Nursing Sciences Journal. Vol. 10, No. 1, April 2026
P- ISSN: 2598-8220, E-ISSN: 2598-8212

EXPLORING THE RELATIONSHIP BETWEEN LACTIC ACID LEVELS AND CLINICAL OUTCOMES OF SEPSIS PATIENTS IN INTENSIVE CARE UNITS: IMPLICATIONS FOR NURSING PRACTICE

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ABSTRACT

Sepsis is a life-threatening condition frequently associated with clinical deterioration, including prolonged hospitalization and increased mortality risk. High lactate concentrations reflect tissue hypoxia and organ dysfunction, which may significantly worsen patient outcomes. However, previous studies on the association between lactate levels and clinical outcomes remain inconsistent. This study aimed to analyze the relationship between lactate levels, length of hospital stay, and mortality in sepsis patients in the intensive care unit. A retrospective observational cohort design was employed, with saturated sampling based on inclusion criteria (n=109). Data were collected from medical records with a total population of 134 patients. Results showed that the majority of sepsis patients were male, predominantly in the pre-elderly and elderly age groups. The most common comorbidities were pneumonia. Most patients had lactate levels >1.7 mmol/L, with prolonged hospitalization (≥3 days) observed and a mortality rate of 71.6%. Chi-square analysis revealed a significant association between lactate levels and both length of stay (p=0.039) and mortality (p=0.018). It can be concluded that elevated lactate levels were associated with prolonged hospitalization and increased mortality in sepsis patients. Lactate levels may serve as a prognostic marker, emphasizing the need for standardized sepsis management, including adherence to the "Hour-1 bundle" protocol, to improve patient outcomes.

Keywords: Sepsis, Lactate Level, Mortality, Length of Hospitalization, Intensive Care Unit

INTRODUCTION

Sepsis is a potentially fatal illness that occurs when the body's response to infection triggers a systemic inflammatory reaction that damages its own tissues and organs, leading to organ failure, tissue damage, and death if left untreated (Moazen et al., 2025). Sepsis remains a significant global health concern associated with high mortality rates (Sakr et al., 2018). According to the World Health Organization (WHO) in 2020, sepsis is one of the top five leading causes of death worldwide, with an estimated 48.9 million cases and 11 million deaths annually, accounting for approximately 20% of global mortality (World Health Organization, 2020). Recent studies in the United States indicate sepsis mortality rates of 17.4% among patients aged 65 and older and 16.6% among those aged 18–64 (Owens et al., 2024). While epidemiological data on sepsis in developing countries,

Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

particularly in Asia and Indonesia, remain limited, a study conducted in an intensive care unit (ICU) of a type B private hospital in South Tangerang revealed that 67.3% of 110 sepsis patients progressed to severe sepsis, with 37.3% developing septic shock and nearly half (49.1%) succumbing to the condition (Wicaksono et al., 2022). A preliminary study further reported 134 sepsis cases between 2020 and 2024 in a regional hospital, with 97 fatalities occurring in the ICU.

Sepsis patients frequently experience prolonged hospital stays compared with non-sepsis patients; for example, a study found a median stay of 11 days in sepsis patients versus 4 days in non-sepsis adults (Abu-Humaidan et al., 2021). According to the World Health Organization fact sheet, although a specific global average length of stay is not provided, sepsis remains a major cause of morbidity and extended hospitalization worldwide (World Health Organization, 2020). In a nationwide Korean multicenter cohort, the median hospital stay after sepsis diagnosis was 15.9 days (IQR 8.2–31.0 days), and prolonged stay before sepsis onset was significantly associated with higher in-hospital mortality (Kim et al., 2024). In Indonesia, research from a South Tangerang hospital found an average hospitalization period of nearly 7 days for sepsis patients (Wicaksono et al., 2022). Extended lengths of stay elevate the risk of adverse outcomes such as hospital-acquired infections, functional decline, and malnutrition—all of which further compromise prognosis in sepsis-affected patients (Loftus et al., 2020).

Sepsis arises from a dysregulated host response to infection, leading to organ dysfunction (Rudd et al., 2020). This dysregulation triggers tissue hypoperfusion, hypoxia, and mitochondrial dysfunction, thereby disrupting pyruvate oxidation in the Krebs cycle and increasing cytosolic pyruvate-to-lactate conversion (Datta and Singh, 2025; Hernandez et al., 2019). Impaired lactate clearance, often due to hepatic or renal failure, further exacerbates hyperlactatemia (lactate ≥ 2 mmol/L) and is strongly associated with worse prognosis in sepsis (Cheng et al., 2020; Donaliazarti, 2022). In particular, patients with persistent hyperlactatemia or impaired lactate kinetics face markedly elevated mortality rates, and evidence suggests that monitoring serial lactate levels and clearance can identify high-risk individuals early (Li et al., 2022; Rezar et al., 2023).

Early detection and prompt intervention are widely recognized as critical determinants of survival among patients with sepsis (Kim and Park, 2019). The international Surviving Sepsis Campaign (SSC) guidelines recommend the "Hour-1 Bundle", which emphasizes measurement of serum lactate, obtaining blood cultures before antibiotic administration, initiation of broad-spectrum antibiotics, rapid fluid resuscitation, and vasopressor use when indicated—all ideally within the first hour of sepsis recognition (Levy et al., 2018). Serum lactate has been endorsed as a biomarker of organ dysfunction and as a guide for resuscitation efforts (Evans et al., 2021). Nurses play a pivotal role in these protocols, performing early physiological assessments, initiating the bundle elements, and collaborating within the multidisciplinary team (Abdalhafith et al., 2025). Despite these recommendations, evidence on the correlation between lactate levels and clinical outcomes remains inconsistent: for example, point-of-care lactate testing was associated with improved guideline adherence and reduced mortality in one study (Lee et al., 2024), whereas a recent meta-analysis found no clear mortality benefit from strict adherence to the Hour-1 Bundle (Freund et al., 2024). Given this discrepancy, the present study aims to analyze the relationship between serum lactate levels, duration of hospital stay, and mortality among sepsis patients admitted to the intensive care unit.

METHODS

This study employed a cross-sectional design with a retrospective approach to analyze the relationship between lactate levels, length of stay, and mortality among sepsis patients in the Intensive Care Unit (ICU) of Dr. Soebandi Regional Hospital, Jember, Indonesia. The hospital serves as a tertiary referral center for the eastern region of East Java, with an ICU capacity of 12 beds.

A total population sampling technique was used due to the limited number of eligible sepsis patients. The study population consisted of all adult sepsis patients admitted to the ICU between January 2020 and December 2024 (N = 134). The final sample included 109 patients who met the inclusion criteria: (1) age > 18 years and (2) documented lactate levels within the first 24 hours of ICU admission. Patients with hospitalization < 24 hours, missing key clinical data, or incomplete medical records were excluded to minimize bias.

Data were collected retrospectively from March to April 2024 using structured observation sheets developed by the researchers. Data were obtained from electronic and paper-based medical records and included (1) demographic characteristics (age, sex), (2) initial lactate levels within 24 hours, (3) length of ICU stay (measured in days from admission to discharge or death), and (4) patient outcomes (alive or deceased). Lactate levels were categorized as ≤1.7 mmol/L or > 1.7 mmol/L based on established cut-off values for tissue hypoperfusion (Villar et al., 2019). Length of stay was dichotomized into < 3 days and ≥ 3 days following previous clinical benchmarks (Kuye et al., 2021).

To ensure data validity, cross-checking was performed by two independent reviewers, and any discrepancies were resolved through consensus. Missing data were excluded using listwise deletion. Statistical analysis was performed using IBM SPSS version 24. Univariate analysis was conducted to describe the sample characteristics, while bivariate analysis employed chi-square tests to examine the relationships between variables, with a significance level set at $\alpha = 0.05$.

This study has obtained ethical approval from the Health Research Ethics Committee, Faculty of Nursing, University of Jember, with reference number 029/UN25.1.14/KEPK/2025. Patient confidentiality was ensured through anonymized data collection and secure storage, following the ethical standards outlined by WHO (2011) and CIOMS (2016).

RESULT

The results of this study are presented in tables to describe the characteristics of sepsis patients, distribution of study variables, and bivariate analyses examining the relationship between lactate levels, length of stay, and mortality.

Table 1. Distribution of Patient Characteristics and Comorbidities (n = 109)

Characteristic	Category	Frequency (n)	Precentage (%)
Gender			
	Male	59	54.1
	Female	50	45.9
	Subtotal	**109**	**100.0**

Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

Characteristic	Category	Frequency (n)	Precentage (%)
Age Group			
	Young Adult (19–44 years)	26	23.9
	Middle-Aged (45–59 years)	42	38.5
	Elderly (≥60 years)	41	37.6
	Subtotal	**109**	**100.0**
Comorbidities[1]			
	Pneumonia	27	24.8
	COVID-19	11	10.1
	Abscess	9	8.3
	Cardiovascular disease	8	7.3
	Renal failure	8	7.3
	Diabetes mellitus	7	6.4
	Acute respiratory failure	5	4.6
	Paralytic ileus	4	3.7
	Hepatitis	3	2.8
	Hernia	3	2.8
	Hydrocephalus	3	2.8
	Colorectal cancer	3	2.8
	Burn injury	3	2.8
	Gastric ulcer	2	1.8
	Tuberculosis	2	1.8
	Gastrointestinal hemorrhage	1	0.9
	Obstructive ileus	1	0.9
	Pregnancy complications	1	0.9
	Gastrointestinal obstruction	1	0.9
	Peritonitis	1	0.9
	COPD	1	0.9
	Cholangitis	1	0.9
	Fibromatosis	1	0.9
	Ulcerative stomatitis	1	0.9
	Hypovolemic shock	1	0.9
	Duodenal ulcer	1	0.9
	Subtotal	**109**	**100.0[2]**

Note: [1]One patient may have more than one comorbidity; therefore, the total number of comorbidities exceeds the total number of patients (N = 109); [2] Percentage calculated relative to total comorbidities, not total patients.

The characteristics of 109 sepsis patients are summarized in Table 1. The majority of patients were male (54.1%), while female patients accounted for 45.9%. Based on age group, most patients were middle-aged (45–59 years) at 38.5%, followed by elderly patients (≥60 years) at 37.6%, and young adults (19–44 years) at 23.9%. Regarding comorbidities, pneumonia was the most common condition (24.8%), followed by COVID-19 (10.1%), abscess (8.3%), cardiovascular disease (7.3%), renal failure (7.3%), and diabetes mellitus (6.4%). Other comorbidities, such as acute respiratory failure, paralytic ileus, hepatitis, hernia, hydrocephalus, colorectal cancer, and burn injury, were present in smaller proportions (<5%). It is important to note that one patient could have more than one comorbidity; therefore, the total number of comorbid conditions exceeds the total number of patients. This pattern indicates that sepsis frequently occurs in individuals with multiple underlying diseases, suggesting that comorbidity burden may contribute to the severity and outcomes of sepsis cases.

Table 2. Frequency Distribution of Clinical Variables among Sepsis Patients (n = 109)

Variables	Category	Frequency (n)	Percentage (%)
Lactate Levels	≤ 1.7 mmol	33	30.3
	> 1.7 mmol	76	69.7
	Subtotal	**109**	**100.0**
Length of Stay	< 3 days	30	27.5
	≥ 3 days	79	72.5
	Subtotal	**109**	**100.0**
Mortality	Survive	31	28.4
	Death	78	71.6
	Subtotal	**109**	**100.0**

Table 2 presents the frequency distribution of the study variables among 109 patients. Most patients had elevated lactate levels (>1.7 mmol), accounting for 69.7% of the total. The majority of patients also had a length of stay of ≥3 days (72.5%), indicating prolonged hospitalization. Regarding patient outcomes, mortality was high, with 71.6% of patients dying during hospitalization, while only 28.4% survived. These findings suggest that higher lactate levels are associated with longer hospital stays and increased mortality rates among the study population.

Table 3. Cross-Tabulation of Lactate Levels and Length of Stay in Sepsis Patients

Lactate Levels	Length of Stay <3 days	Length of Stay ≥3 days	p-value	RR (95% CI)
≤ 1.7 mmol/L	14 (42.4%)	19 (57.6%)	**0.039**	**2.02 (1.12–3.63)**
> 1.7 mmol/L	16 (21.1%)	60 (78.9%)		
Subtotal	**30 (27.5%)**	**79 (72.5%)**		

Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

Table 3 shows a statistically significant association between lactate levels and length of hospital stay (p = 0.039). Patients with lower lactate levels (≤1.7 mmol/L) were approximately twice as likely to have a shorter hospital stay (<3 days) compared to those with elevated lactate levels (RR = 2.02; 95% CI: 1.12–3.63). This finding suggests that higher lactate levels are correlated with prolonged hospitalization among sepsis patients, reflecting greater severity and slower clinical recovery.

Table 4. Cross-Tabulation of Lactate Levels and Mortality in Sepsis Patients

Lactate Levels	Survived	Died	p-value	RR (95% CI)
≤ 1.7 mmol/L	15 (45.5%)	18 (54.5%)	**0.018**	**2.16 (1.22–3.83)**
> 1.7 mmol/L	16 (21.1%)	60 (78.9%)		
Subtotal	**31 (28.4%)**	**78 (71.6%)**		

As shown in Table 4, there was a significant relationship between lactate levels and mortality (p = 0.018). Patients with elevated lactate levels (>1.7 mmol/L) had a markedly higher mortality rate (78.9%) compared to those with lower levels (54.5%). The relative risk (RR = 2.16; 95% CI: 1.22–3.83) indicates that patients with normal lactate levels (≤1.7 mmol/L) were more than twice as likely to survive compared to those with elevated levels. This suggests that increased lactate concentration is a strong predictor of mortality among sepsis patients.

DISCUSSION

The study results show that the majority of sepsis patients were male (54.1%, 59 of 109 patients). This characteristic aligns with previous research showing a male predominance among sepsis patients (Lindström et al., 2021). Research in mice explains that female estrogen hormones can enhance cellular and humoral immune responses, resulting in lower inflammatory responses compared to males. Conversely, male androgen hormones tend to suppress the immune system. Human studies regarding the underlying causes of higher sepsis rates in men remain inconclusive. However, several potential risk factors may play a role, including smoking, alcohol consumption, and different activity patterns between genders (Lakbar et al., 2023).

The age distribution in this study showed the majority of patients were middle-aged (45-59 years), with 42 patients (38.5%), and elderly (≥60 years), with 41 patients (37.6%). These findings are consistent with previous research showing an average sepsis patient age of 67 years (Lindström et al., 2021). Other studies also indicate that most sepsis patients are over 50 years old (Kotfis et al., 2019). Risk factors for sepsis in older age include pre-existing comorbidities, immune dysfunction, decreased physiological reserves related to aging, and polypharmacy. Elderly patients experiencing immunosenescence or age-related immune decline are more susceptible to sepsis (Ibarz et al., 2024). Immune decline affects T-cell and B-cell function, resulting in less effective antibody responses to infection (Alhamyani et al., 2024). Single-cell analysis using scRNA-seq (single-cell RNA sequencing) and scTCR-seq (single-cell T-cell receptor sequencing) reveals various immunological abnormalities in this age group, including increased immune cell apoptosis, severe immune exhaustion, and excessive inflammation

exacerbated by inflammaging. Regulatory T cells (Tregs) show increased numbers and immunosuppressive activity, while CD8+ T cells experience significant depletion. Additionally, immune cell metabolic dysfunction, particularly in mitochondrial function, and increased lysine degradation pathways may contribute to immune dysfunction (He et al., 2024).

The study results also show pneumonia as the most common comorbidity with 27 cases (24.77%), followed by COVID-19 (Coronavirus) with 11 cases (10.09%). Pneumonia has been identified as the most frequent cause of sepsis (Gu et al., 2020). From 1999-2001, pneumonia accounted for 20.77% of all sepsis-related deaths, increasing to 27.63% during 2020-2022. Sepsis mortality rates rose by 30.22% from 2019-2021 due to the COVID-19 pandemic in the United States (Morrissey et al., 2025). Pneumonia and sepsis are two clinically important syndromes with significant global burden and complex pathophysiology. Pneumonia spreads through droplets or aerosols. Nasopharyngeal colonization is a prerequisite for infection. Extrapulmonary dissemination is worsened by immunosuppressive cytokines like IL-37, increasing sepsis risk. Sepsis-induced immunosuppression also facilitates secondary infections including pneumonia, particularly in patients with multi-organ dysfunction. Pneumonia can manipulate dendritic cells, allowing infection to spread from the lungs to systemic circulation (Darkwah et al., 2024).

The present study revealed that 69.7% of sepsis patients exhibited elevated lactate levels (>1.7 mmol/L). Clinically, lactate concentrations between 2-2.5 mmol/L are considered elevated, while levels exceeding 4 mmol/L are classified as high (Amit K et al., 2018). Lactate has been established as a more sensitive indicator of anaerobic metabolism and acidosis compared to blood pressure parameters (Lee et al., 2024). The underlying pathophysiology involves systemic microcirculatory disturbances leading to tissue hypoperfusion (dysoxia) and various metabolic derangements (Gattinoni et al., 2019). The inflammatory cascade in sepsis triggers the release of proinflammatory cytokines, nitric oxide, and lipopolysaccharides, resulting in cytopathic hypoxia and impaired pyruvate dehydrogenase complex function. These mechanisms contribute to mitochondrial dysfunction and subsequent pyruvate-to-lactate conversion (Dartiguelongue, 2024). The accumulation of lactate and protons in bodily fluids significantly worsens clinical outcomes (Ryoo and Kim, 2018).

This study found that the majority of sepsis patients (72.5%) had a hospital stay ≥3 days. Previous research using sepsis patient data from 2010-2016 in the United States reported an average ICU length of stay (LOS) of 5.1 days (Paoli et al., 2018). Compared to patients with other conditions, sepsis patients tend to experience prolonged hospitalization (Naqvi et al., 2022). In this study, most affected patients were elderly and middle-aged adults. The ≥ 3-day hospitalization predominantly occurred in 31 middle-aged and 28 elderly patients. This pattern may be attributed to the increased vulnerability of older patients to infections and sepsis due to immunosenescence (Rezar et al., 2023). Globally, 48.7% of sepsis patients with organ dysfunction experience prolonged hospitalization compared to non-sepsis patients (Markwart et al., 2020).

The mortality rate among sepsis patients in this study was 71.6%. Previous studies reported a 30-day sepsis mortality rate of 16.9% in Norway (Skei et al., 2023). The majority of deaths in our study occurred in middle-aged (30 patients) and elderly (30 patients) groups. Immunosenescence, characterized by cellular and humoral immune system decline, makes older adults more susceptible to severe

Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

infections and sepsis with worse clinical manifestations (Liu et al., 2022). Elderly patients in this study had at least two comorbidities, including both infectious and non-infectious conditions. Pneumonia was the most common comorbidity, with 18 deaths occurring among 27 affected patients (Martín et al., 2017). Immunosuppression has been significantly associated with sepsis mortality (Jiang et al., 2023).

The results of this study demonstrate a significant association between lactate levels and length of hospital stay (p=0.039). Further analysis revealed a relative risk (RR) of 2.015 (95% CI: 1.118-3.634), indicating that patients with lactate levels ≤1.7 mmol/L had twice the probability of experiencing hospitalization <3 days compared to those with levels >1.7 mmol/L. These findings align with previous research showing that suspected sepsis patients with lactate levels ≥2 mmol/L had an increased risk of prolonged ICU stay ≥72 hours (Shetty et al., 2018). Elevated lactate levels in sepsis result from microcirculatory disturbances leading to tissue hypoperfusion and hypoxia (Hernandez et al., 2019; Ward and Levy, 2017). A similar study in acute exacerbation of COPD patients with hypoxia found significantly prolonged hospitalization (p=0.001) in those with lactate levels 2-4 mmol/L (Sagmen and Naziroglu, 2020). However, these results contrast with findings from RSSA showing no correlation between lactate levels and length of stay (r=-0.346, p=0.298) (Pramadhani, 2019).

This study revealed that 19 patients (57.6%) with lactate levels ≤1.7 mmol/L still experienced prolonged hospitalization (≥3 days). While lower lactate levels typically correlate with less organ dysfunction, this finding may reflect delayed lactate elevation in early-stage disease. The low-lactate group also demonstrated delayed achievement of fluid resuscitation targets within the critical first 3-hour window. Elevated lactate levels (>1.7 mmol/L) serve as indicators of physiological distress and metabolic stress, resulting from enzymatic activation and tissue glycolysis combined with mitochondrial dysfunction (Dartiguelongue, 2024; He et al., 2022; Villar et al., 2019). Impaired hepatic and renal lactate clearance significantly contributes to extended hospital stays, highlighting the complex pathophysiology underlying sepsis-related outcomes (Donaliazarti, 2022; Hatman et al., 2021).

The results also showed a significant association between lactate levels and sepsis mortality (p=0.018). The relative risk (RR) was 2.159 (95% CI: 1.216-3.832), indicating patients with lactate ≤1.7 mmol/L had 2.159 times higher survival probability than those >1.7 mmol/L. These findings align with previous studies showing point-of-care lactate was associated with mortality in Thai sepsis patients (p=0.044) (Charoentanyarak et al., 2021). Other studies found that lactate ≥2 mmol/L increased in-hospital mortality risk (Shetty et al., 2018). While higher levels predicted greater short-term mortality (Villar et al., 2019). However, contrasting results from RSSA showed no correlation between lactate and mortality (r=0.018, p=0.917) (Pramadhani, 2019). Another study found no association between lactate 2-6 mmol/L and mortality (Driessen et al., 2018).

The study results demonstrated that 18 patients (54.5%) with lactate levels ≤1.7 mmol/L experienced mortality. Previous studies reported that in the low lactate group, factors such as high APACHEII II scores, elevated C-reactive protein (CRP), and chronic heart failure (CHF) independently influenced mortality rates (Oh et al., 2019). The 38.1% mortality rate in the low lactate group was primarily associated with inadequate fluid resuscitation volume (<30 ml/kg within 6 hours) (He et al., 2023). Admission lactate levels ≥8.0 mmol/L showed significant

correlation with mortality (Bernhard et al., 2020). While levels >4 mmol/L increased mortality risk by 33% (Deulkar et al., 2024). The pathophysiological mechanisms involve microcirculatory disturbances and mitochondrial dysfunction, which subsequently induce immunosuppression through M2 macrophage differentiation and increased myeloid-derived suppressor cells (MDSCs) (He et al., 2022; Hernandez et al., 2019; Nolt et al., 2018). These findings reinforce the recommendation to implement sepsis management according to the Hour-1 Bundle guidelines, which include lactate level monitoring.

This study has several limitations. First, its retrospective design limited the ability to control for confounding factors such as treatment variation, comorbid disease severity, and timing of antibiotic administration. Second, lactate measurements were taken only at admission, without serial follow-up, which restricts interpretation regarding lactate clearance dynamics. Third, this study was conducted in a single hospital, which may limit generalizability to other settings with different patient populations or clinical resources. Future research should employ a multicenter prospective design with serial lactate monitoring to better capture its temporal relationship with outcomes and to validate its prognostic value across diverse clinical contexts.

CONCLUSION AND RECOMMENDATION

This study highlights the critical role of lactic acid levels as prognostic indicators for sepsis outcomes in intensive care units. Elevated lactate levels were significantly associated with longer hospitalization and higher mortality among sepsis patients. The findings reaffirm the importance of lactate monitoring in sepsis management and underscore the necessity of early recognition and timely interventions. From a nursing perspective, continuous patient monitoring, early detection of deterioration, and adherence to evidence-based protocols are crucial to optimizing outcomes.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the University of Jember and Dr. Soebandi Hospital for providing the facilities and institutional support essential for this research. We are deeply indebted to our academic advisors for their expert guidance, critical feedback, and invaluable mentorship throughout this study. Finally, we extend our heartfelt appreciation to our families and friends for their unwavering support and encouragement during the completion of this work.

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Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

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Article History:
Received: September 11, 2025; Revised: October 28, 2025; Accepted: March 2, 2026

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