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Cross-Sectional Study

Syndecan-1 as a predictive biomarker for lung injury in mechanically ventilated pneumonia patients: a cross-sectional study

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ABSTRACT

Pneumonia remains a major global health challenge, with significant mortality rates and complications such as acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). In severe cases, mechanical ventilation becomes essential for managing respiratory failure but can also worsen lung injury through ventilator-induced lung injury (VILI). During lung injury, such as in severe pneumonia, Syndecan-1 (SDC-1) is shed from the cell surface into circulation and the alveolar space. Elevated SDC-1 levels have been associated with the severity of lung injury, making it a potential biomarker for assessing disease progression and guiding treatment strategies. The purpose of this study is to look into the potential of SDC-1, a glycocalyx component, as a predictive biomarker for lung damage severity in pneumonia patients requiring mechanical ventilation. Bronchoalveolar lavage (BAL) samples were obtained from 30 patients in an Intensive Care Unit (ICU), and SDC-1 levels were determined using ELISA. Elevated SDC-1 levels were associated with greater Lung Injury Scores (LIS) and severe hypoxemia ($p < 0.001$). Patients with severe lung injury had significantly greater SDC-1 levels than those with mild-to-moderate injury, indicating that SDC-1 reflects the severity of alveolar epithelial damage and impeded gas exchange. These data suggest that SDC-1 might be a useful biomarker for tracking lung damage development and directing treatment therapies in mechanically ventilated pneumonia patients.

Keywords: Biomarkers, Bronchoalveolar Lavage fluid, Mechanical ventilator, Pneumonia, Syndecan-1

Introduction

Data from the Global Burden of Disease (GBD) study in 2019 shows that the global incidence of lower respiratory infections, including pneumonia, reached 489 million cases [1]. Indonesia has one of the highest pneumonia mortality rates in Southeast Asia, with adult cases showing a mortality rate of up to 11.3% [2]. Given its high incidence and mortality, pneumonia often leads to severe complications such as acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), both of which can dramatically worsen patient outcomes. ALI can manifest through several pathological patterns, including diffuse alveolar damage (DAD), organizing pneumonia (OP), and acute eosinophilic pneumonia (AEP). DAD causes extensive damage to the alveolar epithelium and endothelium, resulting in increased permeability, pulmonary edema, and decreased gas exchange, which is sometimes visible as ground-glass opacification and hyaline membrane development [3].

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ALI in pneumonia is primarily caused by microbial invasion, aggravated by the host's immune response, which leads to inflammation and lung parenchymal damage. This triggers the release of inflammatory mediators, increases permeability, and causes alveolar exudation, leading to hypoxemia and, in severe cases, ARDS or multi-organ failure. Mechanical ventilation, while essential for managing respiratory failure, can exacerbate lung injury through ventilator-induced lung injury (VILI) by causing barotrauma and biotrauma [4]. Studies have shown that prolonged mechanical ventilation not only increases the risk of pneumonia but also leads to worse clinical outcomes, including longer Intensive Care Unit (ICU) stays and higher mortality rates [5]. In pneumonia patients, VILI increases the risk of ARDS and worsens outcomes. Studies have shown that mechanical ventilation can exacerbate endothelial injury, leading to increased levels of Syndecan-1 (SDC-1) in circulation. Elevated serum SDC-1 levels have been found to correlate with the severity of conditions like COVID-19, suggesting that SDC-1 shedding can serve as a useful biomarker for monitoring disease progression and treatment efficacy [6]. Furthermore, glycocalyx degradation, including the loss of SDC-1, is frequently observed in inflammatory states such as sepsis and ARDS [7]. This degradation is thought to be mediated by inflammatory proteases, which are elevated in critically ill patients, further linking mechanical ventilation to endothelial dysfunction [7].

Similarly, in pneumonia, particularly in severe cases requiring mechanical ventilation, SDC-1 shedding is linked to extensive alveolar and endothelial injury. The severity of lung injury can be assessed using scoring systems such as the Lung Injury Score (LIS), which evaluates clinical and radiological parameters, with higher scores indicating more severe injury [8]. In pneumonia, bronchoalveolar lavage fluid (BALF) analysis is a powerful tool for accurately identifying pathogens, guiding treatment, and reflecting inflammatory activity indicative of underlying pathology [9].

The alveolar epithelium plays an important role in gas exchange by maintaining barrier integrity via glycocalyx components such as SDC-1; however, during pulmonary inflammation, this integrity is impaired, resulting in SDC-1 shedding into the alveolar space [10]. While most studies concentrate on plasma levels of SDC-1, which might be altered by comorbidities, research on alveolar shedding is limited [8]. Understanding SDC-1's involvement in lung damage might help improve early detection, predict disease progression, and guide targeted therapies. This study will look at whether SDC-1 may be used as a biomarker to measure lung damage severity in pneumonia patients requiring mechanical ventilation.

Materials and Methods

Study design and setting

This cross-sectional observational analytic study was conducted in the ICU of dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from September to December 2023. The study population consisted of pneumonia patients on mechanical ventilation, with samples selected based on inclusion and exclusion criteria. Consecutive sampling was applied, and data were collected within the first 72 hours following the indication for bronchoscopy, a minimum sample size of 30 determined through standard statistical methods. There was no follow-up period, focusing on a one-time measurement of SDC-1 levels and corresponding lung injury severity at the time of sampling.

Study participants

The study population comprised pneumonia patients on mechanical ventilation admitted to the ICU at Dr. Soetomo General Academic Hospital. This study uses inclusion and exclusion criteria to minimize selection bias. The inclusion criteria consisted of pneumonia patients on mechanical ventilation in the ICU who required bronchoscopy. Additionally, informed consent had to be obtained from the patients' families or legal guardians. Exclusion criteria are patients with other pulmonary conditions such as COVID-19 pneumonia, pulmonary tuberculosis, lung cancer, pulmonary trauma, cardiogenic pulmonary edema, or ARDS. The sample size was calculated using the following formula:

$$n = \{(Z1 - alfa/2 + Z1 - beta) / 1/2\, loge\, (1 + r / 1 - r)\}2 + 3 \quad (1)$$

This calculation resulted in 30 patients who were selected through consecutive sampling. Ethical approval was obtained from the Ethical Committee of Dr. Soetomo Academic General Hospital, Surabaya, Indonesia (0770/KEPK/IX/2023). The patients provided their signed informed consent prior to the study.

Study variables

The study variables included independent, dependent, and intermediary factors. The independent variable was the analysis of SDC-1 levels in BALF from pneumonia patients on mechanical ventilation. The dependent variable was the severity of pneumonia. The intermediary variables encompassed the patient's identity, vital signs, comorbidities, supporting clinical examinations, and the LIS. SDC-1 levels were measured from BALF using an enzyme-linked immunosorbent assay (ELISA) kit, ensuring precise quantification. Lung injury severity, the primary outcome, was assessed using the Lung Injury Score (LIS), which incorporated oxygenation, chest X-ray, Positive End-Expiratory Pressure (PEEP), and compliance data. Demographic and clinical variables, such as age, gender, comorbidities, and vital signs, were collected from patient records and standardized clinical examinations.

Measurement of biomarker

BAL samples were obtained during the first three days of hospitalization from intubated pneumonia patients in the intensive care unit (ICU) by bronchoscopy for this investigation [11-13]. After inserting the bronchoscope into the airways and

instilling a sterile 0.9% NaCl solution, around 10–20 ml of BALF was aspirated and kept at -20°C until analysis. The soluble SDC-1 levels in the BALF were determined using an ELISA kit from Elabscience, USA, after the BAL samples were sent in styrofoam boxes with dry ice to the Clinical Pathology Laboratory at RSUD Dr. Soetomo, Surabaya. Since SDC-1 is released into the BALF after lung injury, this technique yielded accurate SDC-1 values that gave information on the degree of lung epithelial damage in pneumonia patients [14-16].

Statistical analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Quantitative variables, such as SDC-1 levels and LIS, were analyzed using descriptive statistics. Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were presented as means with standard deviations, while non-normally distributed data were reported as medians and ranges. For comparisons, the patients were grouped based on the severity of lung injury (mild-to-moderate vs. severe), with the grouping chosen to explore the relationship between SDC-1 levels and the extent of lung damage. A significance level of $p < 0.05$ was considered statistically significant. The correlation between SDC-1 levels and LIS was analyzed using Spearman's rank correlation.

Results and Discussion

The study included 30 patients diagnosed with pneumonia and requiring mechanical ventilation in the ICU at RSUD dr. Soetomo, Surabaya. The study spanned from September to December 2023. The patient's demographic and clinical characteristics are summarized in **Table 1**.

Table 1. Degree of LIS and SDC-1 Levels Based on Study Subject Characteristics.

Variable	Value, n (%)	Degree of Lung Injury Based on LIS		p	SDC-1 Levels		p
		Mild-moderate, n (%)	Severe, n (%)		*Low,* n (%)	*High,* n (%)	
Gender							
Male	17 (56,7)	14 (58,3)	3 (50)	1,000	14 (58,3)	3 (50)	1,000
Female	13 (43,3)	10 (41,7)	3 (50)		10 (41,7)	3 (50)	
Age (years)	50,8 ± 18,04						
18 – 20	1 (3,3)	1 (4,2)	0 (0)		1 (4,2)	0 (0)	
21 – 30	6 (20,0)	3 (12,5)	3 (50)		3 (12,5)	3 (50)	
31 – 40	2 (6,7)	1 (4,2)	1 (16,7)	0,128	1 (4,2)	1 (16,7)	0,128
41 – 50	4 (13,3)	4 (16,7)	0 (0)		4 (16,7)	0 (0)	
51 – 60	7 (23,3)	6 (25)	1 (16,7)		6 (25)	1 (16,7)	
≥61	10 (33,3)	9 (37,5)	1 (16,7)		9 (37,5)	1 (16,7)	
Body Mass Index/BMI (kg/m^2)	24,04 ± 4,05						
<18,50	1 (3,3)	1 (4,2)	0 (0)		1 (4,2)	0 (0)	
18,50 – 24,99	18 (60)	13 (54,2)	5 (83,3)	0,495	13 (54,2)	5 (83,3)	0,495
25,0 – 29,99	8 (26,7)	8 (33,3)	0 (0)		8 (33,3)	0 (0)	
30,0 – 34,9	3 (10)	2 (8,3)	1 (16,7)		2 (8,3)	1 (16,7)	
Comorbidities*							
None	3 (10)	1 (4,2)	2 (33,3)		1 (4,2)	2 (33,3)	
Present:	27 (90)	23 (95,8)	4 (66,7)		23 (95,8)	4 (66,7)	
Hypertension	6 (20)	5 (20,8)	1 (16,6)		5 (20,8)	1 (16,7)	
Diabetes mellitus	6 (20)	4 (16,7)	2 (33,3)		4 (16,7)	2 (33,3)	
Heart failure	2 (6,7)	1 (4,2)	1 (16,7)	0,094	1 (4,2)	1 (16,7)	0,094
Chronic kidney failure	3 (10)	2 (8,3)	1 (16,7)		2 (8,3)	1 (16,7)	
Stroke	7 (23,3)	6 (25)	1 (16,7)		6 (25)	1 (16,7)	
Neuromuscular disorder	10 (33,3)	8 (33,3)	2 (33,3)		8 (33,3)	2 (33,3)	
Pleura disorder (effusion)	6 (20)	4 (16,7)	2 (33,3)		4 (16,7)	2 (33,3)	
Other	3 (10)	3 (12,5)	0 (0)		3 (12,5)	0 (0)	
Other Risk Factors for Pneumonia*							
Not present	7 (23,3)	7 (29,2)	0 (0)		7 (29,2)	0 (0)	
Present:	23 (76,7)	17 (70,8)	6 (100)		17 (70,8)	6 (100)	
Smoking	1 (3,3)	1 (4,2)	0 (0)		1 (4,2)	0 (0)	
Decreased consciousness (not due to sedation)	12 (40)	11 (45,8)	1 (16,7)	0,290	11 (45,8)	1 (16,7)	0,290
Seizures	1 (3,3)	1 (4,2)	0 (0)		1 (4,2)	0 (0)	
Vomiting	2 (6,7)	1 (4,2)	1 (16,7)		1 (4,2)	1 (16,7)	
Choking	4 (13,3)	3 (12,5)	1 (16,7)		3 (12,5)	1 (16,7)	
Prolonged immobilization	12 (40)	9 (37,5)	3 (50)		9 (37,5)	3 (50)	
Used NGT or ETT	10 (33,3)	8 (33,3)	2 (33,3)		8 (33,3)	2 (33)	
Pneumonia Diagnosis							
CAP	13 (43,3)	10 (41,7)	3 (50)	0,825	10 (41,7)	3 (50)	0,825
HAP	9 (30,0)	7 (29,2)	2 (33,3)		7 (29,2)	2 (33,3)	
VAP	8 (26,7)	7 (29,2)	1 (16,7)		7 (29,2)	1 (16,7)	

*) Each study subject may have more than one comorbidity or risk factor

The majority of the patients were male (56.7%), and the mean age was 50.8 ± 18.04 years. Most patients were aged 51 years or older, with the highest proportion (33.3%) in the ≥61 years age group. The mean body mass index (BMI) was 24.04 ± 4.05 kg/m², with most patients having a normal BMI (18.50-24.99 kg/m², 60%). Comorbid conditions were prevalent among the study population, with 90% of patients having at least one comorbidity. Neuromuscular disorders (33.3%) and stroke (23.3%) were the most common comorbidities. Other significant risk factors for pneumonia included impaired consciousness (40%), prolonged immobilization (40%), and long-term use of nasogastric or endotracheal tubes (33.3%). The types of pneumonia diagnosed were community-acquired pneumonia (CAP) in 43.3%, hospital-acquired pneumonia (HAP) in 30%, and ventilator-associated pneumonia (VAP) in 26.7% of the patients. No significant differences in LIS were observed across various demographic or clinical variables, including gender, age, BMI, presence of comorbidities, or type of pneumonia ($p > 0.05$). However, severe lung injury was more frequently observed in younger patients (21-30 years), those with normal BMI, and those with comorbid conditions and additional pneumonia risk factors.

The box plot in **Figure 1** shows that most subjects have consistent SDC-1 levels in BAL fluid, with a tight distribution around the median. However, the outliers indicate that a few subjects have significantly higher SDC-1 levels, suggesting more severe lung injury.

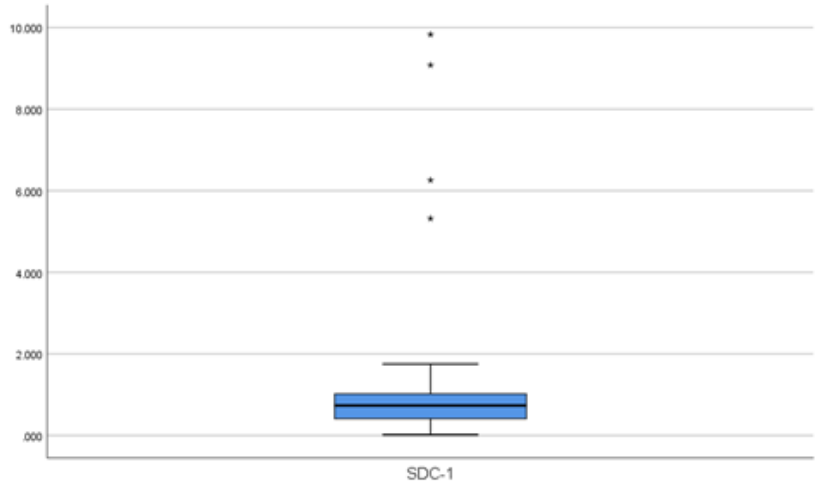

Figure 1. The distribution of soluble epithelial SDC-1 values (ng/mL) in the BAL of the study subjects.

SDC-1 concentrations in BALF were measured in **Table 2** to assess their potential role as biomarkers for pneumonia severity. The LIS was used to evaluate the severity of lung injury in the study subjects. Most patients (80%) fell into the mild to moderate lung injury category (LIS 1-2.5). Patients with severe lung injury (LIS >2.5) had markedly higher SDC-1 levels (mean 5.61 ng/mL, range 1.42-9.83 ng/mL).

Table 2. Degree of Lung Injury in Study Subjects Based on LIS.

LIS Category	SDC-1 (ng/mL)				
	n (%)	Range	Mean	Median	Standard Deviation
Mild-moderate (1-2,5 points)	24 (80)	0,02-1,15	0,59	0,58	0,33
Severe (>2,5 points)	6 (20)	1,42-9,83	5,61	5,79	3,54
Total	30 (100)	0,02-9,83	1,60	0,74	2,53

The receiver operating characteristic (ROC) curve in **Figure 2** demonstrates that SDC-1 levels accurately differentiate between different degrees of lung injury, with an AUC of 1.000 and both sensitivity and specificity at 100%. This suggests that SDC-1 is a reliable biomarker for assessing lung injury severity in the study population.

The cut-off value of 1.15 ng/mL for high SDC-1 concentration was established using ROC curve analysis, highlighting its strong diagnostic potential in lung injury assessment. At this threshold, the biomarker demonstrates 100% sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

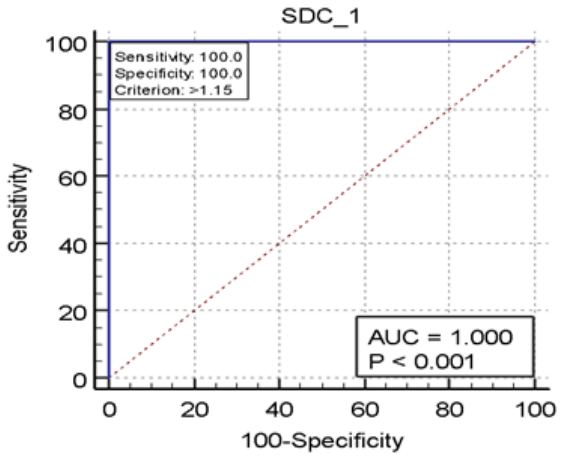

Figure 2. The ROC curve is based on the distribution of SDC-1 values in relation to the degree of LIS among the study subjects.

In this investigation, a high SDC-1 concentration was defined as >1.15 ng/mL. The Shapiro-Wilk test resulted in a p-value < 0.05, suggesting that the SDC-1 data was not regularly distributed. The relationship between SDC-1 and LIS was investigated using Spearman's Rho and Chi-square tests. A Spearman's rank correlation analysis of SDC-1 concentrations and LIS scores reveals a significant association (rs = 0.429, p = 0.018), implying that higher SDC-1 concentrations are related with greater lung damage severity. **Figure 3's** curve fit correlation indicates a positive association between SDC-1 levels in BAL fluid and LIS, showing that greater SDC-1 levels are linked with more serious lung damage.

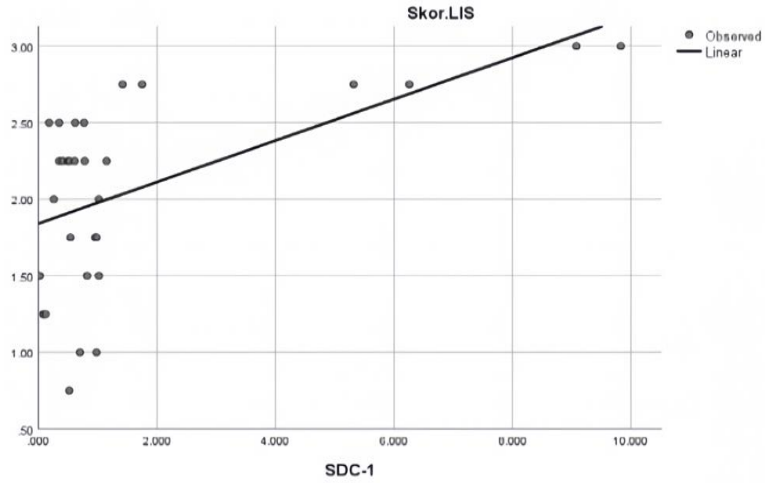

Figure 3. Curve fit correlation of the distribution of soluble epithelial alveolar SDC-1 values in BAL and LIS values.

The chi-square test in **Table 3** revealed a significant link between SDC-1 levels and LIS severity (p < 0.001). All subjects with severe LIS had high SDC-1 levels, while those with mild-moderate LIS had low levels. This result also demonstrates a significant correlation between LIS severity and SDC-1 levels in BALF, as determined by the Mann-Whitney test (p < 0.001). All subjects with severe LIS exhibited elevated SDC-1 levels, while those with mild to moderate LIS had lower SDC-1 levels. Additionally, significant correlations were observed for the PaO2/FiO2 (P/F) ratio (p = 0.005) and PEEP (p = 0.007), whereas no significant associations were found for chest X-ray (p = 0.059) or Cstat (p = 0.163). These findings suggest that SDC-1 is strongly associated with certain components of lung injury severity.

Table 3. Correlation of LIS and Soluble Alveolar Epithelial SDC-1 in BAL Fluid

Parameter		n	SDC-1 BAL		p
			Low, n (%)	*High*, n (%)	
LIS Category	Mild-moderate	24	24 (100)	0	<0,001
	Severe	6	0	6 (100)	
LIS components Chest x-ray	1	7	7 (100)	0	0,059
	2	8	7 (87,5)	1 (12,5)	
	3	15	10 (66,7)	5 (33,3)	

P/F ratio	0	3	3 (100)	0	0,005
	1	8	8 (100)	0	
	2	2	2 (100)	0	
	3	15	11 (73,3)	4 (26,7)	
	4	2	0	2 (100)	
PEEP	0	9	9 (100)	0	0,007
	1	17	14 (82,4)	3 (17,6)	
	2	4	1 (25)	3 (75)	
Cstat	1	1	1 (100)	0	0,163
	2	6	6 (100)	0	
	3	9	7 (77,8)	2 (22,2)	
	4	14	10 (71,4)	4 (28,6)	

People with risk factors are more susceptible to pneumonia. In this study, the highest number of cases was found in subjects aged ≥61 years (33.3%), which aligns with existing literature showing that pneumonia risk increases with age. This includes diminished function of dendritic cells and T cells, thymic involution, reduced immune cell regeneration, and heightened inflammation (inflammaging), all of which impair the body's ability to fight infection and respond to vaccination [17]. Studies have shown that older patients, particularly those over the age of 75, exhibit higher mortality rates when suffering from severe pneumonia. This increased vulnerability is attributed to the age-related decline in immune function, which can exacerbate the severity of lung injury and complicate recovery [18]. While age is a significant factor, gender also influences pneumonia risk. This comprehensive review reinforces the conclusion that females benefit from genetic and epigenetic mechanisms such as X Chromosome Inactivation (XCI) escape and microRNA (miRNA) abundance, which enhance immune efficacy. In contrast, males face vulnerabilities due to loss of the Y (LOY) chromosome, limited X-linked gene dosage, and lower miRNA diversity [19]. These disparities underlie the higher rates of infections and worse outcomes in males [20]. Supporting this theory, this study found more male cases (56.7%) than female [21]. In addition, BMI may influence pneumonia outcomes, although the relationship is not linear and can depend on individual health profiles [22, 23]. One study found that low BMI is a critical characteristic among older adults with aspiration pneumonia, where it was associated with poorer outcomes. The study provides both statistical and pathophysiological reasoning that low BMI, as a marker of malnutrition and frailty, impairs resilience and recovery, thereby increasing the mortality risk in aspiration pneumonia patients [24]. Conversely, obesity can reduce lung volumes and impair respiratory mechanics, complicating pneumonia management [25]. These findings contrast with most patients in this study, who had a normal BMI, suggesting that other factors, such as comorbidities, may play a larger role in increasing pneumonia risk. In this study, 90% of subjects had comorbid conditions, with neuromuscular disorders like stroke being the most common. Neuromuscular diseases increase pneumonia risk by impairing cough and swallowing, leading to secretion retention and aspiration from weakened respiratory muscles [26]. Chronic conditions like Chronic Obstructive Pulmonary Disease (COPD), stroke, and hypertension weaken the immune response, making it harder for the body to fight infections [27]. Moreover, additional factors such as long-term immobility and impaired consciousness further increase the risk of pneumonia, particularly through aspiration. In this study, 43.3% of subjects were diagnosed with CAP, which is consistent with previous studies showing that CAP is the most common type of pneumonia across different populations, such as the United States and Sweden [28].

In a study involving murine models, it was demonstrated that pneumonia infection led to significant lung injury, as evidenced by increased levels of BAL albumin, indicating disruption of the alveolar-capillary barrier [29]. The LIS scoring system has been widely utilized in clinical studies to evaluate the severity of lung injury and predict patient outcomes [30]. Higher LIS scores indicate more severe lung damage, incorporating factors like oxygenation, chest radiology, PEEP, and lung compliance, making it superior to the Berlin criteria, which omits some key variables [31]. Studies have shown LIS can predict intubation duration and severity in ALI patients [32, 33].

In this study, the ROC curve indicated a cut-off of >1.15 ng/mL for high SDC-1 levels, correlating with severe alveolar epithelial damage. Streptococcus pneumoniae induces significant deoxyribonucleic acid (DNA) damage and apoptosis in lung epithelial cells, which could be associated with increased SDC-1 levels due to cellular stress and injury. This damage sets the stage for further complications, as SDC-1 promotes lung fibrosis by facilitating epithelial reprogramming through extracellular vesicles, significantly impacting alveolar epithelial cells (AECs) [34]. Aberrant expression of SDC-1 in alveolar type II (ATII) cells can lead to their dysfunction, contributing to the fibrotic process and subsequent damage to the alveolar epithelium [35]. Furthermore, the damage to alveolar epithelial cells is not only a consequence of SDC-1 elevation but also a driver of inflammatory responses, with damaged AECs secreting pro-inflammatory cytokines such as Interleukin-6 (IL-6) and Tumor Necrosis Factor Alpha (TNF-α), exacerbating lung inflammation and injury [36].

In line with these findings, a significant correlation was identified between elevated soluble SDC-1 levels in BALF and pneumonia severity as measured by LIS scores ($p < 0.001$). All patients with severe pneumonia had high SDC-1 levels, aligning with prior research, which found that the shedding of SDC-1 from the endothelial glycocalyx, induced by lipopolysaccharide (LPS), has

been associated with increased lung edema and inflammatory cell infiltration [37]. The inflammatory response triggered by LPS is characterized by the activation of various signaling pathways, including the Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, which is known to mediate the expression of pro-inflammatory cytokines and further exacerbate lung injury [38]. The resultant inflammatory milieu not only enhances the permeability of the alveolar-capillary barrier but also leads to apoptosis of alveolar epithelial cells, contributing to diffuse alveolar damage (DAD) [39]. Syndecan-1 sheds into the bloodstream due to endothelial glycocalyx degradation, which results from endothelial dysfunction caused by inflammatory mediators like IL-6, high-mobility group box 1 (HMGB1), histone-complexed DNA fragments, soluble thrombomodulin (sTM), and protein C, released during a systemic inflammatory response triggered by trauma [40].

The relationship between SDC-1 and alveolar epithelial damage is further underscored by its role in modulating inflammatory responses and maintaining epithelial barrier function, which is critical in preventing further lung injury [41].

However, despite the strong link between SDC-1 and alveolar damage, there was no significant correlation between SDC-1 levels and radiological findings (p 0.059). This result is supported by studies indicating that although SDC-1 levels are linked to respiratory disorders, they do not always correspond to radiological severity in conditions like pneumonia [6].

In contrast to the lack of correlation with radiological findings, a strong association was found between hypoxemia severity, as indicated by lower P/F ratios, and elevated SDC-1 levels (p 0.005), which is consistent with previous research suggesting That SDC-1 contributes to impaired gas exchange by compromising alveolar integrity. This link reflects the growing severity of pneumonia, as increased SDC-1 shedding corresponds to decreased oxygenation status [40]. This data is consistent with findings from earlier research that show SDC-1 is much higher in patients with severe lung diseases, such as pneumonia, and represents the amount of endothelium damage and inflammation [42]. This study found that higher soluble SDC-1 levels are highly associated with hypoxemia severity in pneumonia patients, highlighting SDC-1's potential as a reliable biomarker for lung damage.

This research found a clear association between SDC-1 levels and clinical severity, as measured by LIS and oxygenation status, which provides valuable insights for assessing disease progression. This study found that SDC-1 levels in BAL fluid were significantly correlated with the severity of lung injury in pneumonia patients requiring mechanical ventilation. Higher SDC-1 levels were associated with more severe lung injury, as measured by the LIS, supporting the hypothesis that SDC-1 is a reliable biomarker for assessing lung damage in this patient population. This makes SDC-1 a promising tool for guiding clinical decisions and optimizing management strategies in patients with severe pneumonia [43-45].

Conclusion

This study found that increased levels of soluble Syndecan-1 (SDC-1) in bronchoalveolar lavage fluid (BALF) are substantially linked with the severity of lung damage in mechanically ventilated pneumonia patients. A substantial association was found between high SDC-1 levels and an elevated Lung Injury Score (LIS), as well as severe hypoxemia, suggesting that SDC-1 represents the amount of alveolar epithelial injury and poor gas exchange. The established threshold value of >1.15 ng/mL for SDC-1 revealed outstanding diagnostic performance, with 100% sensitivity and specificity in detecting severe lung damage. These data confirm SDC-1's clinical use as a reliable, non-invasive biomarker for predicting lung damage progression and guiding treatment options in critical care settings [46-48]. Monitoring alveolar SDC-1 concentrations may assist physicians in stratifying risk, assessing disease progression, and implementing prompt therapies in patients with severe pneumonia needing mechanical ventilation. Future research with bigger sample numbers and longer follow-up is needed to verify these findings and investigate the predictive usefulness of SDC-1 in broader populations and diverse pneumonia subtypes.

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Conflict of interest: None

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References

1. Torres A, Cilloniz C, Niederman MS, Menéndez R, Chalmers JD, Wunderink RG, et al. Pneumonia. Nat Rev Dis Primers. 2021;7:25.
2. Bramantono B, Rachman BE, Marfiani E, Kurniati ND, Arifijanto MV, Jearanaiwitayakul T. The bacterial pneumonia characteristics based on climate and meteorological parameters in Indonesia, the tropical country: a preliminary study. Biomol Health Sci J. 2021;4:15.

3. Sakla NM, Gattu R, Singh G, Sadler M. Vaping-associated acute respiratory distress syndrome. Emerg Radiol. 2020;27:103-6.
4. Nugent K, Berdine G. Mechanical power during mechanical ventilation. Southwest Respir Crit Care Chron. 2024;12:16-23.
5. Rautaporras N, Furuholm J, Uittamo J, Saloniemi M, Puolakka T, Snäll J. Deep odontogenic infections—identifying risk factors for nosocomial pneumonia. Clin Oral Investig. 2021;25:1925-32.
6. Ogawa F, Oi Y, Nakajima K, Matsumura R, Nakagawa T, Miyagawa T, et al. Temporal change in syndecan-1 as a therapeutic target and a biomarker for the severity classification of COVID-19. Thromb J. 2021;19:55.
7. Hayashi K, Koyama D, Hamazaki Y, Kamiyama T, Yamada S, Furukawa M, et al. Syndecan-1 as a prognostic biomarker in COVID-19 patients: a retrospective study of a Japanese cohort. Thromb J. 2024;22:52.
8. Abdelhamid WG, Salah Eldin HM, Abd-Elkarim MA, Abd El Messih MS. Prognostic value of clinical scores, pentraxin3 and C-reactive protein in toxin-related acute lung injury and acute respiratory distress syndrome. Egypt J Forensic Sci Appl Toxicol. 2017;17:93-115.
9. Zhao J, Zhuge R, Hu B, Wang Y, Wang X, Zhang Y, et al. Clinical impact of bronchoalveolar lavage fluid metagenomic next-generation sequencing in immunocompromised patients with severe community-acquired pneumonia in ICU: a multicenter retrospective study. Infection. 2025:1-7.
10. Zhang D, Zhang JT, Pan Y, Liu XF, Xu JW, Cui WJ, et al. Syndecan-1 shedding by matrix metalloproteinase-9 signaling regulates alveolar epithelial tight junction in lipopolysaccharide-induced early acute lung injury. J Inflamm Res. 2021;14:5801-16.
11. Chidambaranathan AS, Culathur T. A prospective clinical study to evaluate the effectiveness of acupuncture treatment for temporomandibular joint muscular disorder. Ann Dent Spec. 2022;10(1):34-8. doi:10.51847/172V2CMsF3
12. Al-Mubarak AM, Alkhaldi FA, Alghamdi AA, Almahmoud MA, Alghamdi FA. Dental students and interns' clinical knowledge toward crown lengthening; a cross-sectional study. Ann Dent Spec. 2023;11(2):75-83. doi:10.51847/2cisEzAkOG
13. AlHussain BS, AlFantoukh MAM, Alasmari KMA, AlHrab FA, Alotaibi FA, Alaybani WH, et al. Clinical knowledge of orthodontics complication and emergencies among interns and dentists in Riyadh City. Ann Dent Spec. 2022;10(2):45-51. doi:10.51847/9H6hhUJo8E
14. Tsekhmister Y, Konovalova T, Bashkirova L, Savitskaya M, Tsekhmister B. Virtual Reality in EU Healthcare: empowering patients and enhancing rehabilitation. J Biochem Technol. 2023;14(3):23-9. doi:10.51847/r5WJFVz1bj
15. Enwa FO, Egbule OS, Oyubu LO, Damera CN, Momoh TO. Characterization of methicillin-resistant Staphylococcus aureusfrom adult out-patients visiting Delta State University Teaching Hospital, Oghara. J Biochem Technol. 2023;14(4):15-8. doi:10.51847/I5U79fysvK
16. Benhmida S, Trabelsi H. Fatty acid composition in bone fluid from knee osteoarthritis patients. J Biochem Technol. 2024;15(2):23-6. doi:10.51847/UNhuTqup51
17. Kang N, Subramanian VS, Agrawal A. Influence of aging and immune alterations on susceptibility to pneumococcal pneumonia in the elderly. Pathogens. 2025;14(1):41.
18. Deng Y, Chen L, Yue M, Huang X, Yang Y, Yu H. Sulbactam combined with tigecycline improves outcomes in patients with severe multidrug-resistant Acinetobacter baumannii pneumonia. BMC Infect Dis. 2022;22:795.
19. Feng Z, Liao M, Zhang L. Sex differences in disease: sex chromosome and immunity. J Transl Med. 2024;22(1):1150.
20. Eteng OE, Bassey N, Eteng EI, Okwe EP, Ekpo G, Ekam V, et al. Effect of vanillic acid and morin on bisphenol s and diethyl phthalate induce-nephrotoxicity in male rats. Bull Pioneer Res Med Clin Sci. 2023;2(1):25-34. doi:10.51847/JipHmYy6fi
21. Enwa FO, Jewo AO, Oyubu LO, Adjekuko CO, Effiong V. Incidence of vaginal infections among females of different age categories in Delta State, Nigeria. Bull Pioneer Res Med Clin Sci. 2022;1(1):18-23. doi:10.51847/C1oahQ115n
22. İlhan N, Telli S, Temel B, Aştı T. Investigating the sexual satisfaction mediating role in the relationship between health literacy and self-care of men with diabetes and women's marital satisfaction. J Integr Nurs Palliat Care. 2022;3:19-25. doi:10.51847/sFjL3OLpqg
23. Yoong SQ, Wang W, Seah ACW, Kumar N, Gan JON, Schmidt LT, et al. Study of the self-care status and factors related to it in heart failure patients. J Integr Nurs Palliat Care. 2022;3:31-5. doi:10.51847/Lqz1ms7fB8
24. Cherchi C, Chiarini Testa MB, Deriu D, Schiavino A, Petreschi F, Ullmann N, et al. All you need is evidence: What we know about pneumonia in children with neuromuscular diseases. Front Pediatr. 2021;9:625751.
25. Wang N, Liu BW, Ma CM, Yan Y, Su QW, Yin FZ. Influence of overweight and obesity on the mortality of hospitalized patients with community-acquired pneumonia. World J Clin Cases. 2022;10:104-16.
26. Yıldızeli ŞO. Determinants of hospital stay, mortality, and readmission in aspiration pneumonia patients. Eur J Geriatr Gerontol. 2024;6:171-7.
27. Quinton LJ, Walkey AJ, Mizgerd JP. Integrative physiology of pneumonia. Physiol Rev. 2018;98:1417-64.
28. Roh EJ, Lee MH, Lee JY, Kim HB, Ahn YM, Kim JK, et al. Analysis of national surveillance of respiratory pathogens for community-acquired pneumonia in children and adolescents. BMC Infect Dis. 2022;22:330.
29. Lin CM, Alrbiaan A, Odackal J, Zhang Z, Scindia Y, Sung S-SJ, et al. Circulating fibrocytes traffic to the lung in murine acute lung injury and predict outcomes in human

acute respiratory distress syndrome: a pilot study. Mol Med. 2020;26:52.
30. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci. 2020;63:364-74.
31. Santos RS, Silva PL, Rocco JR, Pelosi P, Rocco PRM. A mortality score for acute respiratory distress syndrome: predicting the future without a crystal ball. J Thorac Dis. 2016;8:1872-6.
32. Bakhtiar A, Maranatha RA. Acute respiratory distress syndrome. J Respirasi. 2018;4:51.
33. Kangelaris K, Calfee CS, May AK, Zhuo H, Matthay MA, Ware LB. Is there still a role for the lung injury score in the era of the Berlin definition ARDS? Ann Intensive Care. 2014;4:4.
34. Parimon T, Yao C, Habiel DM, Ge L, Bora SA, Brauer R, et al. Syndecan-1 promotes lung fibrosis by regulating epithelial reprogramming through extracellular vesicles. JCI Insight. 2019;5(17):e129359.
35. Correll KA, Edeen KE, Zemans RL, Redente EF, Serban KA, Curran-Everett D, et al. Transitional human alveolar type II epithelial cells suppress extracellular matrix and growth factor gene expression in lung fibroblasts. Am J Physiol Lung Cell Mol Physiol. 2019;317:L283-94.
36. Mills JT, Schwenzer A, Marsh EK, Edwards MR, Sabroe I, Midwood KS, et al. Airway epithelial cells generate pro-inflammatory tenascin-C and small extracellular vesicles in response to TLR3 stimuli and rhinovirus infection. Front Immunol. 2019;10:1987.
37. Huang X, Han S, Liu X, Wang T, Xu H, Xia B, et al. Both UFH and NAH alleviate shedding of endothelial glycocalyx and coagulopathy in LPS induced sepsis. Exp Ther Med. 2019;19(2):913-22.
38. Cui H, Zhang Q. Dexmedetomidine ameliorates lipopolysaccharide-induced acute lung injury by inhibiting the PI3K/Akt/FoxO1 signaling pathway. J Anesth. 2021;35:394-404.
39. Huang CY, Deng JS, Huang WC, Jiang WP, Huang GJ. Attenuation of lipopolysaccharide-induced acute lung injury by hispolon in mice, through regulating the TLR4/PI3K/Akt/mTOR and Keap1/Nrf2/HO-1 pathways, and suppressing oxidative stress-mediated ER stress-induced apoptosis and autophagy. Nutrients. 2020;12:1742.
40. Suzuki K, Okada H, Sumi K, Tomita H, Kobayashi R, Ishihara T, et al. Syndecan-1 as a severity biomarker for patients with trauma. Front Med (Lausanne). 2022;9:985955.
41. Vollenberg R, Tepasse PR, Ochs K, Floer M, Strauss M, Rennebaum F, et al. Indications of persistent glycocalyx damage in convalescent COVID-19 patients: a prospective multicenter study and hypothesis. Viruses. 2021;13:2324.
42. Suzuki K, Okada H, Sumi K, Tomita H, Kobayashi R, Ishihara T, et al. Serum syndecan-1 reflects organ dysfunction in critically ill patients. Sci Rep. 2021;11:8864.
43. AlYousef RA, Abualnaja AA, AlNojaidi JH, AlDosari YN, AlKhalaf SA, AlQahtani NJ, et al. Lower back pain in athletes and non-athletes; a group comparison of risk factors and pain management. World J Environ Biosci. 2022;11(3):36-44. doi:10.51847/kVriSL1OCS
44. Shehata MA, AlDawsari AA, Saeedi AH, AlAyshan ML, Saleh MA, Koshak HA, et al. Acute coronary syndrome diagnosis & management approach in emergency department: literature review. World J Environ Biosci. 2022;11(2):61-4. doi:10.51847/Gihy97OwCC
45. Aldhairyan AH, Alyami SSH, Alsaad AMS, Al Shuqayfah NI, Alotaibi NA, Mujammami NM, et al. Gastroesophageal reflux disease: diagnosis and management approach, literature review. World J Environ Biosci. 2022;11(1):1-3. doi:10.51847/EvuxMWxAai
46. Dehaghi AA, Dolatshahi B, Taremian F, Pourshahbaz A, Ansari H. Acceptance and commitment therapy with islamic aspects as a treatment for scrupulosity in a case study. J Organ Behav Res. 2022;7(2):95-108. doi:10.51847/Fa3ED8HrzB
47. Nguyen NP, Pham TH, Nguyen NH. The effect of financial autonomy on medical treatment in central public Hospitals in Vietnam. J Organ Behav Res. 2024;9(2):95-104. doi:10.51847/M1JcunFDqY
48. Efremov A. Eliminating psychosomatic pain and negative emotions with dehypnosis. J Organ Behav Res. 2023;8(1):1-11. doi:10.51847/RNRhuQMtqY