Bukti Korespondensi Publikasi Dr. Indri Lakhsmi Putri, dr., Sp.B.P.R.E., Subsp.K.M. (K)

Judul : Characteristics of Patients with Pressure Injuries in a COVID-19 Referral Hospital

https://journals.lww.com/aswcjournal/fulltext/2023/04000/characteristics_of_patients_with_pressure_injuries.12.aspx

Penulis:

Indri Lakhsmi Putri (Penulis ke-1 dan Penulis Korespondensi), Aldrich Alexander Afeli Tungga, Rachmaniar Pramanasari, Citrawati Dyah Kencono Wungu.

Jurnal : Advances in Skin and Wound Care

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About the Journal

A monthly peer-reviewed, interprofessional journal, *Advances in Skin & Wound Care* is highly regarded for its unique balance of cutting-edge original research and practical clinical management articles on wound prevention and treatment and other problems of skin integrity. Each issue features CME/NCPD for physicians, nurses, and allied health providers, the first journal in the field to regularly offer continuing education for all healthcare professionals.

The mission of *Advances in Skin & Wound Care* is**:**

- TO MEET the information needs of international interprofessional skin and wound care practitioners through publication of peer-reviewed original research, comprehensive literature reviews, unique case reports, and practical patient management articles that translate evidence to clinical practice.
- TO PROVIDE a forum for current product research and emerging technologies, educational opportunities, and discourse to support clinical and professional development.

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Daftar Bukti Korespondensi

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Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

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2 pesan

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Jun 18 2022 09:34:08:546PM

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Advances in Skin & Wound Care

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Question: Please indicate whether you have financial relationships (regardless of amount of compensation) with entities. You should report relationships that were present during the 36 months prior to submission including board membership, consultancy, employment, expert testimony, grants/grants pending, payment for lectures including service on speakers bureaus, payment for manuscript preparation, patents (planned, pending or issued), royalties, payment for development of educational presentations, stock/stock options, travel/accommodations/meeting expenses unrelated to activities listed (for example, if you report a consultancy above there is no need to report travel related to that consultancy), etc.
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Response: I agree

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Response: I understand

Question: Enter the word count of your article (excluding citations and legends).
Response: 3088No

Question: Is this paper being considered by any other publisher? Yes or No. (We do not accept simultaneous submissions.)
Response: No, this paper is not being considered by any other publisher.

Question: Was this manuscript invited by an editor and/or is it intended for a particular section or column in the journal? If so, please enter the inviting editor's name and/or section/column below.
Response: No, this manuscript is not invited by an editor and/or is it intended for a particular section or column in the journal.

Question: Is this paper being submitted as part of a course requirement?
Response: No

Question: Please provide a 1-2 sentence description of your article and its significance in lay terms.
Response: As a possible risk for severity, health professional should put attention to the increase in d-dimer in COVID-19 patients who develop pressure injury. Pressure injuries in COVID-19 patients may not result in immediate mortality, an increase in morbidity may be prevented with proper treatment.

Question: Please add any relevant social media handles/usernames for promotional purposes.
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Jun 23 2022 11:20:57:978AM

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Jul 06 2022 09:25:23:606AM

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Aug 02 2022 10:10:35:025AM

RE: ASWC-D-22-00154, entitled "Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital"

Dear Mrs. Putri,

Your manuscript was sent for external peer review by content experts. Their feedback is provided below. Please consider their comments and make the necessary revisions. Thank you for your efforts!

Please highlight all changes and include with your revised submission an itemized, point-by-point response to the reviewers' comments, and return the revised manuscript by Aug 16 2022 11:59:59:000PM. By highlighting all changes, the editors are more easily able to see whether reviewers' comments were incorporated into the revision. The author should provide rationale for not making suggested revisions.

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Madeline Talbot
Publishing Assistant
Advances in Skin & Wound Care

Reviewer Comments:

Dear Author,

Thank you for your submission! Our peer reviewers feel that this is an interesting study and have many constructive suggestions for revision. Please consider all of their comments and make the corresponding edits as needed to the manuscript. Please be sure to highlight all changes to the manuscript in yellow so that they are easily assessed upon resubmission. We look forward to receiving your revised manuscript.

Sincerely,
The Editorial Team of Advances in Skin & Wound Care

Reviewer #1:

The submission is very informative, with good citations. Subject matter is of adequate depth. It is interesting that no patients had Stage 1 or Stage 4 ulcers.

Reviewer #2: Thank you very much for invitation to review this manuscript.

This article focuses on the skin problem of the patients with COVID-19. It is an issue could be paid more attention. However, since the 2020, COVID-19 has been a worldwide healthy problem, and management of such patients has become routine, or so-called "post-pandemic". Here, I have some comments.
1. In the manuscript, the rate of PIs is 1.1% (12/1070). The positive rate is low, the number of patients with PIs is small. It means it is not able to do the further statistical correlation analysis but descriptive analysis. If the total sample size is large enough and the positive rate increases, the results can be statistically correlation analyzed, which will be more meaningful.
2. In the introduction part, page 4 line 5--"A "cytokine storm" may arise as the COVID-19 proceeds…." The pathological process of COVID-19 is too much elaborated, which is not closely related to PI, it is suggested to simplify.
3. In page4 line45--"The polymerase chain reaction confirmed that the patients were positive for COVID-19."in terms of the patient recruitment, you recruit patient based on the patient's medical history which diagnosed with COVID-19. But the specific diagnostic methods need not be stated.
4. Reference 18 should be updated. The 2021 version of PI guideline has been published. Please update.
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Please provide more information on the statement: "an increase in morbidity can be avoided with the right care."
Please define the right care

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Author's Response To Reviewer Comments

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Dear Editor,
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Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital

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Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital

Indri Lakhsmi Putri[1,2*], Aldrich Alexander Afeli Tungga[2], Rachmaniar Pramanasari[2], Citrawati Dyah Kencono Wungu[3]

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Introduction: For more than two years, Corona Virus Disease 2019 (COVID-19) has been a global pandemic. As the number of patients admitted to hospitals grows, particularly in the intensive care unit (ICU), more of these individuals are vulnerable to pressure injury (PI) as a result of disease complications.

Methods: This retrospective study describes the data of COVID-19 patients treated at a COVID-19 referral hospital from March 2020 to June 2021, who experienced pressure injuries either before or after admission. The patients' profile, symptoms, comorbidities, location and severity of pressure injury, laboratory values, oxygen therapy, length of stay (LOS), and usage of vasopressors were all presented.

Results: During the study period, 1070 patients were hospitalized for COVID-19 with varying degree of severity, twelve patients were diagnosed with PI. Eight (66.7%) of the patients were men. The median age was 60 (51–71), and half of the patients were obese. Eleven (91.4%) patients had at least one concurrent condition. The sacrum and gluteus were the two most commonly affected sites. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL). The average length of stay (LOS) was 22 days (9.8 – 40.3).

Conclusion: Health professionals should be aware of an increase in d-dimer in COVID-19 patients who suffer from pressure injury**.** Even though pressure injuries in these patients might not result in immediate mortality, an increase in morbidity can be avoided with the right care.

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ACKNOWLEDGMENTS

The authors would like to thank all Airlangga University Hospital staff for the efforts, understanding, and dedication during these difficult times.

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Methods: This retrospective study describes the data of COVID-19 patients treated at a COVID-19 referral hospital who experienced pressure injuries either before or after admission. Age, gender, BMI, symptoms, comorbidities, location and severity of pressure injury, complete blood count, serum creatinine, albumin, d-dimer, oxygen therapy, length of stay (LOS), and use of vasopressors were all presented for each patient.

Results: In this study, 1070 patients were confirmed to have COVID-19, although only twelve (1.1%) had PI. Eight (66.7%) of the patients were men. The median age was 60 (51–71), and half of the patients were obese. Eleven (91.4%) patients had at least one concurrent condition. The sacrum and gluteus were the two most commonly affected sites. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL). The average length of stay (LOS) was 22 days (9.8 – 40.3).

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INTRODUCTION

For more than two years, Corona Virus Disease 2019 (COVID-19) has been a global pandemic. It was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) and began in Wuhan, China[1], before spreading worldwide. In [REDACTED], the first case was discovered in March 2020; since then, over 2 million people have contracted COVID-19, with over 21,000 testing positive as of the end of June 2021[2]. As the number of patients admitted to hospitals grows, particularly in the intensive care unit (ICU), more of these individuals are vulnerable to pressure injury (PI) as a result of disease consequences such as inactivity, immobility, and the use of artificial airways[3].

Pressure injury is a type of local trauma caused by unceasing pressure on the skin, most commonly over bony prominences. This pressure is high enough to interfere with blood flow to the capillaries, reducing oxygen supply to the tissues. This results in ischemia and necrosis of the afflicted tissue[4]. The sacrum, heel, sciatic tuberosity, greater trochanter, and lateral malleolus are frequently impacted[5]. Advanced age, immobility, poor nutrition, excessive wetness and incontinence, altered state of consciousness, poor perfusion, specific skin diseases, and concomitant disorders such as respiratory failure, anemia, diabetes, and septicemia are all risk factors[6]. Patients who acquire PIs are older, have less mobility, and stay in the hospital for a longer period of time than patients who do not[7]. In one study, patients who were hospitalized for 7-20 days had a higher rate of PI than those who were hospitalized for fewer than seven days[8].

A "cytokine storm" may arise as the COVID-19 proceeds. Systemic inflammation, hyperferitinemia, and hemodynamic dysfunction characterize a cytokine storm[9]. This unregulated immune response will cause immune cells, lymphocytes, and macrophages to infiltrate. A substantial amount of proinflammatory cytokines will be produced by these immune cells[10]. The cytokines interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a) [11] are both involved in the production of PI[12,13] and are essential components of the cytokine storm. The rise in d-dimers in COVID-19 indicates that these two cytokines are related with a mix of systemic inflammatory processes and hypercoagulability situations[14].

Nearly half of COVID-19 pneumonia patients developed acute respiratory distress syndrome (ARDS), and more than two - thirds required intensive care and mechanical ventilation[15,16]. Patients who are ventilated are at risk of developing PI because they become immobilized and sedated[17].

Because of the urgency of the issue and the increased risk of PI in COVID-19 patients, this study was conducted at an infectious disease hospital, to describe the clinical characteristics of COVID-19 patients with PI.

METHODS

Ethical considerations and consent

On June 22, 2021, the Clinical Research Ethics Committee accepted this study with ethical approval number 157/KEP/2021. Because this was a retrospective research study based on anonymous and de-identified data, no consent was sought.

Study design and setting

This was a descriptive and retrospective study This was a descriptive and retrospective study. Between March 2020 and June 2021, samples were taken from each patient at our hospital who had been diagnosed with pressure injury and COVID-19.

Participant

The polymerase chain reaction confirmed that the patients were positive for COVID-19. Patients on both invasive and noninvasive mechanical ventilation were included in the study. The study included only patients who were at least 18 years old. Twelve patients with COVID-19 who were admitted and experienced pressure injuries were included in the study. Two of the twelve patients had already suffered a pressure injury before being admitted to the hospital. Only PIs induced by supine position were considered, such as those on the sacrum, occipital, temporal, heels (calcaneus), gluteus, scapula, and trochanter, according to the National Pressure Ulcer Advisory Panel[18]. PIs to the bridge of the nose caused by noninvasive ventilation face masks was ruled out.

Variables and data sources

Secondary data from medical records were used in this study, including: the patients' gender and age; BMI, defined as body weight in kilograms divided by height in meters squared and categorized by definitions as follows: 1) underweight (BMI < 18.5kg/m^2); 2) normal weight (BMI 18.5 – 22.9 kg/m^2); 3) overweight (BMI 23 – 24.9 kg/m^2); 4) obese I (BMI 25 – 29.9 kg/m^2); 5) obese II (BMI< 30 kg/m^2) according to the WHO recommendations for Asian populations[19] ; symptoms related to COVID-19 on admission; coexisting disorder (hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease); type of oxygen therapy used during the time the patient was consulted for pressure injury (room air, nasal cannula, simple oxygen mask, mechanical ventilation); laboratory results of complete blood count, creatinine kinase, albumin, and d-dimer less than or equal to 3 days prior to the pressure injury consultation; location of pressure injury; classification of pressure injury in accordance to the National Pressure Ulcer Advisory Panel[18] and length of stay in the hospital. The data collecting period was determined by the date of hospital admission.

Data analysis

The data was presented in a descriptive analysis. The data collection findings are presented in tabular style, with the median, percentages, and interquartile range displayed.

RESULTS

The authors collected data from confirmed COVID-19 patients treated at our institution during the start of the pandemic from March 2020 to June 2021. Out of 1070 patients hospitalised for COVID-19, 12 (1.1 percent) established PI. All data will be presented in Table 1. Eight (66.7 percent) patients were male. 5 (41.7 percent) of the 12 participants had stage 2 PI, 7 (58.3 percent) had stage 3 PI, and none of the patients in this study had stage 1, stage 4, unstageable, or suspected deep tissue injury (sDTI) PI. These patients had a median age of 60 years. The median age of patients with stage 2 PI was 65 years, which was only slightly older than the median age of patients with stage 3 PI, which was 63.5 years. There was no difference in the number of male patients with stage 2 or stage 3 PI in this study. In female patients, three (75%) had stage 3 PI and one (25%) had stage 2 PI. Two-thirds of the patients were obese. The majority of PI patients in stages 2 and 3 were also obese.

Symptoms

Cough (58.3%), fever (50%), shortness of breath (50%), fatigue (41.7%), and nausea or vomiting were the most prevalent symptoms we saw in these patients (33.3%).

Location

The sacrum (66.7%) was the most frequent site of pressure ulcers in these patients, followed by the gluteus (25%), calcaneus, scapula, temporal, and hip. Sacral ulcers are more prevalent in patients with stage 3 PI.

Coexisting disorder

On admission to the hospital, 11 (91.7 percent) of the 12 patients who suffered from pressure injuries during treatment had at least one comorbidity, including hypertension (50 percent), diabetes (41.7 percent), stroke (41.7 percent), and coronary artery disease (25 percent). More patients in stage 2 PI had hypertension (80%), while most patients in stage 3 PI also had diabetes and cerebrovascular disease.

Median laboratory values

During treatment, the patients were found to be anemic with a median hemoglobin of 10.7 g/dL, hypoalbuminemia (median 3.1 g/dL), and had an elevated leukocyte count. Patients with stage 3 PI had lower hemoglobin levels than those with stage 2 PI (10.2 versus 11.3). In these patients, the median d-dimer value was 3.700 (1,500-8,400) ng/mL. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL).

Oxygen therapy

A ventilator was required in eight patients (66.7%), five of whom had stage 3 PI and three of whom had stage 2 PI. The patient who utilized nasal cannula oxygen therapy acquired a stage 2 PI, while one of the two patients (16.7%) who used a basic oxygen mask developed a stage 3 PI.

Vasopressor support

Because of low blood pressure, the use of vasopressors contributes to poor peripheral tissue perfusion. There were 5 patients (71.4%) with stage 3 PI who were on vasopressors, compared to only 2 patients (40%) with stage 2 PI.

Length of stay

The median length of stay for these patients was 22(9.8 – 40.3) days, with stage 2 PI patients treated for 29(26 - 41) days and stage 3 PI patients treated for 13(8 - 29) days.

DISCUSSION

While all of these individuals received proper care, pressure injuries developed throughout their hospitalization. In this study, the median age of COVID-19 patients with PI was 60 years old, which was close to a Chinese study[20]. The median age difference between individuals with stage 2 and 3 PI was unremarkable. However, a study on pressure injury in COVID-19 patients in Spain included more (37,3%) patients between the ages of 80 and 89[21]. As age is a determinant in the development of PIs[6], older patients made up the majority of the age group in COVID-19 hospitalized cases[22,23].

Two-thirds of the patients were obese. The majority of PI patients in stages 2 and 3 were also obese. Most studies suggest that patients with low weight or severely obese were more likely to develop PI[24,25]. One reason this study had more patients who were obese was almost all (87.5%) of the patients with a BMI > 25 kg/m^2 were using ventilators, whereas only one of the patients with a BMI < 25 kg/m^2 were on a ventilator, thus putting them at risk of developing PI[3].

Most common symptoms seen in this research were cough, fever, shortness of breath, followed by fatigue and nausea or vomiting. Several research also reported cough, shortness of breath, fever as a frequent complaint from COVID-19 patients[20,26]. While diarrhea, loss of sense of taste or smell, and sore throat was less common[26,27]

The majority (66.7%) of patients in this study had PI on their sacrum, while the gluteus came in second (25%). Other research also found the sacrum to be the most common site of PI on COVID-19 patients[20,28]. According to a study in Germany, the strongest predictors for sacral pressure ulcer development were mobility (completely dependent vs. completely independent OR 27.1, 95% CI)[29]. As most of these patients were eventually on mechanical ventilator, immobility would be a factor in their PI development[30,31].

In older persons, the atherosclerosis process reduces blood circulation to vital organs such as the heart, brain, legs, and skin, increasing the risk of PI development. Hypertension was the most frequent coexisting disorder in this study. Cardiovascular disease is frequently associated with PI. Reduced left ventricle ejection fraction predicts PI in patients who have had a myocardial infarction[32]. These patients are more likely to have hypertension, while evidence of its consequences on PI development is conflicting[33]. The second most common coexisting disorders in this study were diabetes and cerebrovascular disease. Diabetes-related peripheral vascular disease and neuropathy appear to be the root causes of PI in diabetic patients[34]. In a Turkish study, diabetes was revealed to be a significant ($p<0.001$) risk factor for PI development in ICU patients[28]. Patients with cerebrovascular disease (CVD) are more likely to become immobile and acquire PI[33].

This study's patients were all anemic. Anemia lowers blood oxygen levels, resulting in a lack of oxygen flow to body tissues[33]. This may enhance the likelihood of tissue ischemia and the development of PI. Two other investigations discovered lower-than-normal hemoglobin levels in pressure injury ICU patients[20,28].

In this study, patients with stage 3 PI had a larger increase in mean d-dimer readings than patients with stage 2 PI. COVID-19 stimulates the immunological response, causing proinflammatory cytokines to be released, causing damage to the vascular endothelium. Following platelet aggregation activation in response to vascular damage, thrombosis and microemboli cause plasmin to promote fibrinolysis, resulting in an increase in d-dimer level[4,35]. Although the mechanism by which COVID-19 affects the development of pressure injury remains unknown, it has been proposed that the myalgia generated by COVID-19 may disguise the discomfort of a pressure injury. Simultaneously, a cytokine storm could exacerbate inflammatory and ischemic tissue damage, as well as create oxygen-induced metabolic acidosis and microemboli[35,36]. Research found that COVID-19 patients in the ICU who developed stage 2 and stage 3 PI had a higher d-dimer value than those with stage 1 PI[20].

The majority (66,7%) of these patients were in the ICU with ARDS and had to be on a ventilator, making them immobile, which contributed to the PI development[30,31,37]. This conclusion is consistent with studies of COVID-19 ICU patients who developed PI[20,28]. COVID-19 predominantly infects lung tissue, resulting in hypoxia due to decreased oxygen exchange. Low blood oxygen levels contribute to the development of PI[33]. As pressure builds up on the skin, the interruption of blood circulation combined with a lack of appropriate oxygen delivery worsens the severity of ischemia.

Characteristics of multi-organ dysfunction syndrome (MODS) might be detected in critically ill COVID-19 patients, such as dysregulation of the body's response to infection characterized by hyperinflammation, alterations in coagulation, and dysregulation of the immunological response[38]. A weakened immune response puts the body vulnerable to opportunistic bacterial infections, which can result in septic shock[39]. Vasopressors constrict blood arteries to assist keep blood pressure stable. The perfusion of smaller blood arteries may be reduced, putting the skin at risk of pressure injury[40].

The shorter hospital stays of patients with stage 3 PI in this study compared to patients with stage 2 PI could be attributed to the quick progression of COVID-19, which led the patient to die before further progression of their pressure injury.

This study recommends that additional attention should be paid to cases of pressure injury in COVID-19 patients. According to one study, having a wound and skin care skilled nurse assigned to these patients reduces the likelihood of PI development by 93%[41].

The study's limitations include the fact that it only reports on a single-center experience with a small group of patients. More analytical observational studies with a bigger sample size could help identify the risk variables for PI in COVID-19 patients.

CONCLUSION

According to the findings of this study, healthcare professionals should pay close attention to cases of pressure injury in COVID-19 patients, particularly those in the ICU. Patients would be immobile due to the constant requirement for ventilators. In these COVID-19 patients, a rise in d-dimer may impact the severity of pressure injury. While pressure injuries in these patients may not result in immediate mortality, an increase in morbidity may be prevented with careful treatment.

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Table 1 Characteristic of Covid-19 patients with pressure injury

Table 1 Characteristics of Covid-19 patients with pressure injury.			
Characteristic	Total (*N*= 12)	Stage 2 (*N*= 5)	Stage 3 (*N*= 7)
General characteristics			
Median age (IQR) - years	60 (51 - 71)	65 (57.5 - 66)	63,5 (52.5 - 68)
Male - no. (%)	8 (66.7)	4 (80.0)	4 (57.1)
Female - no. (%)	4 (33.3)	1 (20.0)	3 (42.9)
Body mass index (kg/m^2) – no. (%)			
Underweight (<18.5)	1(8.3)	0	1(14.3)
Normal (18.5-22.9)	1(8.3)	0	1(14.3)
Overweight (23-24.9)	2(16.7)	2(40.0)	0
Obese I (25-29.9)	6(50.0)	3(60.0)	3(42.9)
Obese II (≥30)	2(16.7)	0	2(28.8)
Symptoms - no. (%)			
Fever	6 (50.0)	4 (80.0)	2 (28.6)
Cough	7 (58.3)	3 (60.0)	4 (57.1)
Shortness of breath	6 (50.0)	1 (20.0)	5 (71.4)
Fatigue	5 (41.7)	3 (60.0)	2 (28.6)
Diarrhea	1 (8.3)	1 (20.0)	0
Nausea or vomiting	4 (33.3)	3 (60.0)	1 (14.3)
Loss of taste or sense of smell	1 (8.3)	0	1 (14.3)
Sore throat	1 (8.3)	1 (20.0)	0
Congested nose	1 (8.3)	1 (20.0)	0
Ulcer characteristic			
Location - no. (%)			
Sacrum	8 (66.7)	2 (40.0)	6 (85.7)
Gluteus	3 (25.0)	3 (60.0)	0
Temporal	1 (8.3)	1 (20.0)	0
Calcaneus	1 (8.3)	0	1 (14.3)
Scapula	1 (8.3)	0	1 (14.3)
Hip	1 (8.3)	0	1 (14.3)
Coexisting disorder - no. (%)			
Hypertension	6 (50.0)	4 (80.0)	2 (28.6)
Diabetes	5 (41.7)	2 (40.0)	3 (42.9)
Cerebrovascular disease	5 (41.7)	1 (20.0)	4 (57.1)
Coronary artery disease	3 (25.0)	1 (20.0)	2 (28.6)
Median laboratory values (IQR)			
Leukocytes (per mm^3)	14,265 (12,547.5-22,992.5)	14,830 (12,480-24,020)	13,700 (12,830-19,885)
Differential Count (per mm^3)			
Total neutrophils	12,288.7 (10,830-21,012.9)	11,967.8 (10,886.9-21,401.8)	12,356.9 (11,439.9-18,479.5)
Total lymphocytes	1,023.9 (782.3-1,442.7)	1,764.8 (1,335.4-1,969.4)	838.1 (698.9-1,023.9)
NLR	20.4 (10.6-24)	10.9 (7.7-36.6)	21.1 (15.5- 22.6)
Hemoglobin (g/dL)	10.7 (10-11.8)	11.3 (10.6-11.4)	10.2 (8.8-11.3)
Platelet count (per $mm^{3)}$	260,500 (187,000-443,250)	241,000 (190,000-399,000)	280,000 (203,500-447,500)
Albumin (g/dL)	3.08 (2.9-3.1)	3 (2.8-3.1)	3.1 (3-3.1)
D-dimer (ng/mL)	3,700 (1,500-8,400)	1,100 (600-1,700)	7,900 (5,200-11,200)
Oxygen therapy - no.(%)			
Room Air	1 (8.3)	0	1 (14.3)
Nasal cannula	1 (8.3)	1 (20.0)	0
Simple oxygen mask	2 (16.7)	1 (20.0)	1 (14.3)
Mechanical ventilation	8 (66.7)	3 (60.0)	5 (71.4)
Vasopressor support - no. (%)	7 (58.3)	2 (40.0)	5 (71.4)
Length of stay (LOS) – days (IQR)	22 (9.8 – 40.3)	29 (26 - 41)	13 (8 - 29)

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Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital

Abstract

Introduction: For more than two years, Corona Virus Disease 2019 (COVID-19) has been a global pandemic. As the number of patients admitted to hospitals grows, particularly in the intensive care unit (ICU), more of these individuals are vulnerable to pressure injury (PI) as a result of disease complications.

Methods: This retrospective study describes the data of COVID-19 patients treated at a COVID-19 referral hospital from March 2020 to June 2021, who experienced pressure injuries either before or after admission. The patients' profile, symptoms, comorbidities, location and severity of pressure injury, laboratory values, oxygen therapy, length of stay (LOS), and usage of vasopressors were all presented.

Results: During the study period, 1070 patients were hospitalized for COVID-19 with varying degree of severity, twelve patients were diagnosed with PI. Eight (66.7%) of the patients were men. The median age was 60 (51–71), and half of the patients were obese. Eleven (91.4%) patients had at least one concurrent condition. The sacrum and gluteus were the two most commonly affected sites. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL). The average length of stay (LOS) was 22 days (9.8 – 40.3).

Conclusion: Health professionals should be aware of an increase in d-dimer in COVID-19 patients who suffer from pressure injury**.** Even though pressure injuries in these patients might not result in immediate mortality, an increase in morbidity can be avoided with the right care.

Keywords: COVID-19, d-dimer, Pressure injury

INTRODUCTION

For more than two years, Corona Virus Disease 2019 (COVID-19) has been a global pandemic. It was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) and began in Wuhan, China[1], before spreading worldwide. In Indonesia, the first case was discovered in March 2020; since then, over 2 million people have contracted COVID-19, with over 21,000 testing positive as of the end of June 2021[2]. As the number of patients admitted to hospitals grows, particularly in the intensive care unit (ICU), more of these individuals are vulnerable to pressure injury (PI) as a result of disease consequences such as inactivity, immobility, and the use of artificial airways[3].

Pressure injury is a type of local trauma caused by unceasing pressure on the skin, most commonly over bony prominences. This pressure is high enough to interfere with blood flow to the capillaries, reducing oxygen supply to the tissues. This results in ischemia and necrosis of the afflicted tissue[4]. The sacrum, heel, sciatic tuberosity, greater trochanter, and lateral malleolus are frequently impacted[5]. Advanced age, immobility, poor nutrition, excessive wetness and incontinence, altered state of consciousness, poor perfusion, specific skin diseases, and concomitant disorders such as respiratory failure, anemia, diabetes, and septicemia are all risk factors[6]. Patients who acquire PIs are older, have less mobility, and stay in the hospital for a longer period of time than patients who do not[7]. In one study, patients who were hospitalized for 7-20 days had a higher rate of PI than those who were hospitalized for fewer than seven days[8].

A "cytokine storm" may arise as the COVID-19 proceeds. This unregulated immune response will cause immune cells, lymphocytes, and macrophages to infiltrate and produce a substantial amount of proinflammatory cytokines[9]. The cytokines interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a)[10] are both involved in the production of PI[11,12] and are essential components of the cytokine storm. The rise in d-dimers in COVID-19 indicates that these two cytokines are related with a mix of systemic inflammatory processes and hypercoagulability situations[13].

Nearly half of COVID-19 pneumonia patients developed acute respiratory distress syndrome (ARDS), and more than two - thirds required intensive care and mechanical ventilation[14,15]. Patients who are ventilated are at risk of developing PI because they become immobilized and sedated[16].

Because of the urgency of the issue and the increased risk of PI in COVID-19 patients, this study was conducted at an infectious disease hospital, to describe the clinical characteristics of COVID-19 patients with PI.

METHODS

Ethical considerations and consent

On June 22, 2021, the Clinical Research Ethics Committee accepted this study with ethical approval number 157/KEP/2021. Because this was a retrospective research study based on anonymous and de-identified data, no consent was sought.

Study design and setting

This was a descriptive and retrospective study This was a descriptive and retrospective study. Between March 2020 and June 2021, samples were taken from each patient at our hospital who had been diagnosed with pressure injury and COVID-19.

Participant

Participants were chosen from medical records by their polymerase chain reaction (PCR) confirmed result for COVID-19 after being admitted to the COVID-19 referral hospital. The study included only patients who were at least 18 years old, patients with a diagnosis of pressure injury by the attending plastic surgeon on their medical records. Only PIs induced by supine position were considered, such as those on the sacrum, occipital, temporal, heels (calcaneus), gluteus, scapula, and trochanter according to the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance[17]. Medical device-related pressure injuries were ruled out.

Variables and data sources

Secondary data from medical records were used in this study, including: the patients' gender and age; BMI, defined as body weight in kilograms divided by height in meters squared and categorized by definitions as follows: 1) underweight (BMI < 18.5kg/m^2); 2) normal weight (BMI 18.5 – 22.9 kg/m^2); 3) overweight (BMI 23 – 24.9 kg/m^2); 4) obese I (BMI 25 – 29.9

kg/m^2); 5) obese II (BMI< 30 kg/m^2) according to the WHO recommendations for Asian populations[18~~8~~] ; symptoms related to COVID-19 on admission; coexisting disorder (hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease); type of oxygen therapy used during the time the patient was consulted for pressure injury (room air, nasal cannula, simple oxygen mask, mechanical ventilation); laboratory results of leucocyte, total neutrophil, total lymphocyte, NLR (ratio of neutrophils/lymphocytes), platelets, albumin, and d-dimer dated less than or equal to 3 days prior to the pressure injury consultation; location of pressure injury and stages of pressure injury were classified in accordance to the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance[17].

Length of stay was the number of days spent in the hospital until the patient was discharged. The data collecting period was defined as the time from the collection of data from the first participant to the latest follow-up of the study participants

Data analysis

The data was presented in a descriptive analysis. The data collection findings are presented in tabular style, with the median, percentages, and interquartile range displayed.

RESULTS

The authors collected data from confirmed COVID-19 patients treated at our institution during the start of the pandemic from March 2020 to June 2021. During that period, 1070 patients were hospitalized for COVID-19 with varying severity. twelve patients were diagnosed with PI. Two of the twelve patients had already suffered a pressure injury before being admitted to the hospital. All data will be presented in Table 1. Eight (66.7 percent) patients were male. 5 (41.7 percent) of the 12 participants had stage 2 PI, 7 (58.3 percent) had stage 3 PI, and none of the patients in this study had stage 1, stage 4, unstageable, or suspected deep tissue injury (sDTI) PI. These patients had a median age of 60 years. The median age of patients with stage 2 PI was 65 years, which was only slightly older than the median age of patients with stage 3 PI, which was 63.5 years. There was no difference in the number of male patients with stage 2 or stage 3 PI in this study. In female patients, three (75%) had stage 3 PI and one (25%) had stage 2 PI. Two-thirds of the patients were obese. The majority of PI patients in stages 2 and 3 were also obese.

Symptoms

Cough (58.3%), fever (50%), shortness of breath (50%), fatigue (41.7%), and nausea or vomiting were the most prevalent symptoms we saw in these patients (33.3%).

Location

The sacrum (66.7%) was the most frequent site of pressure ulcers in these patients, followed by the gluteus (25%), calcaneus, scapula, temporal, and hip. Sacral ulcers are more prevalent in patients with stage 3 PI.

Coexisting disorder

On admission to the hospital, 11 (91.7 percent) of the 12 patients who suffered from pressure injuries during treatment had at least one comorbidity, including hypertension (50 percent), diabetes (41.7 percent), stroke (41.7 percent), and coronary artery disease (25 percent). More patients in stage 2 PI had hypertension (80%), while most patients in stage 3 PI also had diabetes and cerebrovascular disease.

Median laboratory values

During treatment, the patients were found to be anemic with a median hemoglobin of 10.7 g/dL, hypoalbuminemia (median 3.1 g/dL), and had an elevated leukocyte count. The NLR median values were much higher in stage III pressure injury group compared to the stage II group (21.1 vs 10.9). Platelet values were relatively normal in stage II and stage III pressure injury group. Patients with stage 3 PI had lower hemoglobin levels than those with stage 2 PI (10.2 versus 11.3). In these patients, the median d-dimer value was 3.700 (1,500-8,400) ng/mL. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL).

Oxygen therapy

A ventilator was required in eight patients (66.7%), five of whom had stage 3 PI and three of whom had stage 2 PI. The patient who utilized nasal cannula oxygen therapy acquired a stage 2 PI, while one of the two patients (16.7%) who used a basic oxygen mask developed a stage 3 PI.

Vasopressor support

Because of low blood pressure, the use of vasopressors contributes to poor peripheral tissue perfusion. There were 5 patients (71.4%) with stage 3 PI who were on vasopressors, compared to only 2 patients (40%) with stage 2 PI.

Length of stay

The median length of stay for these patients was 22(9.8 – 40.3) days, with stage 2 PI patients treated for 29(26 - 41) days and stage 3 PI patients treated for 13(8 - 29) days.

DISCUSSION

While all of these individuals received proper care, pressure injuries developed throughout their hospitalization. In this study, the median age of COVID-19 patients with PI was 60 years old, which was close to a Chinese study[19]. The median age difference between individuals with stage 2 and 3 PI was unremarkable. However, a study on pressure injury in COVID-19 patients in Spain included more (37,3%) patients between the ages of 80 and 89[20]. As age is a determinant in the development of PIs[6], older patients made up the majority of the age group in COVID-19 hospitalized cases[21,22].

Two-thirds of the patients were obese. The majority of PI patients in stages 2 and 3 were also obese. Most studies suggest that patients with low weight or severely obese were more likely to develop PI[23,24]. One reason this study had more patients who were obese was almost all (87.5%) of the patients with a BMI > 25 kg/m^2 were using ventilators, whereas only one of the patients with a BMI < 25 kg/m^2 were on a ventilator, thus putting them at risk of developing PI[3].

Most common symptoms seen in this research were cough, fever, shortness of breath, followed by fatigue and nausea or vomiting. Several research also reported cough, shortness of breath, fever as a frequent complaint from COVID-19 patients[19,25]. While diarrhea, loss of sense of taste or smell, and sore throat was less common[25,26]

The majority (66.7%) of patients in this study had PI on their sacrum, while the gluteus came in second (25%). Other research also found the sacrum to be the most common site of PI on COVID-19 patients[19,27]. According to a study in Germany, the strongest predictors for sacral pressure ulcer development were mobility (completely dependent vs. completely independent OR 27.1, 95% CI)[28]. As most of these patients were eventually on mechanical ventilator, immobility would be a factor in their PI development[29,30].

In older people, the atherosclerosis process reduces blood circulation to vital organs such as the heart, brain, legs, and skin, increasing the risk of PI development. Hypertension was the most frequent coexisting disorder in this study. Cardiovascular disease is frequently associated with PI. Reduced left ventricle ejection fraction predicts PI in patients who have had a myocardial infarction[31]. These patients are more likely to have hypertension, while evidence of its consequences on PI development is conflicting[32]. The second most common coexisting disorders in this study were diabetes and cerebrovascular disease. Diabetes-related peripheral vascular disease and neuropathy appear to be the root causes of PI in diabetic patients[33]. In a Turkish study, diabetes was revealed to be a significant ($p<0.001$) risk factor for PI development in ICU patients[27]. Patients with cerebrovascular disease (CVD) are more likely to become immobile and acquire PI[32].

This study's patients were all anemic. Anemia lowers blood oxygen levels, resulting in a lack of oxygen flow to body tissues[32]. This may enhance the likelihood of tissue ischemia and the development of PI. Two other investigations discovered lower-than-normal hemoglobin levels in pressure injury ICU patients[19,27].

Neutrophil to lymphocyte ratio (NLR) is considered as a sign of physiological stress[34], but may also a predictor for sepsis[35]. A NLR value above 10 could also be a potential parameter for assessing sepsis severity[36], proposed by one study. In this research, it is shown that NLR median values were much higher in stage III pressure injury group compared to the stage II group (21.1 vs 10.9). The patients in this study also showed elevated levels of leucocytes, and although their platelets were relatively normal, leukocytosis and thrombocytopenia are commonly present during sepsis [(34,37)]. As sepsis was found to impair wound healing [(38,39)], these findings may indicate adverse effects on the development of pressure injury. One study on 104 patients admitted to the ICU suggests NLR could be a marker for subjects in increased risk of pressure injury development[40].

In this study, patients with stage 3 PI had a larger increase in mean d-dimer readings than patients with stage 2 PI. COVID-19 stimulates the immunological response, causing proinflammatory cytokines to be released, causing damage to the vascular endothelium. Following platelet aggregation activation in response to vascular damage, thrombosis and microemboli cause plasmin to promote fibrinolysis, resulting in an increase in d-dimer level[4,41]. Although the mechanism by which COVID-19 affects the development of pressure injury remains unknown, it has been proposed that the myalgia generated by COVID-19 may disguise the discomfort of a pressure injury. Simultaneously, a cytokine storm could exacerbate inflammatory and ischemic tissue damage, as well as create oxygen-induced metabolic acidosis and microemboli[41,42]. Research found that COVID-19 patients in the ICU who developed stage 2 and stage 3 PI had a higher d-dimer value than those with stage 1 PI[19].

The majority (66,7%) of these patients were in the ICU with ARDS and had to be on a ventilator, making them immobile, which contributed to the PI development[29,30,43]. This conclusion is consistent with studies of COVID-19 ICU patients who developed PI[19,27].

COVID-19 predominantly infects lung tissue, resulting in hypoxia due to decreased oxygen exchange. Low blood oxygen levels contribute to the development of PI[32]. As pressure builds up on the skin, the interruption of blood circulation combined with a lack of appropriate oxygen delivery worsens the severity of ischemia.

Characteristics of multi-organ dysfunction syndrome (MODS) might be detected in critically ill COVID-19 patients, such as dysregulation of the body's response to infection characterized by hyperinflammation, alterations in coagulation, and dysregulation of the immunological response[44]. A weakened immune response puts the body vulnerable to opportunistic bacterial infections, which can result in septic shock[45]. Vasopressors constrict blood arteries to assist keep blood pressure stable. The perfusion of smaller blood arteries may be reduced, putting the skin at risk of pressure injury[46].

The shorter hospital stays of patients with stage 3 PI in this study compared to patients with stage 2 PI could be attributed to the quick progression of COVID-19, which led the patient to die before further progression of their pressure injury.

This study recommends that additional attention should be paid to cases of pressure injury in COVID-19 patients. During the COVID-19 pandemic, it was suggested that to help prevent and manage PIs, improvement of mobility, improvement of contributing factors such as anti-shock therapy to improve skin perfusion, positioning and use of pressure relieving devices, minimization of excess moisture and correction of malnutrition, and close daily monitoring of pressure injury and the dressing could be helpful[47]. According to one study, having a wound and skin care skilled nurse assigned to these patients reduces the likelihood of PI development by 93%[48].

The study's limitations include the fact that it only reports on a single-center experience with a small group of patients. More analytical observational studies with a bigger sample size could help identify the risk variables for PI in COVID-19 patients.

CONCLUSION

According to the findings of this study, healthcare professionals should pay close attention to cases of pressure injury in COVID-19 patients, particularly those in the ICU. Patients would be immobile due to the constant requirement for ventilators. In these COVID-19 patients, a rise in d-dimer and NLR values may impact the severity of pressure injury. While pressure injuries in these patients may not result in immediate mortality, an increase in morbidity may be prevented with the right care.

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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Dear Editor,

Here we have reviewed the reviewer's comments and answered them accordingly. The answers are in italics.

Editor/Reviewers' comments:

Reviewer #1:

The submission is very informative, with good citations. Subject matter is of adequate depth. It is interesting that no patients had Stage 1 or Stage 4 ulcers.

Thank you for the comment. It is possible that no patients had stage 1 or stage 4 ulcers because stage 1 is frequently misdiagnosed, and no patients had stage 4 because good management was provided during stages 2 and 3 (we have included it in the revision of the manuscript, in the discussion).

Reviewer #2:

1. In the manuscript, the rate of PIs is 1.1% (12/1070). The positive rate is low, the number of patients with PIs is small. It means it is not able to do the further statistical correlation analysis but descriptive analysis. If the total sample size is large enough and the positive rate increases, the results can be statistically correlation analyzed, which will be more meaningful.

Thank you for the comment, the 1070 patients admitted for COVID-19 were of varying degree of severity. We feel that it cannot be considered as a true ratio, since the denominator should only be patients with less activity such as ICU patients, as immobilization is a known risk factor. We are open for further suggestions, thank you.

2. In the introduction part, page 4 line 5--"A "cytokine storm" may arise as the COVID-19 proceeds...." The pathological process of COVID-19 is too much elaborated, which is not closely related to PI, it is suggested to simplify.

Thank you for the comment. We have simplified it in the revision of the manuscript.

3. In page4 line45--"The polymerase chain reaction confirmed that the patients were positive for COVID-19."in terms of the patient recruitment, you recruit patient based on the patient's medical history which diagnosed with COVID-19. But the specific diagnostic methods need not be stated.

Thank you for the comment. The reason that we stated the specific diagnostic method was because during the elimination process, a subjective test done by rapid antigen test might yield a negative PCR test for COVID-19, thus we feel a positive result by PCR was more credible. We are open for futher suggestion.

4. Reference 18 should be updated. The 2021 version of PI guideline has been published. Please update.

Thank you for the comment. We have updated it in the revision of the manuscript.

5. In the Participant part, why do you state the number of PI patient? It is should be in the Result part. Instead, where, who, when and how the data was selected? Those should be addressed.

Thank you for the comment. We apologized for this error. We have edited it in the revision of the manuscript.

6. "PIs to the bridge of the nose caused by noninvasive ventilation face masks was ruled out." were all MDRPI excluded? Such as gastric tube, oxygen tube, pulse oxygen clip, etc.

Thank you for the comment. Yes, on all these patients, various MDRPI have been excluded. We have edited it in the revision of the manuscript.

7. Do the item in "Median laboratory values" such as Leukocytes、 Total neutrophils、Total lymphocytes、Platelet count、D-dimer、Creatinine have relation with the development of PI? Why did you select these data?

Thank you for the comment. Increase in Leukocytes, thrombocytopenia are commonly present during sepsis. Whereby sepsis disrupts wound healing and might worsen the pressure injury.

Neutrophil to lymphocyte ratio (NLR) is considered as a sign of physiological stress, but may also a predictor for sepsis. A NLR value above 10 could also be a potential parameter for assessing sepsis severity.

An increase in d-dimer as a result of cytokine storm may indicate an increase state of hypercoagulability, which then increase formations of microembolis that may worsen the development of PI.

We have added further explanation on the matter in the discussion on page 5 line 22.

Reviewer #3:

Thank you for submitting this paper to Advances.

This is a retrospective study with small numbers but you have included some very important information

* confirmed COVID 19 with PCR

* identified comorbidities and obesity

*confirmed the association of morbidity or more severe disease with increased D-dimer levels as previously reported in the literature

1. Please provide more information on the statement: "an increase in morbidity can be avoided with the right care."

Please define the right care

Thank you for the comment. The definition of right care suggested during the COVID-19 pandemic was to help prevent and manage PIs, improvement of mobility, improvement of contributing factors such as anti-shock therapy to improve skin perfusion, positioning and use of pressure relieving devices, minimization of excess moisture and correction of malnutrition, and close daily monitoring of pressure injury and the dressing could be helpful. We have included it in the revision of the manuscript on page 6 line 16.

Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Advances in Skin and Wound Care Submission Confirmation for ASWC-D-22-00154R1

1 pesan

LWW E-Submissions <em@editorialmanager.com> 8 Agustus 2022 pukul 21.13
Balas Ke: LWW E-Submissions <taylor.hayes@wolterskluwer.com>
Kepada: Indri Lakhsmi Putri <indrilakhsmiputri@fk.unair.ac.id>

Aug 08 2022 10:13:09:229AM

Dear Mrs. Putri,

The LWWeSubmissions.com has received your revised submission ASWC-D-22-00154R1 entitled, "Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital."

You may check the status of your manuscript by logging onto the Editorial Manager.

https://www.editorialmanager.com/lwwesubmissions/

Your username is: indrilakhsmiputri
https://www.editorialmanager.com/lwwesubmissions/l.asp?i=388127&l=P85NUF7P

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Advances in Skin and Wound Care

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/lwwesubmissions/login.asp?a=r). Please contact the publication office if you have any questions.

Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Advances in Skin and Wound Care Decision

1 pesan

LWW E-Submissions <em@editorialmanager.com> 11 Agustus 2022 pukul 22.59
Balas Ke: LWW E-Submissions <taylor.hayes@wolterskluwer.com>
Kepada: Indri Lakhsmi Putri <indrilakhsmiputri@fk.unair.ac.id>

CC: "Aldrich Alexander Afeli Tungga" draldrichalexander@gmail.com, "Rachmaniar Pramanasari" rachma.pramanasari@gmail.com, "Citrawati Dyah Kencono Wungu" citrawati.dyah@fk.unair.ac.id

Aug 11 2022 11:59:04:070AM

RE: ASWC-D-22-00154R1, entitled "Characteristics of COVID-19 patients with pressure injuries in a COVID-19 referral hospital"

Dear Mrs. Putri,

After carefully reviewing your manuscript, we're happy to inform you that we feel it will make a valuable contribution to *Advances in Skin & Wound Care*, and that we plan to use it in a future issue of the journal.

Prior to publication, we will send you a copy of the edited version for your approval. Although this may be 12 months or more from now, in most cases it signals that your article has been tentatively scheduled for an issue.

OPEN ACCESS

If you indicated in the revision stage that you would like your submission, if accepted, to be made open access, please go directly to step 2. If you have not yet indicated that you would like your accepted article to be open access, please follow the steps below to complete the process:
1. Notify the journal office via email that you would like this article to be available open access. Please send your Email to taylor.hayes@wolterskluwer.com. Please include your article title and manuscript number.
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With Kind Regards,

Madeline Talbot
Publishing Assistant
Advances in Skin & Wound Care

Dear Author,

Thank you for your thoughtful revisions - we are pleased to accept your manuscript to publication.

Congratulations!

Sincerely,
The Editorial Team of Advances in Skin & Wound Care

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Remove my information/details). Please contact the publication office if you have any questions.

SMART UNIVERSITY

Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Article in Advances in Skin & Wound Care

6 pesan

Bunje, Holly <Holly.Bunje@wolterskluwer.com> 20 Januari 2023 pukul 02.01
Kepada: "indrilakhsmiputri@fk.unair.ac.id" <indrilakhsmiputri@fk.unair.ac.id>

Dear Dr Putri,

We have prepared your article, "Characteristics of Patients with Pressure Injuries in a COVID-19 Referral Hospital" for an upcoming issue of *Advances in Skin & Wound Care*.

Please review the attached files, answer all author queries, and make changes/comments directly to the files using track changes (already on). If possible, please return your corrections to me by next Thursday, January 26.

Please let me know if you have any questions, and please confirm receipt of this message. Thank you!

Best,

Holly Bunje

Holly Bunje (she/her)

Editor

Advances in Skin & Wound Care

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Holly.Bunje@wolterskluwer.com

2 lampiran

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Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id> 22 Januari 2023 pukul 10.04
Kepada: "Bunje, Holly" <Holly.Bunje@wolterskluwer.com>

Dear Mrs. Holly Bunje,

Thank your

We have revised and attached our article, “Characteristics of Patients with Pressure Injuries in a COVID-19 Referral

Hospital” for an upcoming issue of *Advances in Skin & Wound Care*.

Warmest regards,
Indri Lakhsmi Putri, MD., Ph.D

[Kutipan teks disembunyikan]

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2 lampiran

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wcf154_Putri revised.docx
53K

Bunje, Holly <Holly.Bunje@wolterskluwer.com> 24 Januari 2023 pukul 02.14
Kepada: Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Dear Dr. Putri,

Thank you so much for sending these files – they both came through perfectly. I’ll let you know if any other questions arise during the production process.

All the best,

Holly

Holly Bunje (she/her)

Editor

Advances in Skin & Wound Care

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Holly.Bunje@wolterskluwer.com

From: Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>
Sent: Saturday, January 21, 2023 7:04 PM
To: Bunje, Holly <Holly.Bunje@wolterskluwer.com>
Subject: Re: Article in Advances in Skin & Wound Care

Caution, this email may be from a sender outside Wolters Kluwer. Verify the sender and know the content is safe.

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Bunje, Holly <Holly.Bunje@wolterskluwer.com> 14 Februari 2023 pukul 09.18
Kepada: Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Dear Dr. Putri,

A few more questions arose during the production process related to the following sections:

Ethics

Who extracted the data, and how were patients identified?

When were data extracted?

How were data stored (what kind of security measures)?

Study Design and Setting

Did the study take place at the authors' hospital? Located in Indonesia? A single site? What kind of hospital - primary populations, rural, urban; how many beds, etc

Thank you in advances for addressing these questions!

Best,

Holly

Holly Bunje (she/her)

Editor

Advances in Skin & Wound Care

Health Learning, Research & Practice

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Holly.Bunje@wolterskluwer.com

From: Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>
Sent: Saturday, January 21, 2023 7:04 PM
To: Bunje, Holly <Holly.Bunje@wolterskluwer.com>
Subject: Re: Article in Advances in Skin & Wound Care

Caution, this email may be from a sender outside Wolters Kluwer. Verify the sender and know the content is safe.

Dear Mrs. Holly Bunje,

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[Kutipan teks disembunyikan]

Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id> 14 Februari 2023 pukul 10.35
Kepada: "Bunje, Holly" <Holly.Bunje@wolterskluwer.com>

Dear Holly Bunje,

Thank you for your email,

Here are the answers for the questions:

Ethics

Who extracted the data, and how were patients identified?
The data was gathered from hospital medical records and analyzed with CDWK by the authors (ILP, AAAT, and RP). The plastic surgery department at our hospital manages pressure injuries, with ILP and RP as the doctors in charge.

When were data extracted?
The data were extracted on August 2021.

How were data stored (what kind of security measures)?
The raw data from hospital medical records is only accessible to the primary researcher and is not shared with others.

Study Design and Setting

Did the study take place at the authors' hospital? Located in Indonesia? A single site? What kind of hospital - primary populations, rural, urban; how many beds, etc.
This is a study of a single site. The study was conducted at the author's hospital, Airlangga University Hospital, one of the referral hospitals for COVID-19, which is located in Surabaya, Indonesia's second largest city. With 307 beds, Airlangga University Hospital is the largest university hospital in East Java.

Thank you in advances for the questions

Warmest regards,

Indri Lakhsmi Putri, MD, PhD.
[Kutipan teks disembunyikan]

Bunje, Holly <Holly.Bunje@wolterskluwer.com> 14 Februari 2023 pukul 23.58
Kepada: Indri Lakhsmi <indrilakhsmiputri@fk.unair.ac.id>

Dear Dr Putri,

Thank you so much for your quick response! I appreciate you sending these additional details.

All the best,

[Kutipan teks disembunyikan]

[[Original Investigation]]

Characteristics of Patients with Pressure Injuries in a COVID-19 Referral Hospital

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ABSTRACT

Objective: This retrospective study aimed to describe the characteristics of patients treated at a COVID-19 referral hospital from March 2020 to June 2021 who experienced pressure injuries (PIs) either before or after admission.

Methods: The researchers collected and analyzed data on patients' demographic characteristics, symptoms, comorbidities, location and severity of PI, laboratory values, oxygen therapy, length of stay, and usage of vasopressors.

Results: During the study period, 1,070 patients were hospitalized for COVID-19 with varying degrees of severity, and 12 patients were diagnosed with PI. Eight (66.7%)

of the patients with PI were men. The median age was 60 (range, 51–71) years, and half of the patients had obesity. Eleven of the patients with PI (91.4%) had at least one comorbid condition. The sacrum and gluteus were the two most commonly affected sites. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL). The average length of stay was 22 (range, 9.8–40.3) days.

Conclusions: Health professionals should be aware of an increase in d-dimer in patients with COVID-19 and PI. Even though PIs in these patients might not result in immediate mortality, an increase in morbidity can be avoided with the right care.

Keywords: comorbidity, COVID-19, d-dimer, PI, pressure injury, wound healing

INTRODUCTION

In Indonesia, the first case of COVID-19 was diagnosed in March 2020; since then, over 2 million people have contracted COVID-19, with over 21,000 testing positive as of the end of June 2021.[2] As the number of patients admitted to hospitals increases, particularly ICU admissions, a greater number of individuals are vulnerable to pressure injury (PI) as a result of inactivity, immobility, and the use of artificial airways.[3,16]

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Pressure injury is a type of local trauma caused by constant pressure on the skin, most commonly over bony prominences. This pressure is high enough to interfere with blood flow to the capillaries, reducing oxygen supply to the tissues. This results in ischemia and necrosis of the afflicted tissue.[4] The sacrum, heel, sciatic tuberosity, greater trochanter, and lateral malleolus are frequently impacted.[5] Advanced age, immobility, poor nutrition, excessive moisture, incontinence, altered state of consciousness, poor perfusion, specific skin diseases, and concomitant disorders (eg, respiratory failure, anemia, diabetes, and septicemia) are all risk factors.[6] Patients who develop PIs tend to be older, less mobile, and have longer hospital stays than patients who do not.[7] Gedamu et al[8] reported that patients who were hospitalized for 7 to 20 days had a higher rate of PI than those who were hospitalized for fewer than 7 days.

A "cytokine storm" may arise as COVID-19 infection develops. This unregulated immune response causes immune cells, lymphocytes, and macrophages to infiltrate and produce a substantial amount of proinflammatory cytokines.[9] The cytokines interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)[10] are both involved in PI development[11,12] and are essential components of the cytokine storm. The rise in d-dimers in COVID-19 indicates that these two cytokines are related with a mix of systemic inflammatory processes and hypercoagulability situations.[13]

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Because of the urgency of the issue and the increased risk of PI in patients with COVID-19, this study was conducted at an infectious disease hospital to describe the clinical characteristics of patients with COVID-19 and PI.

METHODS

Ethics

On June 22, 2021, the Clinical Research Ethics Committee accepted this study with ethical approval number 157/KEP/2021. Because this was a retrospective research study based on anonymous and de-identified data, no consent was sought.

Study Design and Setting

This was a descriptive and retrospective study. Between March 2020 and June 2021, samples were taken from each patient at the hospital who had been diagnosed with PI and COVID-19.

Participants

Participants were chosen from medical records by their polymerase chain reaction confirmed result for COVID-19 after being admitted to the COVID-19 referral hospital. The study included patients who were at least 18 years old and had a diagnosis of PI by the attending plastic surgeon in their medical records. Only PIs induced by supine position were considered, such as those on the sacrum, occipital, temporal, heels (calcaneus), gluteus, scapula, and trochanter according to the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel and Pan Pacific PI Alliance.[17] Medical device-related PIs were excluded.

Variables and Data Sources

The secondary data drawn from patient medical records included sex; age; body mass index (BMI; categorized as follows: 1) underweight, BMI <18.5kg/m^2); 2) normal weight, BMI 18.5–22.9 kg/m^2); 3) overweight, BMI 23–24.9 kg/m^2); 4) obese I, BMI 25–29.9 kg/m^2); and 5) obese II, BMI >30 kg/m^2 according to the WHO recommendations for Asian populations);[18] symptoms related to COVID-19 on admission; coexisting disorder (hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease); type of oxygen therapy used during the time the patient was consulted for PI (room air, nasal cannula, simple oxygen mask, mechanical ventilation); laboratory results of leucocyte, total neutrophil, total lymphocyte, neutrophil-to-lymphocyte ratio (NLR), platelets, albumin, and d-dimer dated less than or equal to 3 days prior to the PI consultation; and PI location and stage. Pressure injury stages were classified in accordance with guidelines from the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel, and Pan Pacific PI Alliance.[17]

Length of stay (LOS) was the number of days a patient spent in the hospital before being discharged. The data-collection period was defined as the time from the collection of data from the first participant to the latest follow-up of the study participants.

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Data Analysis

Investigators conducted a descriptive analysis of the data, reporting medians, percentages, and interquartile ranges (Table).

RESULTS

The authors collected data from patients with confirmed COVID-19 who were treated at their institution during the start of the pandemic, from March 2020 to June 2021. During that period, 1,070 patients were hospitalized for COVID-19 with varying severity; of those, 12 patients were also diagnosed with a PI. Two of the 12 patients had already experienced a PI before being admitted to the hospital. Eight of these patients (66.7%) were men. Five of the 12 patients (41.7%) had a stage 2 PI and 7 (58.3%) had a stage 3 PI; none of the patients in this study had stage 1, stage

4, or unstageable PI or suspected deep-tissue injury. Overall, these patients had a median age of 60 years. When looking at median age by PI stage, the median age of patients with stage 2 PI was only slightly older than the median age of those with stage 3 PI (65 vs 63.5 years, respectively). Equal numbers of men had stage 2 (n = 4) or stage 3 PIs (n = 4) in this study. Among women, three (75%) had a stage 3 PI and one (25%) had a stage 2 PI. Two-thirds of the patients were obese. The majority of patients with PIs were also obese.

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Symptoms

Cough (58.3%), fever (50%), shortness of breath (50%), fatigue (41.7%), and nausea or vomiting (33.3%) were the most prevalent symptoms among the patients with both COVID-19 and a PI.

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Location

The sacrum (66.7%, n = 8) was the most frequent site of PI in these patients, followed by the gluteus (25%, n = 3), calcaneus, scapula, temporal, and hip. Sacral wounds were more prevalent in patients with stage 3 PI than in those with stage 2 PI.

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Comorbid Conditions

On admission to the hospital, 11 (91.7%) of the 12 patients who experienced PIs during treatment had at least one comorbidity, including hypertension (50%), diabetes (41.7%), stroke (41.7%), and coronary artery disease (25%). Most patients with a stage 2 PI had hypertension (80%), whereas most patients with a stage 3 PI also had diabetes and cerebrovascular disease.

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Median Laboratory Values

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During treatment, the patients were found to be anemic with a median hemoglobin of 10.7 g/dL, hypoalbuminemia (median 3.1 g/dL), and an elevated leukocyte count. The NLR median values were much higher among patients with stage 3 PI compared with the stage 2 group (21.1 vs 10.9). Platelet values were relatively normal across all patients with PI. Patients with a stage 3 PI had lower hemoglobin levels than those with a stage 2 PI (10.2 vs 11.3 g/dL). In these patients, the median d-dimer value was 3,700 (range, 1,500-8,400) ng/mL. Those with a stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with a stage 2 PI (1,100 ng/mL).

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Oxygen Therapy

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Eight patients (66.7%) required the use of a ventilator, five of whom had stage 3 PIs and three of whom had stage 2 PIs. One patient (8.3%) used nasal cannula oxygen therapy and acquired a stage 2 PI. Two patients (16.7%) used a basic oxygen mask; one developed a stage 2 PI and one developed a stage 3 PI.

Vasopressor Support

Because of low BP, the use of vasopressors contributes to poor peripheral tissue perfusion. Overall, seven of 12 patients required vasopressor support. Five patients (71.4%) on vasopressors had stage 3 PI whereas only two patients (40%) had stage 2 PI.

Length of Stay

The median LOS for these patients was 22 (range, 9.8–40.3) days. Patients with stage 2 PI were treated for 29 (range, 26-41) days and patients with stage 3 PI were treated for 13 (range, 8-29) days.

DISCUSSION

Although all of these individuals received appropriate care, PIs developed throughout their hospitalization. In this study, the median age of patients with PI was 60 years old, which was similar to the findings of a recent Chinese study.[19] The median age difference between individuals with stage 2 and 3 PI was nonsignificant. However, a study on PI in patients with COVID-19 in Spain included more (37.3%) patients between the ages of 80 and 89.[20] Because age is a determinant in the development of PIs,[6] older patients made up the majority of the age group in COVID-19 hospitalized cases.[21,22]

Two-thirds of the patients diagnosed with COVID-19 were obese. The majority of patients with PI were also obese. Research suggests that patients who have a low body mass index (BMI) or are severely obese are more likely to develop PI.[23,24] The present study likely included a high proportion of patients who were obese because almost all of the patients with a BMI over 25 kg/m^2 (87.5%) were using ventilators, thus putting them at higher risk of PI development.[3]

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The most common symptoms seen in this research were cough, fever, and shortness of breath, followed by fatigue and nausea or vomiting. According to the literature, cough, shortness of breath, and fever are frequent complaints from patients with COVID-19,[19,25] whereas diarrhea, loss of sense of taste or smell, and sore throat may be less common.[25,26]

The majority of patients in this study (66.7%) had PI on their sacrum, followed by the gluteus (25%). Other research also found the sacrum to be the most common site of PI on patients with COVID-19.[19,27] According to a study in Germany, the strongest predictor for sacral PI development was mobility.[28] Because most of these patients were eventually mechanically ventilated, immobility would be a factor in their PI development.[29,30]

In older adults, atherosclerosis reduces blood circulation to vital organs such as the heart, brain, legs, and skin, increasing the risk of PI development. Hypertension was the most common comorbid condition in this study. Cardiovascular disease is frequently associated with PI. Reduced left ventricle ejection fraction predicts PI in patients who have had a myocardial infarction.[31] These patients are more likely to have hypertension, but evidence of its consequences on PI development is conflicting.[32]

The second most common comorbid conditions in this study were diabetes and cerebrovascular disease. Diabetes-related peripheral vascular disease and neuropathy appear to be the root causes of PI in patients with diabetes.[33] In a Turkish study, diabetes was revealed to be a significant risk factor for PI development in ICU patients.[27] Patients with cerebrovascular disease are more likely to become immobile and acquire PIs.[32]

The patients in the present study were all anemic. Anemia lowers blood oxygen levels, resulting in a lack of oxygen flow to body tissues.[32] This may enhance the likelihood of tissue ischemia and PI development. Two other investigations also reported lower-than-normal hemoglobin levels in ICU patients with PI.[19,27]

The NLR is considered a marker of physiologic stress,[34] but may also a predictor for sepsis.[35] An NLR value above 10 could also be a potential parameter for assessing sepsis severity.[36] In this research, the median NLR value was higher among patients with stage 3 PI compared with that of patients with stage 2 PI (21.1 vs 10.9). The patients in this study also showed elevated levels of leucocytes, although their platelets were relatively normal. Leukocytosis and thrombocytopenia are commonly present during sepsis.[34,37] Because sepsis impairs wound healing,[38,39] these findings may indicate adverse effects related to PI development. One study on 104 patients admitted to the ICU suggested that NLR could be a marker for patients in increased risk of PI development.[40]

In this study, patients with stage 3 PI had a larger increase in mean d-dimer readings than did patients with stage 2 PI. COVID-19 stimulates an immune response, causing proinflammatory cytokines to be released and damaging the vascular endothelium. Following platelet aggregation activation in response to vascular damage, thrombosis and microemboli cause plasmin to promote fibrinolysis, resulting in an increase in d-dimer level.[4,41] Although the mechanism by which COVID-19 affects the development of PI remains unknown, it has been proposed that the myalgia generated by COVID-19 may disguise the discomfort of a developing PI. Simultaneously, a cytokine storm could exacerbate inflammatory and ischemic tissue damage, as well as create oxygen-induced metabolic acidosis and microemboli.[41,42] Yu et al[19] found that patients with COVID-19 in the ICU who developed stage 2 and stage 3 PI had a higher d-dimer value than those with stage 1 PI.

The majority of these patients (66.7%) were in the ICU with acute respiratory distress syndrome and had to be on a ventilator, making them immobile, which contributed to their PI development.[29,30,43] This conclusion is consistent with other studies of ICU patients with COVID-19 who developed PI.[19,27] COVID-19 predominantly infects lung tissue, resulting in hypoxia due to decreased oxygen exchange. Low blood oxygen levels contribute to the development of PI.[32] As pressure builds up on the skin, the interruption of blood circulation combined with a lack of appropriate oxygen delivery worsens the severity of ischemia.

Characteristics of multiorgan dysfunction syndrome might be detected in critically ill patients with COVID-19, such as dysregulation of the body’s response to infection characterized by hyperinflammation, alterations in coagulation, and dysregulation of the immune response.[44] A weakened immune response makes the body vulnerable to opportunistic bacterial infections, which can result in septic shock.[45] Vasopressors constrict blood arteries to help keep BP stable. However, the perfusion of smaller blood arteries may be reduced, thus putting the skin at risk of PI.[46]

The shorter hospital stays of patients with stage 3 PI in this study compared to patients with stage 2 PI could be attributed to the quick progression of COVID-19, which led the patient to die before further progression of their PI.

The authors recommend that additional attention should be paid to cases of PI in patients with COVID-19. During the COVID-19 pandemic, Tang et al[47] suggested that improvements in mobility and skin perfusion (eg, by anti-shock therapy), careful positioning, use of pressure-relieving devices, minimization of excess moisture, correction of malnutrition, and close daily monitoring would be helpful in preventing and managing PIs.[47] According to one study, having a nurse who is skilled in wound and skin care assigned to high-risk patients reduces the likelihood of PI development by 93%.[48]

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Limitations

This study only reports on a single-center experience with a small group of patients, so it has limited generalizability. More analytical observational studies with larger sample sizes could help identify the risk variables for PI in patients with COVID-19.

CONCLUSIONS

Healthcare professionals should pay close attention to cases of PI in patients with COVID-19, particularly those in the ICU because these patients have increased PI risk from immobility due to ventilator use. In patients with COVID-19 who develop PI, a rise in d-dimer and NLR values may indicate the severity of PI. Although PIs in these patients may not result in immediate mortality, an increase in morbidity may be prevented with the right care.

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Table.

CHARACTERISTICS OF PATIENTS WITH COVID-19 AND PRESSURE INJURY

Characteristic	Total (N = 12)	Stage 2 (n = 5)	Stage 3 (n = 7)
Demographic characteristics			
Median age, y (interquartile range)	60 (51 - 71)	65 (57.5 - 66)	63,5 (52.5 - 68)
Men, n (%)	8 (66.7)	4 (80.0)	4 (57.1)
Women, n (%)	4 (33.3)	1 (20.0)	3 (42.9)
Body mass index (kg/m^2), n (%)			
Underweight (<18.5)	1 (8.3)	0	1 (14.3)
Normal (18.5-22.9)	1 (8.3)	0	1 (14.3)
Overweight (23-24.9)	2 (16.7)	2 (40.0)	0
Obese I (25-29.9)	6 (50.0)	3 (60.0)	3 (42.9)
Obese II (≥30)	2 (16.7)	0	2 (28.8)
Symptoms, n (%)			
Cough	7 (58.3)	3 (60.0)	4 (57.1)
Fever	6 (50.0)	4 (80.0)	2 (28.6)
Shortness of breath	6 (50.0)	1 (20.0)	5 (71.4)
Fatigue	5 (41.7)	3 (60.0)	2 (28.6)
Nausea or vomiting	4 (33.3)	3 (60.0)	1 (14.3)
Diarrhea	1 (8.3)	1 (20.0)	0
Loss of taste or smell	1 (8.3)	0	1 (14.3)
Sore throat	1 (8.3)	1 (20.0)	0
Nasal congestion	1 (8.3)	1 (20.0)	0
Ulcer location, n (%)			
Sacrum	8 (66.7)	2 (40.0)	6 (85.7)
Gluteus	3 (25.0)	3 (60.0)	0
Temporal	1 (8.3)	1 (20.0)	0
Calcaneus	1 (8.3)	0	1 (14.3)
Scapula	1 (8.3)	0	1 (14.3)
Hip	1 (8.3)	0	1 (14.3)
Comorbid condition, n (%)			

Hypertension	6 (50.0)	4 (80.0)	2 (28.6)
Diabetes	5 (41.7)	2 (40.0)	3 (42.9)
Cerebrovascular disease	5 (41.7)	1 (20.0)	4 (57.1)
Coronary artery disease	3 (25.0)	1 (20.0)	2 (28.6)
Median laboratory values (interquartile range)			
Leukocytes (per mm^3)	14,265 (12,547.5-22,992.5)	14,830 (12,480-24,020)	13,700 (12,830-19,885)
Differential count (per mm^3)			
Total neutrophils	12,288.7 (10,830-21,012.9)	11,967.8 (10,886.9-21,401.8)	12,356.9 (11,439.9-18,479.5)
Total lymphocytes	1,023.9 (782.3-1,442.7)	1,764.8 (1,335.4-1,969.4)	838.1 (698.9-1,023.9)
Neutrophil/lymphocyte ratio	20.4 (10.6-24)	10.9 (7.7-36.6)	21.1 (15.5- 22.6)
Hemoglobin (g/dL)	10.7 (10-11.8)	11.3 (10.6-11.4)	10.2 (8.8-11.3)
Platelet count (per mm^3)	260,500 (187,000-443,250)	241,000 (190,000-399,000)	280,000 (203,500-447,500)
Albumin (g/dL)	3.08 (2.9-3.1)	3 (2.8-3.1)	3.1 (3-3.1)
D-dimer (ng/mL)	3,700 (1,500-8,400)	1,100 (600-1,700)	7,900 (5,200-11,200)
Oxygen therapy, n (%)			
Room air	1 (8.3)	0	1 (14.3)
Nasal cannula	1 (8.3)	1 (20.0)	0
Simple oxygen mask	2 (16.7)	1 (20.0)	1 (14.3)
Mechanical ventilation	8 (66.7)	3 (60.0)	5 (71.4)
Vasopressor support, n (%)	7 (58.3)	2 (40.0)	5 (71.4)
Length of stay, d (interquartile range)	22 (9.8 – 40.3)	29 (26 - 41)	13 (8 - 29)

[[Original Investigation]]

Characteristics of Patients with Pressure Injuries in a COVID-19 Referral Hospital

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ABSTRACT

Objective: This retrospective study aimed to describe the characteristics of patients treated at a COVID-19 referral hospital from March 2020 to June 2021 who experienced pressure injuries (PIs) either before or after admission.

Methods: The researchers collected and analyzed data on patients' demographic characteristics, symptoms, comorbidities, location and severity of PI, laboratory values, oxygen therapy, length of stay, and usage of vasopressors.

Results: During the study period, 1,070 patients were hospitalized for COVID-19 with varying degrees of severity, and 12 patients were diagnosed with PI. Eight (66.7%) of the patients with PI were men. The median age was 60 (range, 51–71) years, and half of the patients had obesity. Eleven of the patients with PI (91.4%) had at least one comorbid condition. The sacrum and gluteus were the two most commonly affected sites. Those with stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with stage 2 PI (1,100 ng/mL). The average length of stay was 22 (range, 9.8–40.3) days.

Conclusions: Health professionals should be aware of an increase in d-dimer in patients with COVID-19 and PI. Even though PIs in these patients might not result in immediate mortality, an increase in morbidity can be avoided with the right care.

Keywords: comorbidity, COVID-19, d-dimer, ~~PI,~~ pressure injury, wound healing, medical care

INTRODUCTION

In Indonesia, the first case of COVID-19 was diagnosed in March 2020; since then, over 2 million people have contracted COVID-19, with over 21,000 testing positive as of the end of June 2021.[1~~2~~] As the number of patients admitted to hospitals increases, particularly ICU admissions, a greater number of individuals are vulnerable to pressure injury (PI) as a result of inactivity, immobility, and the use of artificial airways.[2-5~~3,16~~]

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Pressure injury is a type of local trauma caused by constant pressure on the skin, most commonly over bony prominences. This pressure is high enough to interfere with blood flow to the capillaries, reducing oxygen supply to the tissues. This results in ischemia and necrosis of the afflicted tissue.[6~~4~~] The sacrum, heel, sciatic tuberosity, greater trochanter, and lateral malleolus are frequently impacted.[7~~5~~] Advanced age, immobility, poor nutrition, excessive moisture, incontinence, altered state of consciousness, poor perfusion, specific skin diseases, and concomitant disorders (eg, respiratory failure, anemia, diabetes, and septicemia) are all risk factors.[8~~6~~] Patients who develop PIs tend to be older, less mobile, and have longer hospital stays than patients who do not.[9~~7~~] Gedamu et al[~~8~~10] reported that patients who were hospitalized for 7 to 20 days had a higher rate of PI than those who were hospitalized for fewer than 7 days. Slow-healing wounds might diminish one's quality of life.[11]

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A “cytokine storm” may arise as COVID-19 infection develops. This unregulated immune response causes immune cells, lymphocytes, and macrophages to infiltrate and produce a substantial amount of proinflammatory cytokines.[12~~9~~] The cytokines interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)[13~~10~~] are both involved in PI development[14~~1~~,15~~2~~] and are essential components of the cytokine storm. The rise in d-dimers in COVID-19 indicates that IL-6 and TNF-α

~~these two cytokines~~ are related with a mix of systemic inflammatory processes and hypercoagulability situations.[16]~~[3]~~

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Because of the urgency of the issue and the increased risk of PI in patients with COVID-19, this study was conducted at an infectious disease hospital to describe the clinical characteristics of patients with COVID-19 and PI.

METHODS

Ethics

On June 22, 2021, the Clinical Research Ethics Committee accepted this study with ethical approval number 157/KEP/2021. Because this was a retrospective research study based on anonymous and de-identified data, no consent was sought.

Study Design and Setting

This was a descriptive and retrospective study. Between March 2020 and June 2021, samples were taken from each patient at the hospital who had been diagnosed with PI and COVID-19.

Participants

Participants were chosen from medical records by their polymerase chain reaction confirmed result for COVID-19 after being admitted to the COVID-19 referral hospital. The study included patients who were at least 18 years old and had a diagnosis of PI by the attending plastic surgeon in their medical records. Only PIs induced by supine position were considered, such as those on the sacrum, occipital, temporal, heels (calcaneus), gluteus, scapula, and trochanter according to the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel and Pan Pacific PI Alliance.[17] Medical device-related PIs were excluded.

Variables and Data Sources

The secondary data drawn from patient medical records included sex; age; body mass index (BMI; categorized as follows: 1) underweight, BMI <18.5kg/m^2); 2) normal weight, BMI 18.5–22.9 kg/m^2); 3) overweight, BMI 23–24.9 kg/m^2); 4) obese I, BMI 25–29.9 kg/m^2); and 5) obese II, BMI >30 kg/m^2 according to the WHO recommendations for Asian populations);[18] symptoms related to COVID-19 on admission; coexisting disorder (hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease); type of oxygen therapy used during the time the patient was consulted for PI (room air, nasal cannula, simple oxygen mask, mechanical ventilation); laboratory results of leucocyte, total neutrophil, total lymphocyte, neutrophil-to-lymphocyte ratio (NLR), platelets, albumin, and d-dimer dated less than or equal to 3 days prior to the PI consultation; and PI location and stage. Pressure injury stages were classified in accordance with guidelines from the European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel, and Pan Pacific PI Alliance.[17]

Length of stay (LOS) was the number of days a patient spent in the hospital before being discharged. ~~The data-collection period was defined as the time from the collection of data from the first participant to the latest follow-up of the study participants.~~

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Data Analysis

Investigators conducted a descriptive analysis of the data, reporting medians, percentages, and interquartile ranges (Table).

RESULTS

The authors collected data from patients with confirmed COVID-19 who were treated at their institution during the start of the pandemic, from March 2020 to June 2021. During that period, 1,070 patients were hospitalized for COVID-19 with varying severity; of those, 12 patients were also diagnosed with a PI. Two of the 12 patients had already experienced a PI before being admitted to the hospital. Eight of these patients (66.7%) were men. Five of the 12 patients (41.7%) had a stage 2 PI and 7 (58.3%) had a stage 3 PI; none of the patients in this study had stage 1, stage 4, or unstageable PI or suspected deep-tissue injury. Overall, these patients had a median age of 60 years, ranging from 51 to 71 years. When looking at median age by PI stage, the median age of patients with stage 2 PI was only slightly older than the median age of those with stage 3 PI (65 vs 63.5 years, respectively). Equal numbers of men had stage 2 (n = 4) or stage 3 PIs (n = 4) in this study. Among women, three (75%) had a stage 3 PI and one (25%) had a stage 2 PI. Two-thirds of the patients (67%) were obese. ~~The majority of patients with PIs were also obese.~~

Symptoms

Cough (58.3%), fever (50%), shortness of breath (50%), fatigue (41.7%), and nausea or vomiting (33.3%) were the most prevalent symptoms among the patients with both COVID-19 and a PI.

Location

Some of the 12 patients have had numerous pressure injuries. The sacrum (66.7%, n = 8) was the most frequent site of PI in these patients, followed by the gluteus (25%, n = 3), calcaneus, scapula, temporal, and hip. Sacral wounds were more prevalent in patients with stage 3 PI (n=6) than in those with stage 2 PI (n=2).

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Comorbid Conditions

On admission to the hospital, 11 (91.7%) of the 12 patients who experienced PIs during treatment had at least one comorbidity, including hypertension (50%), diabetes (41.7%), stroke (41.7%), and coronary artery disease (25%). Most patients with a stage 2 PI had hypertension (80%), whereas most patients with a stage 3 PI also had diabetes (42.9%) and cerebrovascular disease (57.1%).

Median Laboratory Values

During treatment, the patients were found to be slight anemic with a median hemoglobin of 10.7 g/dL (normal values: 12-16), a median hypoalbuminemia of ~~(median~~ 3.1 g/dL~~)~~ (normal values: 3,4-4,8), and an elevated leukocyte count with a median 14.265 (normal values: 4.000-11.000). The NLR median values were much higher among patients with stage 3 PI compared with the stage 2 group (21.1 vs 10.9). Platelet values were relatively normal across all patients with PI. Patients with a stage 3 PI had lower hemoglobin levels than those with a stage 2 PI (10.2 vs 11.3 g/dL). In these patients, the median d-dimer value was 3,700 (range, 1,500-8,400) ng/mL. Those with a stage 3 PI had a substantially greater median d-dimer (7,900 ng/mL) than patients with a stage 2 PI (1,100 ng/mL).

Oxygen Therapy

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Eight patients (66.7%) required the use of a ventilator, five of whom had stage 3 PIs and three of whom had stage 2 PIs. One patient (8.3%) used nasal cannula oxygen therapy and acquired a stage 2 PI. Two patients (16.7%) used a basic oxygen mask; one developed a stage 2 PI and one developed a stage 3 PI.

Vasopressor Support

Because of low BP, the use of vasopressors contributes to poor peripheral tissue perfusion. Overall, seven of 12 patients required vasopressor support. Five patients (71.4%) on vasopressors had stage 3 PI whereas only two patients (40%) had stage 2 PI.

Length of Stay

The median LOS for these patients was 22 (range, 9.8–40.3) days. Patients with stage 2 PI were treated for 29 (range, 26-41) days and patients with stage 3 PI were treated for 13 (range, 8-29) days.

DISCUSSION

Although all of these individuals received appropriate care, PIs developed throughout their hospitalization. In this study, the median age of patients with PI was 60 years old, which was similar to the findings of a recent Chinese study.[19] The median age difference between individuals with stage 2 and 3 PI was nonsignificant. However, a study on PI in patients with COVID-19 in Spain included more (37.3%) patients between the ages of 80 and 89.[20] Because age is a determinant in the development of PIs,[6] older patients made up the majority of the age group in COVID-19 hospitalized cases.[21,22]

Two-thirds of the patients diagnosed with COVID-19 were obese. The majority of patients with PI were also obese. Research suggests that patients who have a low body mass index (BMI) or are severely obese are more likely to develop PI.[23,24] The present study likely included a high proportion of patients who were obese because almost all of the patients with a BMI over 25 kg/m^2 (87.5%) were using ventilators, thus putting them at higher risk of PI development.[3]

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The most common symptoms seen in this research were cough, fever, and shortness of breath, followed by fatigue and nausea or vomiting. According to the literature, cough, shortness of breath, and fever are frequent complaints from patients with COVID-19,[19,25] whereas diarrhea, loss of sense of taste or smell, and sore throat may be less common.[25,26]

The majority of patients in this study (66.7%) had PI on their sacrum, followed by the gluteus (25%). Other research also found the sacrum to be the most common site of PI on patients with COVID-19.[19,27] According to a study in

Germany, the strongest predictor for sacral PI development was mobility.[28] Because most of these patients were eventually mechanically ventilated, immobility would be a factor in their PI development.[29,30]

In older adults, atherosclerosis reduces blood circulation to vital organs such as the heart, brain, legs, and skin, increasing the risk of PI development. Hypertension was the most common comorbid condition in this study. Cardiovascular disease is frequently associated with PI. Reduced left ventricle ejection fraction predicts PI in patients who have had a myocardial infarction.[31] These patients are more likely to have hypertension, but evidence of its consequences on PI development is conflicting.[32]

The second most common comorbid conditions in this study were diabetes and cerebrovascular disease. Diabetes-related peripheral vascular disease and neuropathy appear to be the root causes of PI in patients with diabetes.[33] In a Turkish study, diabetes was revealed to be a significant risk factor for PI development in ICU patients.[27] Patients with cerebrovascular disease are more likely to become immobile and acquire PIs.[32]

The patients in the present study were all anemic. Anemia lowers blood oxygen levels, resulting in a lack of oxygen flow to body tissues.[32] This may enhance the likelihood of tissue ischemia and PI development. Two other investigations also reported lower-than-normal hemoglobin levels in ICU patients with PI.[19,27]

The NLR is considered a marker of physiologic stress,[34] but may also a predictor for sepsis.[35] An NLR value above 10 could also be a potential parameter for assessing sepsis severity.[36] In this research, the median NLR value was higher among patients with stage 3 PI compared with that of patients with stage 2 PI (21.1 vs 10.9). The patients in this study also showed elevated levels of leucocytes, although their platelets were relatively normal. Leukocytosis and thrombocytopenia are commonly present during sepsis.[34,37] Because sepsis impairs wound healing,[38,39] these findings may indicate adverse effects related to PI development. One study on 104 patients admitted to the ICU suggested that NLR could be a marker for patients in increased risk of PI development.[40]

In this study, patients with stage 3 PI had a larger increase in mean d-dimer readings than did patients with stage 2 PI. COVID-19 stimulates an immune response, causing proinflammatory cytokines to be released and damaging the vascular endothelium. Following platelet aggregation activation in response to vascular damage, thrombosis and microemboli cause plasmin to promote fibrinolysis, resulting in an increase in d-dimer level.[4,41] Although the mechanism by which COVID-19 affects the development of PI remains unknown, it has been proposed that the myalgia generated by COVID-19 may disguise the discomfort of a developing PI. Simultaneously, a cytokine storm could exacerbate inflammatory and ischemic tissue damage, as well as create oxygen-induced metabolic acidosis and microemboli.[12,41~~41,42~~] Yu et al[19] found that patients with COVID-19 in the ICU who developed stage 2 and stage 3 PI had a higher d-dimer value than those with stage 1 PI.

The majority of these patients (66.7%) were in the ICU with acute respiratory distress syndrome and had to be on a ventilator, making them immobile, which contributed to their PI development.[29,30,42~~3~~] This conclusion is consistent with other studies of ICU patients with COVID-19 who developed PI.[19,27] COVID-19 predominantly infects lung tissue, resulting in hypoxia due to decreased oxygen exchange. Low blood oxygen levels contribute to the development of PI.[32] As pressure builds up on the skin, the interruption of blood circulation combined with a lack of appropriate oxygen delivery worsens the severity of ischemia.

Characteristics of multiorgan dysfunction syndrome might be detected in critically ill patients with COVID-19, such as dysregulation of the body’s response to infection characterized by hyperinflammation, alterations in coagulation, and dysregulation of the immune response.[43~~4~~] A weakened immune response makes the body vulnerable to opportunistic bacterial infections, which can result in septic shock.[44] Vasopressors constrict blood arteries to help keep BP stable. However, the perfusion of smaller blood arteries may be reduced, thus putting the skin at risk of PI.[45]

The shorter hospital stays of patients with stage 3 PI (median= 13 days) in this study compared to patients with stage 2 PI (median= 29 days) could be attributed to the quick progression of COVID-19, which led the patient to die before further progression of their PI. Fifty percent of patients died during their hospital stay: four of seven patients with stage 3 PI (57.1%), and two of five patients with stage 2 PI (40%).

The authors recommend that additional attention should be paid from healthcare workers to cases of PI in patients with COVID-19. During the COVID-19 pandemic, Tang et al[47] suggested that improvements in mobility and skin perfusion (eg, by anti-shock therapy), careful positioning, use of pressure-relieving devices, minimization of excess moisture, correction of malnutrition, and close daily monitoring would be helpful in preventing and managing PIs.[2] According to one study, having a nurse who is skilled in wound and skin care assigned to high-risk patients reduces the likelihood of PI development by 93%.[47]

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Limitations

This study only reports on a single-center experience with a small group of patients, so it has limited generalizability. More analytical observational studies with larger sample sizes could help identify the risk variables for PI in patients with COVID-19.

CONCLUSIONS

Healthcare professionals should pay close attention to cases of PI in patients with COVID-19, particularly those in the ICU because these patients have increased PI risk from immobility due to ventilator use. In patients with COVID-19 who develop PI, a rise in d-dimer and NLR values may indicate the severity of PI. Although PIs in these patients may not result in immediate mortality, an increase in morbidity may be prevented with the right care.

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Commented [FC36]: Author: is this the same as ref. 3?

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Table.

CHARACTERISTICS OF PATIENTS WITH COVID-19 AND PRESSURE INJURY

Characteristic	**Total (N = 12)**	**Stage 2 (n = 5)**	**Stage 3 (n = 7)**
Demographic characteristics			
Median age, y (interquartile range)	60 (51 - 71)	65 (57.5 - 66)	63,5 (52.5 - 68)
Men, n (%)	8 (66.7)	4 (80.0)	4 (57.1)
Women, n (%)	4 (33.3)	1 (20.0)	3 (42.9)
Body mass index (kg/m^2), n (%)			
Underweight (<18.5)	1 (8.3)	0	1 (14.3)
Normal (18.5-22.9)	1 (8.3)	0	1 (14.3)
Overweight (23-24.9)	2 (16.7)	2 (40.0)	0
Obese I (25-29.9)	6 (50.0)	3 (60.0)	3 (42.9)
Obese II (≥30)	2 (16.7)	0	2 (28.8)
Symptoms, n (%)			
Cough	7 (58.3)	3 (60.0)	4 (57.1)
Fever	6 (50.0)	4 (80.0)	2 (28.6)
Shortness of breath	6 (50.0)	1 (20.0)	5 (71.4)
Fatigue	5 (41.7)	3 (60.0)	2 (28.6)
Nausea or vomiting	4 (33.3)	3 (60.0)	1 (14.3)
Diarrhea	1 (8.3)	1 (20.0)	0
Loss of taste or smell	1 (8.3)	0	1 (14.3)
Sore throat	1 (8.3)	1 (20.0)	0
Nasal congestion	1 (8.3)	1 (20.0)	0
Ulcer location, n (%)			
Sacrum	8 (66.7)	2 (40.0)	6 (85.7)
Gluteus	3 (25.0)	3 (60.0)	0
Temporal	1 (8.3)	1 (20.0)	0
Calcaneus	1 (8.3)	0	1 (14.3)
Scapula	1 (8.3)	0	1 (14.3)
Hip	1 (8.3)	0	1 (14.3)
Comorbid condition, n (%)			

Hypertension	6 (50.0)	4 (80.0)	2 (28.6)
Diabetes	5 (41.7)	2 (40.0)	3 (42.9)
Cerebrovascular disease	5 (41.7)	1 (20.0)	4 (57.1)
Coronary artery disease	3 (25.0)	1 (20.0)	2 (28.6)
Median laboratory values (interquartile range)			
Leukocytes (per mm^3)	14,265 (12,547.5-22,992.5)	14,830 (12,480-24,020)	13,700 (12,830-19,885)
Differential count (per mm^3)			
Total neutrophils	12,288.7 (10,830-21,012.9)	11,967.8 (10,886.9-21,401.8)	12,356.9 (11,439.9-18,479.5)
Total lymphocytes	1,023.9 (782.3-1,442.7)	1,764.8 (1,335.4-1,969.4)	838.1 (698.9-1,023.9)
Neutrophil/lymphocyte ratio	20.4 (10.6-24)	10.9 (7.7-36.6)	21.1 (15.5- 22.6)
Hemoglobin (g/dL)	10.7 (10-11.8)	11.3 (10.6-11.4)	10.2 (8.8-11.3)
Platelet count (per mm^3)	260,500 (187,000-443,250)	241,000 (190,000-399,000)	280,000 (203,500-447,500)
Albumin (g/dL)	3.08 (2.9-3.1)	3 (2.8-3.1)	3.1 (3-3.1)
D-dimer (ng/mL)	3,700 (1,500-8,400)	1,100 (600-1,700)	7,900 (5,200-11,200)
Oxygen therapy, n (%)			
Room air	1 (8.3)	0	1 (14.3)
Nasal cannula	1 (8.3)	1 (20.0)	0
Simple oxygen mask	2 (16.7)	1 (20.0)	1 (14.3)
Mechanical ventilation	8 (66.7)	3 (60.0)	5 (71.4)
Vasopressor support, n (%)	7 (58.3)	2 (40.0)	5 (71.4)
Length of stay, d (interquartile range)	22 (9.8 – 40.3)	29 (26 - 41)	13 (8 - 29)
Died during hospital stays, n (%)	6 (50.0)	2 (40.0)	4 (57.1)