

# Association of qSOFA with Ludwig's Angina Patient Mortality at Dr. Sutomo Hospital, Surabaya

Muhamad Saifuddin<sup>1</sup>, Dwi Hari Susilo<sup>1</sup>, Marjono Dwi Wibowo<sup>1</sup>, Sahudi<sup>1</sup>

<sup>1</sup>Department of General Surgery, Head and Neck Division, Faculty of Medicine Airlangga University, Surabaya, Indonesia

Corresponding Author: Muhamad Saifuddin, Email: [doktersaif@gmail.com](mailto:doktersaif@gmail.com)

## ABSTRACT

**Objective:** This study aims to determine the association between the quick Sequential Organ Failure (qSOFA) score and the mortality of Ludwig's Angina.

**Material and Methods:** Secondary data from the medical records of Ludwig's Angina patients in the period January 2019 - December 2020. Data included demographic feature, qSOFA data, Outcome patient, comorbidity diseases and complications before treatment. The number of samples was determined using the total sampling method. This study was enrolled into analytical observational study.

**Results:** There were 49 medical records that were included in the inclusion criteria, 6 medical records were excluded because the data were missing. There were more men 36 (73,5%) than women 13 (26,5%). There were 12 (24,5%) high qSOFA and 37 (75,5%) low qSOFA. There were 12 (24,5%) patient outcome dead and 37 (75,5%) outcome alive. The results of Chi-square analysis show qSOFA and confounding Diabetes Mellitus (DM) respectively were statistically significant association with Ludwig's Angina mortality. The results of multivariate logistic regression analysis, shows that there is a significant association between qSOFA and Ludwig's Angina mortality (p: 0.018) with an OR of 20.9 (CI 95%: 1,673 – 263,367). Diabetes mellitus comorbidity factors were also significantly associated with the mortality of Ludwig's angina.

**Conclusion:** There is a significant association between qSOFA and Ludwig's Angina mortality.

**Keywords:** Ludwig's Angina, Mortality, qSOFA, Sepsis

## INTRODUCTION

The mortality incidence of Ludwig's Angina increased significantly at Dr. Sutomo Hospital Surabaya in the period January 2019 - December 2020. The mortality rate at Dr Sutomo Hospital Surabaya is up to 24.5%. This mortality actually need to be detected early. Some experts in the world use qSOFA to predict mortality early.<sup>1-2</sup> Therefore, we conducted a study to prove the association between the qSOFA variable and the mortality variable for Ludwig's Angina patients.

## LITERATURE REVIEW

Ludwig's angina was first described by Wilhelm Frederick von Ludwig as a fast-processing cellulitis in the region of the submandibular gland that spreads through anatomical contiguity without leading to abscess formation.<sup>3-4</sup> The spread of odontogenic infections accounts for 57% of deep neck abscesses. With the potential for spread of infection to the intrapleural space and mediastinal tissue, the mortality rate for mediastinitis ranges from 17 - 50%. Death is usually caused by sepsis.<sup>5</sup> In addition, airway obstruction is a serious complication and requires airway management such as tracheostomy.<sup>6</sup> In the pre-antibiotic era, Ludwig's angina mortality was up to 50%. Currently, aggressive management with airway protection, intravenous antibiotics and surgical intervention can significantly reduce mortality by less than 10%.<sup>7-10</sup>

The mortality rate at Dr Sutomo Hospital Surabaya is up to 24.5% compared to the mortality rate for Ludwig's Angina in the world which is less than 10%.<sup>4</sup> These deaths actually need to be detected early.<sup>6</sup> Some experts in the world use qSOFA which consists of assessments conscious status, systolic blood pressure  $\leq 100$  mm Hg and respiratory rate  $\geq 22$  times / minute to predict mortality in patients with suspected sepsis.<sup>1-2</sup> However, studies on the association of qSOFA to mortality in Ludwig's Angina patients are still limited.

The use of the qSOFA score is quite easy to do in the Emergency Room (ER), without waiting for laboratory results and has a very large benefit value for doctors in the ER.<sup>11</sup>

## **MATERIALS & METHODS**

This was a cross-sectional analytical observational study to analyze the association of qSOFA with mortality in Ludwig's Angina patients. The data used are secondary data from the medical records of Ludwig's Angina patients in the Medical Records Division of Dr. Sutomo Surabaya for the period January 2019 - December 2020. The data were obtained from the records of the surgical resident doctor when the patient first came to the ER. Medical record data were collected from January 2021 - February 2021. Informed consent was obtained from all patients.

The inclusion criteria were all Ludwig's Angina patients who were treated at Dr. Sutomo Hospital since they were in the emergency room until they returned home after treatment during the period January 2019 - December 2020. The records were excluded if (1) the sufferer was Death on Arrival, (2) data were missing, and (3) the outcome was unknown.

The data collected were patient demographic data such as age and gender. Supporting data qSOFA consciousness status on admission to the hospital by assessing Glasgow Coma Scale (GCS), systolic blood pressure, respiratory rate per minute. Recording of outcomes after

treatment whether dead or alive. Recording of emergency measures that have been performed such as incision drainage with or without tracheostomy. Records of administration of antibiotics during treatment. Recording of patient comorbidity diseases such as diabetes mellitus, hypertension, Human Immunodeficiency Virus and others. Recording of disease complications before treatment such as acute respiratory distress syndrome, mediastinitis, and sepsis.

The independent variables of Ludwig's Angina qSOFA are high qSOFA and low qSOFA. The definition of qSOFA is high if the qSOFA score is  $\geq 2$  and qSOFA is low if the qSOFA score is  $< 2$ .<sup>1</sup> The dependent variable for Ludwig's Angina mortality is death and life. Confounding factors were diabetes mellitus, hypertension and the elderly.

The number of samples was determined using the total sampling method for the period January 2019 - December 2020. Data were collected and processed using IBM SPSS version 23. Data were then analyzed descriptively to recognize the data distribution. Bivariate analysis was used to analyze the association between qSOFA and mortality using the chi-square ( $p < 0,05$ ). The normality test for data distribution was not carried out because the data were nominal. Multivariate logistic regression analysis was used to determine the association between qSOFA and confounding factors that were significant to patient outcomes.

This study has been approved by the Hospital Ethics Committee. Dr. Sutomo Hospital Surabaya (No. 0296/LOE/301.4.2/I/2021).

## **RESULT**

During this study period, there were 49 medical records that were included in the inclusion criteria, 6 medical records were excluded because the medical record data were missing. All patients underwent emergency surgical incision drainage with or without tracheostomy. The patient was

given empirical therapy of Ceftriaxon and Metronidazole according to Dr. Sutomo Hospital's standards until the tissue microbiology culture results came out.

**Table 1 Subject Demographics**

Parameter		n	%
Sex	Male	36	73,5%
	Female	13	26,5%
Age	< 60 years	40	81,6%
	≥ 60 years	9	18,3%

**Table 2. Proportions of qSOFA and Ludwig's Angina outcome**

Parameter		n	%
qSOFA	Low	37	(75,5%)
	High	12	(24,5%)
Outcome	Alive	37	(75,5%)
	Dead	12	(24,5%)

*qSOFA : The quick Sequential Organ Failure*

**Table 3 Association of qSOFA with Ludwig's Angina mortality**

		Outcome		Total	P value
		Alive	Dead		
qSOFA	Low	34 (91,9%)	3 (8,1)	37 (100%)	<b>0,000</b>
	High	3 (25%)	9 (75%)	12 (100%)	

*qSOFA : The quick Sequential Organ Failure*

**Table 4 Association of DM with Ludwig's Angina mortality**

		Outcome		Total	P value
		Alive	Dead		
DM	Negatif	35 (94,6%)	2 (5,4%)	37 (100%)	<b>0,000</b>
	Positif	2 (16,7%)	10 (83,3%)	12 (100%)	

*DM : Diabetes Mellitus*

Table 1 shows that there were more men 36 (73,5%) than women 13 (26,5%). The majority of sufferers were in the age group < 60 years 40 (81,6%) and less in the elderly age group > 60 years 9 (18,3%). The average age was 46,22. Table 2 shows the proportion of qSOFA in Ludwig's Angina patients with low qSOFA 37 (75,5%) more than those with high qSOFA 12 (24,5%). The proportion with the outcome of living 37 (75,5%) is more than the outcome of dying 12 (24,5%). Table 3, the results of the chi-square analysis, shows that there is a significant association between qSOFA and Ludwig's Angina mortality (p: 0.00). There is also a significant association between DM and Ludwig's Angina mortality (p: 0,00). Conversely, other confounding factors (hypertension and the elderly) are not associated with mortality (p : 0,123 and p : 0,495). Table 5, the results of multivariate

logistic regression analysis, shows that there is a significant association between qSOFA and Ludwig's Angina mortality (p: 0.018) with an OR of 20.9, which means that patients with high qSOFA Ludwig's Angina have a risk of dying 20.93 times higher than those with low qSOFA patients. DM comorbidity factors were also significantly associated with the mortality of Ludwig's angina (p: 0.001).

**Table 5. qSOFA and DM Multivariate Logistic Regression on Mortality**

Variable	P value	Adjusted OR	95% Confidence Interval	
			Lower	Upper
qSOFA	<b>0.018</b>	<b>20,993</b>	1,673	263,367
DM	<b>0.001</b>	<b>59,148</b>	4,865	719,111

*qSOFA : The quick Sequential Organ Failure ; DM : Diabetes Mellitus ; OR : Odd Ratio*

## DISCUSSION

Ludwig's angina is a progressive diffuse cellulitis and edema due to a mandibular infection that spreads rapidly to the perimandibular (submandibular, sublingual, and submental) spaces bilaterally. <sup>1</sup> Infection can cross the midline of the neck or spread posteriorly to the deep fascial spaces of the neck. This condition is life threatening to the patient. <sup>3</sup> Apart from airway obstruction, death is usually caused by sepsis. Ludwig's angina tends to occur in immunocompromised patients such as AIDS, glomerulonephritis, diabetes mellitus and aplastic anemia. <sup>4</sup>

Assessment of the qSOFA association of Ludwig's Angina patients is important to do in the ER to predict patient outcomes whether at risk of dying or living. Patients with a high risk of dying need to be handled aggressively, quickly and accurately, supported by room facilities such as the Intensive Care Unit (ICU). If this is not possible, the patient should be immediately referred to a hospital with specialist surgery and supporting facilities such as the ICU room.

This analytic observational study proves that there is a statistically significant association between qSOFA and Ludwig's Angina mortality. Based on table 3, 9 (75%) of patients with high qSOFA died.

The results of this study are similar to previous studies which stated that high qSOFA has a sensitivity of 61% and a specificity of 80% for predicting hospital mortality. The positive likelihood ratio  $\geq 2$  to hospital mortality is 3.09 (2.86 - 3.35). When patients received antibiotics prior to culture examination, qSOFA sensitivity decreased and its specificity increased for predicting patient outcome compared to patients who were cultured before antibiotic administration.<sup>12</sup> Singer, AJ's study evaluated qSOFA to predict mortality of patients with or without suspected infection in the emergency department showed a qSOFA score 0, 1, 2 and 3 were associated with mortality as much as 0.6% (score 0), 2.8% (score 1), 12.8% (score 2) and 25% (score 3). The qSOFA value was associated with mortality with an odds ratio of 3.05 (95% CI 2.66 - 3.49). The sensitivity and specificity of qSOFA  $\geq 2$  were 29% and 97%, respectively, with a negative predictive value of 99%. The sensitivity and specificity with the qSOFA score 1 were 71% sensitivity and 74% specificity.<sup>13</sup> The study of Jha, G.N et al. who examined qSOFA score as a predictive tool in the emergency department concluded that there was a correlation between qSOFA and the incidence of mortality. Correlation qSOFA score 0, 1, 2, and 3 with mortality respectively 0.8% (score 0), 2.5% (score 1), 11.38% (score 2) and 25.75% (score 3) with  $p < 0.001$ .<sup>10</sup> Another study showed that patients with severe sepsis, qSOFA scores (sensitivity 96% and specificity 87%) were better than SOFA scores (sensitivity 71% and specificity 57%) for predicting mortality. In patients with septic shock, qSOFA was also better (sensitivity 92% and specificity 85%) than the SOFA score (sensitivity 70% and specificity 59%).<sup>14</sup>

In this study, patients with Ludwig's Angina with high qSOFA values had a tendency to develop sepsis since the start of treatment. Along the way, sepsis patients will suffer from multiorgan dysfunction. This is exacerbated if the patient has

comorbidity such as Diabetes Mellitus.<sup>8</sup> Diabetes Mellitus is an important comorbidity condition in sepsis because of its high prevalence.<sup>15</sup> Diabetic patients are generally believed to be more prone to infections than the general population.<sup>16</sup> Diabetes mellitus exacerbates the decline of many functions of the body organs and cause immune disorders.<sup>8, 17-18</sup> This study states that 9 (75%) of patients who died were found to be in sepsis when they first came to the ER. In addition, as many as 10 (83.3%) of patients who died were known to have comorbidity diabetes mellitus. This means that most of Ludwig's Angina patients who come then die in the hospital is patients with comorbidity Diabetes Mellitus who may have been immunocompromised and came in a septic condition since they first came to the hospital. Systemic diseases such as diabetes mellitus increase the severity of Ludwig's Angina patients. Mathew, G et al., 5 years retrospective study in Punjab, demonstrated the results of a univariate evaluation of patients at risk of life with comorbidity diabetes mellitus ( $p: 0.02$ ).<sup>4</sup> Study Botha, Andrew et al in Pretoria, South Africa, involving 93 patients with 73.1% odontogenic causes and the most comorbidity diseases with diabetes mellitus 21 (22.6%).<sup>19</sup>

In this study, the results of the qSOFA and DM multivariate logistic regression analysis on mortality showed that there was a significant association between qSOFA and Ludwig's Angina mortality ( $p: 0.018$ ) with Adjusted OR 20.93 (95% CI: 1.673 - 263.367). That is, high qSOFA patients in Ludwig's Angina patients had a 20.93 times higher risk of dying than those of low qSOFA patients. In addition, there was a significant association between diabetes and mortality of Ludwig's Angina ( $p: 0.001$ ) with Adjusted OR 59.148 (95% CI: 4,865 - 719,111). That is, Ludwig's Angina patients with DM positive risk of dying 59,148 times compared with patients without DM.

The drawback of this research is that the study only focuses on looking for the association of qSOFA with Ludwig's Angina mortality. In fact, mortality is influenced by many other comorbidity factors besides diabetes such as hypertension, obesity, heart disease and kidney failure as well as preoperative complications such as airway obstruction, pleural effusion, and empyema. In this study, data on these diseases were scanty and inadequate for analysis looking for their association with Ludwig's Angina mortality. We recommend that this study be further developed into a cohort study with qSOFA adjustment with a more adequate amount of data on comorbidity diseases and preoperative complications that contribute to Ludwig's Angina mortality.

## CONCLUSION

We can conclude that qSOFA is significantly associated with mortality in Ludwig's Angina patients. DM in Ludwig's Angina patients was also significantly associated with Ludwig's Angina patient mortality. This finding is in line with previous studies on sepsis cases in general which assessed the association of qSOFA to mortality with a significant association.<sup>3, 8, 11, 20-21</sup> Comorbidity DM is known to be associated with the life threat of Ludwig's Angina patients.<sup>8, 22-24</sup> clinical management of Ludwig's Angina patients in the emergency room to improve the outcome.

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