

(CASE REPORT)



Predicting factors for patients with Ludwig's angina have been treated at Viet Duc University hospital

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Abstract

Introduction: Ludwig's angina remains a severe infection pathology with a high mortality risk despite many advances in treatment. Prognostic death factors such as age, underlying disease, spreading infection, and airway compression have been mentioned. The purpose of the study was to determine the predicting factors to improve management outcomes.

Materials and methods: All patients diagnosed with Ludwig's angina were treated at Viet Duc University Hospital from 2019 to 2021, including death. Data were processed by software SPSS.20.0

Results: A total of 29 patients were enrolled during the study period. Male patients covered 79.3%, female patients accounted for 20%. The age group between 50 and 69 accounted for 51.7%. The most common cause was dental infection, which accounted for 82.8%; meanwhile, comorbidities accounted for 69%, including diabetes mellitus 34.5%, hypertension 24.1%, and cardiovascular disease 31.0%.

Classification of airway compression according to Mallampatti score: Class III accounted for 51.7%, and class IV accounted for 10.3%. There were 20 patients associated with comorbidities, accounting for 69%.

Spreading infection: Localized floor of mouth accounts for 49.7% including one side 41.4%, two sides 48.3%, extending to mediastinum accounts for 10.3%. Most common manifestations were neck swelling 100%, pain 82.8%, dyspnea 62.1%, fever 62.1%, dysphagia 41.4%. Septic shock and trimus accounted for 27.6% and 24.1% respectively.

Bacterial isolations: *Streptococcus species* was the most common at 31%, and *Peptostreptococcus* accounted for 24.1%. *Acinetobacter Baumannii* and *Klebsiella pneumoniae* both accounted for 13.8%

Airway management: 3 cases needed tracheostomy at emergency department, accounting for 10.3%.

There were 12 cases of postoperative complications, accounted for 41.4%. Six died, accounted for 20.7%.

Conclusions and recommendations: Ludwig's angina mortality remains high so far. Risk factors should be assessed as soon as the patient is admitted to the hospital for aggressive management, notably airway management and antibiotic strategies.

Keywords: Ludwig's angina; Mediastinitis; Airway decompression; Submandibular space

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1. Introduction

German physician Wilhelm Frederick von Ludwig first described Ludwig's angina in 1836, later called Ludwig's angina after his name. It's a potentially life-threatening diffuse cellulitis of the neck, the floor of the mouth, and submandibular regions bilaterally, leading to airway obstruction. The disease is notorious for its aggressiveness, quick progression resulting in airway compromise, and high mortality when there is a delay in intervention. Infection usually comes from a condition of the mouth [1, 2, and 3].

If left untreated, the infection rapidly spreads to the mediastinal thorax. Pathogenic bacteria caused by the combination of anaerobic and aerobic bacteria lead to severe systemic disease with a high mortality rate. Before the antibiotic phase, most patients died. The prognosis for this type of infection is guarded. In 1938, according to Pearse HE [5], mediastinitis was reported to have a mortality rate greater than 50%.

Today despite advances in resuscitation and surgery, mortality is still as high as 30% in some recent reports [3, 4, and 6]. Predisposing factors include dental caries, current dental treatment, systemic illness, such as acquired immune deficiency syndrome, organ transplantation, mandibular trauma, penetrating injuries of the floor of the mouth, and oral neoplasm. Death is mainly related to airway compromise, shocked septic, multi-organ failure, or bleeding because of damage to some significant vessels in the neck [4, 5, and 6].

Although there are many cases of Ludwig's angina in Vietnam, there are very few reports on this disease. For these reasons, we conducted the study to determine the predicting factors through treatment outcomes.

2. Material and methods

2.1. Subjects

2.1.1. Selection Criteria

Patients diagnosed with Ludwig's angina were treated at Viet Duc hospital from 2019 to 2021, including death. If the patient died without surgery, there must be a biopsy record to determine the Ludwig's angina.

2.2. Methods

It's a retrospective, and prospective clinical description study then followed longitudinally.

- Design a sample medical record to collect information
- Study variables retrieved from the patient's medical history included the demographics, aetiology, signs and symptoms at presentation, and possible predisposing factors.
- Laboratory investigations included Full Blood Count, Electrolytes and Urea, Blood Sugar profile and Microscopy, and culture and sensitivity (MCS) of all abscess pus.
- Mallampati score (Mallampati classification) was used for the assessment or prediction of ease of endotracheal intubation or airway compromise [7]

In addition, complications and duration of hospital stay, and treatment outcomes were also noted.

2.2.1. Data processing

Collected data were analyzed using SPSS 20.0 software.

2.3. Medical ethics

The Ethics Committee in Biomedical Science of Viet Duc University Hospital has approved the study.

3. Results

3.1. Demographic information

There were 29 patients with Ludwig's angina who met the criteria selection, including 23 male patients, 79.3 %, and 6 female patients, 20.7%. Commonly patients in a group aged 50 to 69 years old accounted for 51.7%, and those more than 70 years old accounted for 27.6%, respectively.

3.1.1. Causes

Table 1 Medical history

Description	(n=29)	(%)
Tonsillar infection	4	13.8
Dental infection	24	82.8
Tooth extraction	1	3.4

There were 20 patients associated with comorbidities, accounting for 69%. The details are shown in the following table.

Table 2 Comorbidities associated

Description	(n)	(%)
High blood pressure	7	24.1
Diabetes mellitus	10	34.5
Cardiovascular diseases	9	31.0

3.1.2. Clinical features

Table 3 Clinical features

Description	(n)	(%)
Neck swelling	29	100
Dyspnea	18	62.1
Pain	24	82.8
Dysphagia	12	41.4
Fever	18	62.1
Hemoptysis	3	10.3
Trimus	7	24.1
Septic shock	8	27.6

3.1.3. Mallampatti classification

Table 4 Classification of dyspnea according to Mallampatti score

Description	(n=29)	(%)
Class I	2	6.9
Class II	9	31.0
Class III	15	51.7
Class IV	3	10.3

3.1.4. Paraclinical features

CT scan results

Table 5 CT scan results

Description		(n=29)	(%)
Extension of pus	One side of the neck	12	41.4
	Extension to both sides of the neck	14	48.3
	Extension to mediastinum	3	10.3

Bacterial isolation

All cultures were positive. The results are shown in the following table.

Table 6 Isolated bacteria's

Description	(n)	(%)
Streptococcus species	9	31
Staphylococcus species	3	10.3
Acinetobacter Baumanii	4	13.8
Klebsiella pneumonia	4	13.8
Pseudomonas aeruginosa	2	6.9
Peptostreptococcus	7	24.1

3.1.5. Management on emergency

Airway management

These 3 cases were treated the airway obstruction at emergency department by tracheotomy, which accounted for 10.3%

3.1.6. Antibiotherapy, according to the results of the antibiogram

Table 7 Antibiotherapy following results of antibiogram.

Description	Antibiotic used by experience	Sensibility	%
Cephalosporin III	21	17	81
Clindamycin	5	5	100
Meronem	5	4	80
Sulbactam	2	1	50
Metronidazole *	25	12	48

*Metronidazole has low sensibility, accounting for 48%.

3.1.7. Surgical management

All patients were operated on for emergency; the procedures included: pus drainage, debridement of necrotizing tissues.

Postoperative complications

The postoperative complications that occurred in 12 cases accounted for 41.4%. The details are in the table.

Table 8 Postoperative complications

Descriptions	(n=12)	(%)
Pneumonia	3	25.0
Pleural effusion	5	41.7
Bleeding from wound	3	25.0
Extensions of necrotizing soft tissues *	9	75.0

*This complication required more debridement

Length of hospitalization

Table 9 Length of hospitalization

Description (day)	(n=29)	(%)
< 7	2	6.9
8-14	9	31.0
15-21 *	15	51.7
>22	3	10.4

*Most common patients in this group had comorbidities, and ages were older than 70 years

Outcomes of treatment

6 deaths occurred, accounting for 20.7 %. Of them, there two cases had Mallampatti score IV, two cases with Mallampatti score III, one case with Mallampatti score II.

4. Discussions

Since the German physician W. F. von Ludwig first described Ludwig's angina until now with advances in treatment and management, the mortality rate has decreased significantly from 50% to 10 % in recent reports [1, 8, 9, and 10]

Most cases of Ludwig's angina are due to dental infections, especially second and third molars. Other possible causes of Ludwig's angina include submandibular abscess, mandibular fracture, oral laceration or mandibular sinusitis, and oral malignancy. The infection can also spread continuously to the oropharynx, compressing the airways and to the mediastinum, causing difficulty breathing.

Predisposing factors include tooth decay, recent dental treatment, systemic illness such as diabetes, malnutrition, alcoholism, a compromised immune system such as AIDS, and post-organ transplantation.

According to the study of Nikhil M J et al. [10] (2016) at Bangalore Medical College & Research Institute, Bengaluru, India, there had thirty patients with Ludwig's angina. Most patients were in the third decade of life; there was a preponderance of females in this study. Dental infection was the most common etiological factor (70%). In the report of Ian M Furst [11], in adults, 52% of cases of Ludwig's angina are caused by dental caries³ and have a mortality rate of 8-10%.

In our study, the demographic characteristics showed that the percentage of male patients was 79%, and the age group from 50 to 69 was the majority (51.7%). Regarding the causes, it showed that purulent pharyngitis accounted for 13.8% of dental infections for 82.8% (Table1). Comorbidities accounted for 69.0 % (Table2), including diabetes mellitus 44.8%, followed by high blood pressure 24.1%, and cardiovascular disease 13.8% respectively.

Clinical signs to assess the extent of airway involvement can be seen in patients often wheezing due to the height of the floor of the mouth and the tongue receding posteriorly with the risk of airway obstruction. Neck swelling (100%), pain (83%), fever (75%), and trismus (33%) were the most common complaints in a report of Nikhil M J. Clinical presentations of the patients were found to be different. Most patients presented with multiple complaints. Neck

swelling, pain, and fever were the most familiar presentations. The following common presentation was dysphagia. Dental infection was found to be the most common source of infection [10].

Almost report mentioned that if the patient presents with pain, tongue lift, malaise, fever, neck swelling, and difficulty swallowing, the submandibular region may be saturated, sometimes palpable. Inability to swallow saliva and difficulty speaking raises concern because of airway damage. The most dangerous complication is airway obstruction due to compression of the extended and backward tongue [12, 13, and 14]. According to Nogueira [15] and Nguyen Duc Chinh et al. (2020) [16], tongue elevation is associated with dysphagia, sore throat, and cyanosis. Possible systemic manifestations: high fever, malaise, loss of appetite, tachycardia, and chills. On the other hand, increasing compressive pressure in the oral cavity increases clinical muscle tone.

In our series, the clinical manifestations included 100% swelling; the pain was 82.8%; High fever accounted for 62.1%; Trismus was 24.1%. Notably, there were three cases of hemoptysis (10.3%), which are signs of a high risk of airway obstruction; 27.6% were septic shock, and all were at increased risk of death (Table 3).

A study by Sharma V in 2011 [18] showed that fever and neck swelling was present in 100% of cases, halitosis was present in 68% of cases, and difficulty in swallowing was present in 63.8% of cases, hoarseness of voice was present in 61.7% cases. Trismus was present in 36.2% of patients and respiratory difficulty in 8.5% of cases. Other reports have also mentioned the breathing problem due to airway compromise or complications of pleural effusion or mediastinitis [10,11,19].

In our study, 62.1 % of patients had difficulty breathing. We applied the **Mallampati score (Mallampati classification) [7]** to predict endotracheal intubation or airway compromise. The most common patients were classified as class IV, at high risk of airway compromise (Table 4).



Figure 1 The patient had breathing problems, the pillars and the uvula were obstructed, and only the soft palate was visible (medical record coded 21002497547), classified III of Mallampati score

Currently, computed tomography (CT) scan is very valuable in diagnosing Ludwig's angina not only to determine the cause but also to show specific lesions: soft edema, air fluid, abscess, especially mediastinal abscess due to spreading infections. Miller CR et al. [20] showed CT scan with 89% accuracy, 95% sensitivity, and 80% specificity. According to Fogaça PFL [21], clinical examination is decisive in diagnosing Ludwig's angina. A combination of laboratory tests such as hematology, biochemistry assessment of liver and kidney function, culture, and antibiogram is also of essential importance to monitor the patient's general condition and to plan the proper treatments in an emergency. A report by Ian M Furst [11] found that where neck infections descend to the mediastinum it is usually through the retropharyngeal space (71% of cases); however, the carotid sheath is the conduit in 21%. If a deep neck infection is suspected, early CECT imaging should be considered, as clinical exam alone has a sensitivity of 55%. In other words, a 45% chance that a deep neck abscess will be misdiagnosed as cellulitis when using a clinical exam alone. However, the combination of CECT and clinical exam has an accuracy rate of 89% with a sensitivity rate of 95%.



Figure 2 Patient classified IV: breathing problems: The soft palate is also obstructed from view, and only the hard palate is visible (medical record coded 21002570381)

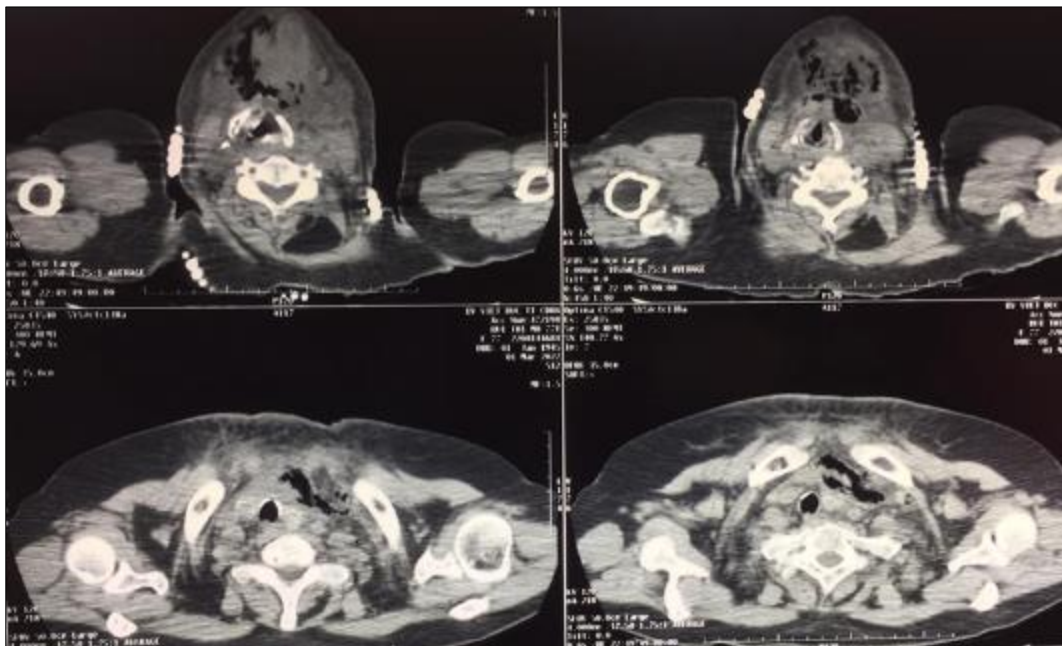


Figure 3 Abscess was extended to mediastinitis (medical record coded 21002497547)

Our study's CT scan findings (Table 5) showed that the abscess was extended to both neck sites in 48.3% and mediastinitis in 10.3%. The results were used not only for accurate diagnosis but also for predicting factors for treatment outcomes. In the case of mediastinitis, a high risk of complications and death might occur.

Antibiotic therapy is a critical issue for managing Ludwig's angina. Ludwig's angina is caused by mixed bacteria (aerobic and anaerobic bacteria), usually located in the oropharynx, and is commonly isolated by *streptococci*, *staphylococci*, *pseudomonas*, *B melaninogenicus*, and *peptostreptococcus*. Some studies reported the isolated organism of β -hemolytic *streptococcus* in association with anaerobic bacteria such as *peptostreptococcus* and *pigment* bacteria was described as the causative agent [6, 11, 15, 22]. Anaerobic bacteria were responsible for the gas formation in the soft tissues. In this case, the extension along the carotid sheath or the retropharyngeal space may have caused the mediastinitis. Both spaces extend into the superior mediastinum.

According to the study by Nikhil M J et al. [10] (2016), the most common pathogens found were *Streptococcus viridans* (36.6%), followed by *Staphylococcus aureus* (16.6%), *Streptococcus pyogenes* (13.3%), and *Klebsiella species* (10%). A

report by I Brook in 2003 [23] found that the microorganisms commonly identified as anaerobes include *Bacteroides sp.*, *Micrococcus sp.*, *Fusobacterium sp.*, and *Peptostreptococcus sp.* The antibiotic recommended to use was broad-spectrum antimicrobial therapy as the rule of thumb for management. Recommended antibiotic treatment includes a broad-spectrum, β -lactam-based, usually penicillin (\pm penicillinase inhibitor). Intravenous high-dose combined with metronidazole is the antibiotic therapy of choice in treating Ludwig's angina. Some authors also recommend the combination of gentamycin. In the report on Nikhil M J et al. [10] (2016), 86.6% were treated with ceftriaxone and metronidazole before pus culture sensitivity was obtained and was found to be effective. For the resistance of antibiotic, linezolid was indicated.

In our series, all 29 cases, the bacteria were isolated (100%) (Table 6). The most isolated bacteria were *Streptococcus species* 31%, *Peptostreptococcus* accounted for 24.2%. *Acinetobacter Baumannii* and *Klebsiella pneumoniae* both accounted for 13.8%. For antibiotics, some common medications indicated to use as experienced were clindamycin (100%), cephalosporin III (81%), meronem (80%). Metronidazole was also suggested for the first line. However, the resistance rate was relatively high, and we had to change according to the results of antibiogram (Table. 7)

Respiratory failure is always synonymous with Ludwig's angina and is the leading cause of death. Therefore, airway management is the primary treatment concern when resuscitating patients. The stage of the disease, comorbidities at the presentation, the physician's experience, and available resources are all essential factors in decision making. Blind endotracheal intubation should not be performed in patients with Ludwig's angina who are likely to bleed and rupture the abscess. Flexible intubation requires skill, experience, and, if not feasible, tracheostomy under local anesthesia.

Tracheostomy with local anesthesia has been considered the "gold standard" of airway management in patients with deep neck infections but may be difficult or impossible in severe conditions due to the location of tracheostomy or due to anatomical deformity of the anterior neck [12, 24, 25,26].

Many authors recommend intubation while awake to secure the airway if CT shows deviation and narrowing of the airway. Larawin V et al. [27] retrospectively studied 103 patients with VT from 1993 to 2005; 10% required tracheostomy. In 29 cases in 9 years by Greenberg SL et al. [28] showed 1 (3%) emergency intubation, 7 (24%) intubation with a flexible bronchoscope, and 1 (3 %) required tracheostomy under local anesthesia.

Drainage of pus is to control the airway (due to compression), and the treatment goal is to resolve the infection. The location and size of the incision will depend on the anatomy of where the pus-related disease has spread. Freire-Filho et al. [29] recommend extensive surgical drainage combined with antibiotic therapy for Ludwig's angina to avoid pus spreading into the mediastinum.

For airway management of our series, there were 3 cases of tracheostomy because the endotracheal tube could not be placed.

In our study, the postoperative complications accounted for 41.4%. Respiratory complications were the most common, followed by septic shock and necrosis continued to extend respectively (Table 8).

For the outcome of management, in the study of Nikhil M John [10] the majority of patients (80%) were discharged by 2 weeks following the day of admission. The author concluded that managing Ludwig's angina can often be challenging. Appropriate and aggressive antibiotic therapy, surgical decompression if required, and removal of infected foci can arrest the progress of the disease and prevent further complications.

According to Harpreet Singh [30], the moderately severe Ludwig's angina such as age ≤ 40 years with difficulty in breathing or hoarseness, age $>40 \leq 60$ with or without difficulty in breathing or hoarseness, age >60 without difficulty in breathing or hoarseness, rest of features of mild Ludwig's angina, severe Ludwig's angina, age >60 years with difficulty in breathing or hoarseness, any age with a systemic illness like diabetes, chronic renal failure, aplastic anemia, HIV.

In our series, the most common length of stay was from 15 to 21 days, accounting for 51.7% (Table 9). Six patients died, so the mortality accounted for 20.7%. The patients with complications and died were in the group of age >60 , having comorbidities, Mallampati class III and IV, and abscess extended to mediastinum.

5. Conclusion

Ludwig's angina is still a potentially life-threatening infectious disease with a high risk of death.

Dental infection is a significant risk factor predisposing to the development of Ludwig's angina. Broad-spectrum parenteral antibiotics play an essential role in the control of infection.

Most of the patients needed surgical decompression in an emergency.

The predisposing factors of outcomes are men over 70 years old with comorbidities, airway compromise, septicemia, mediastinal extension of infection.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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