti-inflammatory effect of angiotensin 1–7. Thus, by reducing one of the formation of angiotensin II in the case of ACE inhibitors, this agent can actually contribute to reducing systemic inflammation and especially in the lungs, heart, and kidneys. Thus, ACE inhibitors and ARBs can reduce the potential for the development of acute respiratory distress syndrome, myocarditis or acute kidney disorders, which can occur in COVID-19 patients.[9]

Obesity as a risk factor for COVID-19 is of little concern. This risk is very relevant in the US because the prevalence of obesity is around 40%, compared to the prevalence of 6–2% in China, 20% in Italy, and 24% in Spain. Obesity can restore ventilation by blocking the diaphragm travel, impairing the immune response to viral infections, being proinflammatory, and inducing diabetes and oxidant stress which adversely affects cardiovascular function. It can be concluded that in populations with a high prevalence of obesity, COVID-19 will affect a younger population than previously reported.[12]

We reported 6 patients with confirmed sepsis COVID-19, with 1 patient died and 5 patients recovering. The cause of death of these patient is multiple comorbid from the patient, his comorbid not only respiratory failure but also diabetes mellitus and heart failure. In China increase in the number of COVID-19 cases with CFR 3.4%, and patients with cardiovascular disease have a significantly increased risk of death.[1,13]

Treatment of Covid 19 patients with sepsis does not differ considerably with sepsis in general, only on Covid 19 need to be considered concerning infection control such as, the use of personal protective equipment when performed certain actions (intubation, mechanical ventilation and other actions) treating patients in isolation room with negative pressure, reduce aerosol action, and others.[3]

CONCLUSION

We have described the patients with confirmed COVID-19 accompanied with sepsis condition in our Hospital. Diagnosis of sepsis in COVID-19 patients should be made quickly and treated promptly and accordingly to prevent

worsening in these patients. SOFA Score is a quick, easy tool to determine sepsis condition. Respiratory parameter of the SOFA Score is the dominant factor seen in our patients. Therefore, Respiratory parameter of the SOFA Score has a great impact in determining sepsis condition among patients with COVID-19.

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