Characteristics and Predictors of Mortality in Descending Necrotizing Mediastinitis: A Retrospective Cohort Study

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Abstract

Background: Descending necrotizing mediastinitis (DNM) is a life-threatening infection originating from necrotizing soft tissue infections, particularly in the cervical and oropharyngeal regions. DNM has a high mortality rate if not promptly diagnosed and treated surgically. Despite its severity, there is limited research on the characteristics and outcomes of DNM patients in Indonesia, especially in East Java. Methods: We conducted a single-center retrospective cohort study at Dr. Soetomo Hospital, Surabaya, Indonesia, analyzing the medical records of DNM patients treated between January 2021 and June 2023. Data on demographic, clinical, and surgical characteristics, along with treatment approaches, were collected. Statistical analyses included univariate and bivariate analyses to identify predictors of mortality. Results: Among 37 patients (mean age 45.6 years; 64.9% male), the primary infection source was odontogenic (86.5%). Most patients (51.4%) were classified as DNM type I, with cervicotomy and substernal drainage as the most common surgical approach (97.3%). The mean ICU stay was 6.6 days, and the overall hospital stay was 11.3 days. The mortality rate was 48.6%. Shorter hospital stays were significantly associated with increased mortality (p=0.000). Conclusion: DNM remains a severe condition with high mortality, primarily originating from odontogenic sources. Prompt diagnosis, appropriate surgical intervention, and targeted antibiotic therapy are critical to improving outcomes. Our study underscores the need for standardized management guidelines to enhance patient survival rates in regions with limited resources.

Keywords: Descending Necrotizing Mediastinitis, Mortality Predictors, Odontogenic Infections, Surgical Outcomes, Retrospective Cohort Study

Significance | This study demonstrated key characteristics and mortality predictors in Descending Necrotizing Mediastinitis patients, aiding timely diagnosis and effective management strategies in Surabaya, Indonesia.

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Introduction

The mediastinum, a central compartment within the thoracic cavity, is bounded by the mediastinal parietal pleura and extends from the superior thoracic inlet to the diaphragm. This anatomical region houses critical structures, such as the heart, major blood vessels, trachea, and esophagus, making it a vital area for various pathologies. Mediastinitis, a potentially life-threatening infection, specifically affects the connective tissue of the mediastinum and may present as either acute or chronic, with causes ranging from infectious to non-infectious etiologies (Jiwangga, 2018). One particularly severe form of this condition is Descending Necrotizing Mediastinitis (DNM), which originates from necrotizing soft tissue infections (NSTI) in the head or neck region and extends downward into the mediastinum (Ulusan & Koc, 2016).

DNM is characterized by rapid progression and extensive tissue necrosis, resulting in a mortality rate of up to 60% if not diagnosed early and managed promptly with aggressive surgical intervention

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(Gorlitzer et al., 2007). The condition was first described by Pearse in 1938, who outlined its devastating nature and clinical challenges (Pearse, 1938). DNM is primarily linked to necrotizing fasciitis (NF) of the cervicofacial region, with approximately 40-45% of NF cases potentially progressing to DNM (Sumi, 2015). The infection's aggressive nature, coupled with its rapid descent along the fascial planes of the neck into the thoracic cavity, underscores the importance of early diagnosis and intervention.

Timely control of the infection source, combined with adequate surgical drainage, is paramount for effective DNM management. However, there are no standardized guidelines for the treatment of this condition, leading to significant variability in clinical practice (A. Putra et al., 2016). The management approach often involves a combination of broad-spectrum antibiotic therapy and surgical drainage procedures, such as cervicotomy, sternotomy, and thoracotomy, tailored to the individual patient's condition and the infection's extent (Ulusan & Koc, 2016). The lack of standardized treatment protocols poses a challenge in the management of DNM, necessitating further research and the development of consensus guidelines.

Despite the severe implications of DNM, the condition remains under-researched, particularly in certain geographic areas, such as Indonesia. Most of the existing literature originates from Western countries, leaving a gap in understanding the disease's regional characteristics, outcomes, and associated factors in Southeast Asia. This study aims to address this gap by analyzing the characteristics and predictors of mortality among patients diagnosed with DNM in the East Java region of Indonesia. Conducted at the Department of Cardiothoracic & Vascular Surgery, Dr. Soetomo Hospital, Surabaya, this retrospective cohort study focuses on patients treated between January 2021 and June 2023. Through a comprehensive analysis of demographic, clinical, and surgical variables, this study seeks to contribute valuable insights into the management and outcomes of DNM in a Southeast Asian context, thus aiding in the formulation of more effective treatment strategies and improving patient prognosis.

Understanding the local epidemiology, risk factors, and clinical outcomes of DNM is crucial for optimizing patient management and reducing mortality rates. By identifying key predictors of poor outcomes, healthcare providers can better stratify patients according to their risk profiles, thereby facilitating timely and targeted interventions. This study endeavors to shed light on the specific challenges and outcomes associated with DNM in Indonesia, ultimately aiming to enhance the quality of care and survival rates for patients affected by this devastating condition.

Methodology

Study Design and Population

This is a single-center retrospective cohort study that was conducted at the Departement Cardiothoracic & Vascular Surgery, Dr. Soeotomo Hospital Surabaya, Indonesia, with the aim to identify the characteristics and predictors of mortality of DNM patients. The study included DNM patients who received treatment at the hospital between January 1st, 2021, and June 31st, 2023. Thorax X-rays and CT scans were performed on our cohort (Figure 2A-B). The diagnosis of DNM is established using the criteria outlined by Estrera et al., which encompass the following key elements:1) evidence of oropharyngeal infection; 2) imaging characteristics consistent with mediastinitis; 3) intraoperative findings or postmortem evidence confirming the presence of infection; 4) establishing a direct link between the oropharyngeal infection and the occurrence of mediastinitis (AS et al., 1983). The inclusion criteria were patients who were treated in the surgical ward of the Dr. Soeotomo Hospital Surabaya, Indonesia with clinical manifestations of infection in the oral cavity and neck related to the mediastinal space. Exclusion criteria were DNM patients who died prior to further treatment and DNM patients who refused further treatment. Patients with incomplete medical records and those without a confirmed diagnosis of DNM were also excluded from the study.

Data Collection

This study utilized secondary data from existing medical records to perform the retrospective analysis. The researchers collected data from medical records and patient registration data at the Departement Cardiothoracic & Vascular Surgery, Dr. Soeotomo Hospital Surabaya, Indonesia. Demographic and clinical characteristics of the subjects were collected, including age, sex, presence of diabetes Mellitus (DM), source of infection (odontogenic, esophageal, head and neck, and tracheobronchial), down spreading type (anterior, middle, and posterior mediastinum, pleura, mediastinum, and pleura), and the DNM classification (type I, IIA, IIB, IIC). The researchers also investigated the surgical characteristics, the timing of surgery, surgical approach (herniotomy, VAST, sternotomy, left thoracotomy, right thoracotomy), and drain insertion (substernal, right or left intrapleural, substernal, and intrapleural). The antibiotics used, and results from culture examination with the isolated microorganism were also recorded. Patient outcomes were assessed by recording the average length of ICU and overall hospital stay and also the overall survival. Some of the collected variables were then compared between patient groups who survived and those who unfortunately passed away.

Statistical Analyses

Data analysis for this study was conducted using SPSS version 20 for Windows. Two types of analyses were performed: univariate analysis and bivariate analysis. Univariate analysis was conducted to provide an overview of the subject characteristics and the

distribution of subject data. For categorical data, such as gender and surgical characteristics, the number and percentage of each category were presented. For numerical data, such as age or length of hospital stay, descriptive statistics such as mean and standard deviation (SD) or median and interquartile range (IQR) were used, based on whether the data was normally distributed. Bivariate analysis was then performed to compare specific variables between different groups. For categorical data, the Chi-square test was employed to determine whether there were substantial differences in proportions across groups. For numerical data, the independent T-test was utilized to compare the means between groups. The significance level was set with a p-value of less than 0.05 for all tests.

Results

In this study period, 37 patients (mean age of 45.59 (±14.884) years; 64.9% male) diagnosed as DNM were admitted to the division of cardiac and vascular surgery with complete data. The demographic, clinical, and surgical characteristics of our study population are described in Table 1. In this study, the primary source of infection was odontogenic in nature, accounting for approximately 86.5% of cases. Among the DNM patients, about half of them (51.4%) were categorized as DNM type I. The most frequently utilized surgical approach was cervicotomy substernal drainage, which was employed in 97.3% of cases. The mean length of ICU stay for the cohort was 6.62 (±4.542) days, and the mean hospital length of stay was 11.32 (±8.014) days. A total of 18 patients (48.6%) died during the course of this study (Figure1A-B)

Table 2 presents a comparison of characteristics between the groups of patients who died and those who survived. The deceased group had a significantly shorter hospital stay in comparison to survived group (6.56 [±3.944] days vs. 15.84 [±8.335] days; p=0.000). However, the other variables examined did not demonstrate statistical significance between the two groups.

Discussion

Mediastinitis is characterized as an inflammatory condition affecting the connective tissue within the mediastinum, which includes the structures and spaces between the pleural membranes. When this condition arises from an infectious source in the oral or cervical regions, it is specifically referred to as "descending mediastinitis" (Inaco Cirino et al., 2006). Symptoms commonly present within the first 48 hours and may encompass retrosternal pain, swelling, redness, stiffness in the neck and anterior thoracic wall, sepsis-related manifestations such as shivering and fever, cough, and dyspnea. Mediastinal involvement usually becomes evident within 12 hours to 2 weeks. Radiological examination reveals distinctive features, primarily centered on mediastinal extension (Inaco Cirino et al., 2006; Ulusan & Koc, 2016). These findings encompass widening of the mediastinum, with or without air-fluid levels in the retropharyngeal region, mediastinal emphysema, cervical lordosis widening, anterior shift of the tracheal air column, enlargement of the cardiac silhouette, pneumothorax, and hydropneumothorax (Foroulis, 2011). Chest computed tomography (CT) scans serve as a valuable diagnostic tool for confirming this condition and assessing its extent (Inaco Cirino et al., 2006; Ulusan & Koc, 2016).

Our study cohort comprised adult patients with a mean age of 46 years, and the majority of participants (65%) were male. A previous report by Harar et al. stated that DNM primarily affects young adults with a median age of 36 years, and 86% of them being men (Harar et al., 2002). Results of other studies also documented that DNM is more frequent in male patients (Jiwangga, 2018; Lara et al., 2013; M. A. Putra et al., 2016; Sumi, 2015). The mean age of our subjects was found to be comparable to the mean age of 43.73 years observed in a separate study involving 50 DNM patients at Dr. Soetomo Hospital, Surabaya, Indonesia.1 Previous study in Italy involved 34 DNM patients with an average age was 46.8 ± 11.2 years and a ratio of male to female of 3.25 (Palma et al., 2016). A third of the participants in our research had a documented history of type 2 diabetes. Indeed, diabetes has been recognized as a risk factor for the occurrence of DNM. Other significant risk factors for DNM include advanced malnutrition, age, obesity, immunodeficiency, peripheral vascular disease, hypoalbuminemia, cancer, corticosteroid use, and chronic renal failure (Headley, 2003; Inaco Cirino et al., 2006; Reuter et al., 2023; Weaver et al., 2010).

Within this study cohort, the predominant origin of DNM infection was identified as odontogenic sources, accounting for approximately 86.5% of cases. These findings align closely with the results of a previous extensive series conducted by Kiernan et al., where DNM cases were investigated, and odontogenic sources were reported as the primary cause in approximately 58% of the cases.17 Cirino et al., in their review stated that odontogenic infection accounts for 40-60% of DNM cases (Inaco Cirino et al., 2006). DNM is frequently encountered in cases of odontogenic infections involving the second and third molar teeth, a condition also known as Ludwig's angina. Negative thoracic pressure along the cervical fascia in the retropharyngeal area promotes infection transmission to the mediastinum (Ulusan & Koc, 2016). In the context of causative organisms, it is common to find a co-existence of both aerobic and anaerobic microorganisms. Among the aerobic bacteria, *Streptococcus pyogenes*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* are frequently identified. Additionally, anaerobic bacteria such as *Klebsiella pneumoniae*, *Bacteroides fragilis*, and *Clostridium* species are also commonly detected (Foroulis, 2011; Sumi, 2015; Ulusan & Koc, 2016). These findings are consistent with the culture results obtained from our study cohort.

The dissemination of infection to the mediastinal compartment occurs through three principal fascial pathways. These pathways include the pre tracheal (superficial) route, terminating in the anterior mediastinum; the later pharyngeal (perivascular) pathway, terminating in the middle mediastinum; and the retropharyngeal (prevertebral space) route, ending in the posterior mediastinum (Inaco Cirino et al., 2006; Ulusan & Koc, 2016). This is consistent with the findings of the down-spreading type in our DNM patients, which included the anterior (64.9%), middle (8.1%), and posterior mediastinum (21.6%). A recent study in Surabaya also found that the most common form of down spreading infection was anterior mediastinum extension (78.57%) (Jiwangga, 2018).

Endo et al. in 1999 proposed a classification system for DNM depend on the extent of dissemination observed on CT scans. The classification comprises two main types: focal and diffuse. In type I (focal type) DNM, the infection is concentrated in the superior mediastinal space above the tracheal bifurcation. Type II (diffuse type) is further subdivided into two forms: subtype IIA, in which the infection is limited to the inferior anterior mediastinum, and subtype IIB, in which the disease process has spread to the inferior posterior mediastinum (Endo et al., 1999). In 2021, Sugio et al. proposed the fourth type of DNM, type IIC, that is confined within the posterior mediastinum (Sugio et al., 2021).

The primary treatment approach for DNM involves the administration of appropriate antibiotics in conjunction with surgical drainage (Ulusan & Koc, 2016). The initial treatment approach should involve the use of broad-spectrum antibiotics, providing comprehensive coverage against both aerobic and anaerobic microorganisms (Inaco Cirino et al., 2006). We used empirical therapy based on microbial mapping and antibiotic sensitivity in our hospital while awaiting culture results. Debridement of necrotic tissues is essential, and thorough irrigation of both the mediastinal and pleural regions is crucial for effective management (Figure 2D) (Ulusan & Koc, 2016).

Almost all (97.3%) of our patients were treated with substernal drainage cervicotomy, which is similar to the study by Jiwangga who did cervicotomy substernal drainage for 96.43% of their DNM cases (Jiwangga, 2018). Cervicotomy was carried out by an incision created anterior to the sternocleidomastoid muscle on the affected side or via a cervical collar incision (Figure 3A-C). The primary objectives of this approach were to access and open the involved cervical space, facilitate drainage of infected materials, and remove necrotic tissue through debridement (Krüger et al., 2016).

We found one patient with type IIB DNM who underwent a video-assisted thoracoscopy (VATS) surgery in our research group (Figure 3D-E). The utilization of VATS in DNM cases has been documented by Isowa et al. and Min et al., and its application is currently restricted to specific indications, primarily in the initial phases of infection or for dealing with posterior mediastinal collections (Isowa et al., 2004; Min et al., 2004). Indeed, VATS offers several universal advantages associated with minimally invasive surgical techniques. These benefits include reduced postoperative pain, improved cosmetic outcomes due to smaller incisions, and faster recovery times for patients (A. Putra et al., 2016; Sumi, 2015). Yun et al. demonstrated that compared to the transcervical group, the VATS group had duration of antibiotic therapy, shorter drainage duration, and decreased hospital length of stay (Yun et al., 2023).

In our patient cohort, nearly all individuals underwent drain insertion, with a majority (48.6%) of them having a substernal drain placed, similar to the study conducted by Jiwangga (Jiwangga, 2018). These drains enable continuous washing with antiseptic solutions, contributing to effective infection control. However, the drains must be regularly monitored since necrotic tissue particles might obstruct them. On average, the drains are kept in place for approximately three weeks. When abscesses or non-drained collections persist, a second operative procedures is required to prevent clinical worsening (Inaco Cirino et al., 2006; Makeieff et al., 2004).

Tracheostomy was performed on 1 of our patients, who spent 15 days in the ICU and a total of 38 days in the hospital. There are differing opinions among authors regarding the use of tracheostomy in cases of DNM. Some experts argue that tracheostomy is necessary and should be considered, especially when prolonged mechanical ventilation is required. However, there are worries that tracheostomy may transmit the illness to non-involved regions and hamper later surgical treatments (Brunelli et al., 1996; Inaco Cirino et al., 2006).

Late diagnosis and insufficient drainage represent the leading reasons of mortality in DNM. The consequences of these factors may lead to bleeding complications, metastatic cranial infection, aspiration, fulminant sepsis, emphysema, purulent pericarditis, and tamponade (Sumi, 2015; Ulusan & Koc, 2016). The main complication of DNM is sepsis, which was evident in our study as all of the patients were diagnosed with preoperative septicemia. DNM is a serious and potentially fatal disorder with a high fatality rate. The mortality rate of DNM is typically around 50%, and this is consistent with the findings observed in our study cohort, where the mortality rate was reported to be 48.6% (Inaco Cirino et al., 2006; A. Putra et al., 2016).

In our study cohort, the mean length of ICU stay was 6.62 (±4.542) days, and the mean hospital stay was 11.32 (±8.014) days. DNM patients typically had prolonged ICU and hospital stays. Comparing our findings with the results from other studies, such as the one conducted by Chen et al. involving 18 DNM patients, they reported an ICU length of stay of 14.6 ± 13.4 days and a hospital stay of 40.1 ± 23.3 days, with a mortality rate of 16.7% (Chen et al., 2008). Another study by Uwa et al., which included 5 DNM

Table 1. Demographic, clinical, and surgical characteristics

	Number of Cases (n=37)
Age (years)	45.59 (±14.884)
Sex	
Male	24 (64.9%)
Female	13 (35.1%)
Diabetes mellitus	11 (29.7%)
Source of infection	
Odontogenic	32 (86.5 %)
Esophageal	0
Head and neck	5 (13.5 %)
Tracheobronchial	0
Timing of surgery (days after onset)	8.35 (±4.756)
Surgical approach	
Cervicotomy substernal drainage	36 (97.3%)
VATS	1 (2.7%)
Left thoracotomy	0
Right thoracotomy	0
Drain insertion	
Substernal drain	18 (48.6%)
Right / left intrapleural	6 (16.2%)
Substernal and intrapleural	11 (29.7%)
No drain	2 (5.4%)
Down spreading type†	
Anterior mediastinum	24 (64.9%)
Middle mediastinum	3 (8.1%)
Posterior mediastinum	8 (21.6%)
Pleura	0
Mediastinum and pleura	0
Classification	
Type I	19 (51.4%)
Type IIA	2 (5.4%)
Type IIB	13 (35.1%)
Type IIC	3 (8.1%)
Isolated organism	
Klebsiella pneumonia	4 (10.8%)
Pseudomonas aurigenosa	3 (8.10%)
Staphylococcus aureus	3 (8.10%)
Acinetobacter baumanii	3 (8.10%)
Escherichia coli ESBL	3 (8.10%)
Staphylococcus haemolyticus	2 (5.4%)
Streptococcus anginosus	2 (5.4%)
Rothia mucilaginous	2 (5.4%)
Staphylococcus arlettae	1 (2.7%)
Enterobacter cloacae	1 (2.7%)
MRSA	1 (2.7%)
Streptococcus costellatus	1 (2.7%)
Streptococcus alpha hemolytic	1 (2.7%)
Candida glabrata	1 (2.7%)
Not detected	10 (27.0%)
Antibiotic used	
Metronidazole + Ceftriaxone	14 (37.8%)
Metronidazole + Levoflocacin	9 (24.3%)
Metronidazole + Cefoperazone Sulbactam	6 (16.2%)
Metronidazole + Amikasin	3 (8.10%)
Levoflocacin	2 (5.4%)
Metronidazole + Meropenem	1 (2.7%)
Ampicllin Sulbactam	1 (2.7%)
Cefopreazone + Micafungin	1 (2.7%)
Mean ICU length of stay (days)	6.62 (±4.542)
Mean hospital length of stay (days)	11.32 (±8.014)
Preoperative septicemia	37 (100%)
Outcomes	
Survived	19 (51.4%)
Died	18 (48.6%)

Table 2. The comparison between deceased and surviving groups

Variables	Deceased (n=18)	Survived (n=19)	P value
Age (years)	48.39 (±15.162)	42.95 (±14.516)	0.272
Diabetes mellitus	4 (22.2%)	7 (36.8%)	0.331
Timing of surgery (days since onset)	7.39 (±4.754)	9.26 (±4.700)	0.236
Classification			0.105
Type I	8 (44.4%)	11(57.9%)	
Type IIa	2 (11.1%)	0	
Type IIb	5 (27.8%)	8 (42.1%)	
Type IIc	3 (16.7%)	0	
Mean ICU stay (days)	6.56 (±3.944)	6.68 (±5.154)	0.933
Mean hospital stay (days)	6.56 (±3.944)	15.84 (±8.335)	**0.000**[a]

significant p-value based on the Independent T-test analysis.

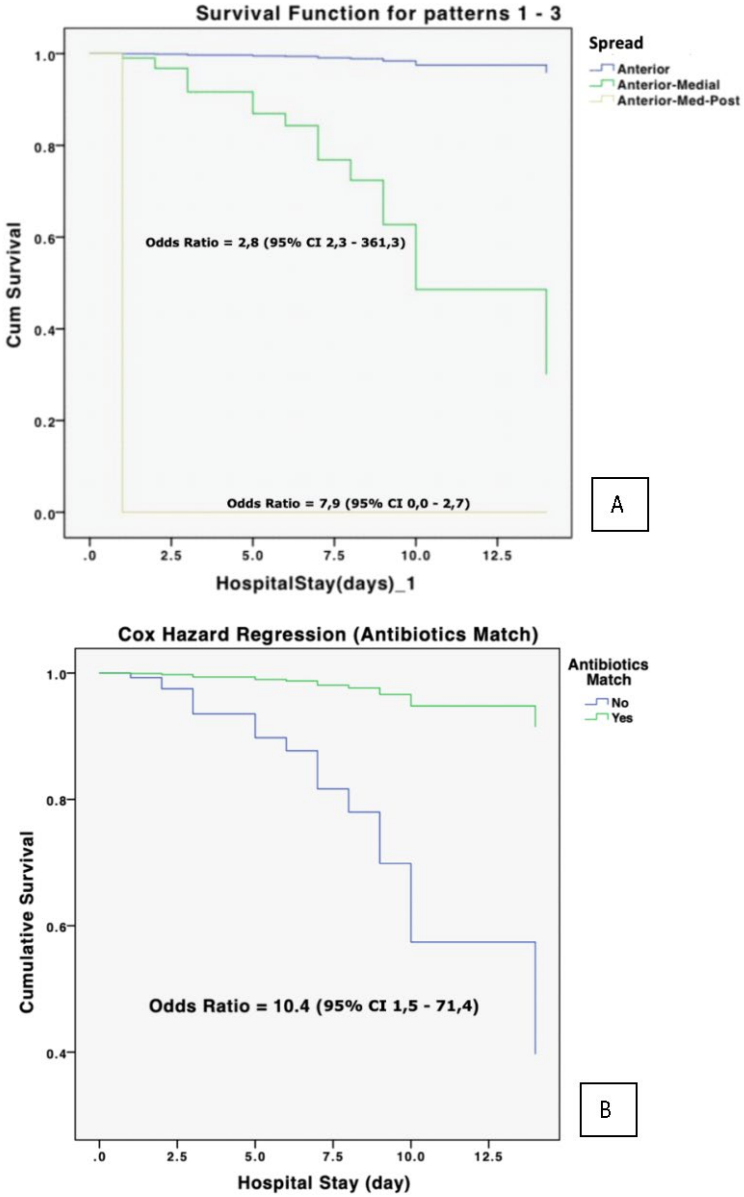

Figure 1. (A) Explain the extent of infection spreading in the mediastinum, have significantly lower the survival rate. (B) Show antibiotics and Culture match confers significant survival benefit in patient with DNM

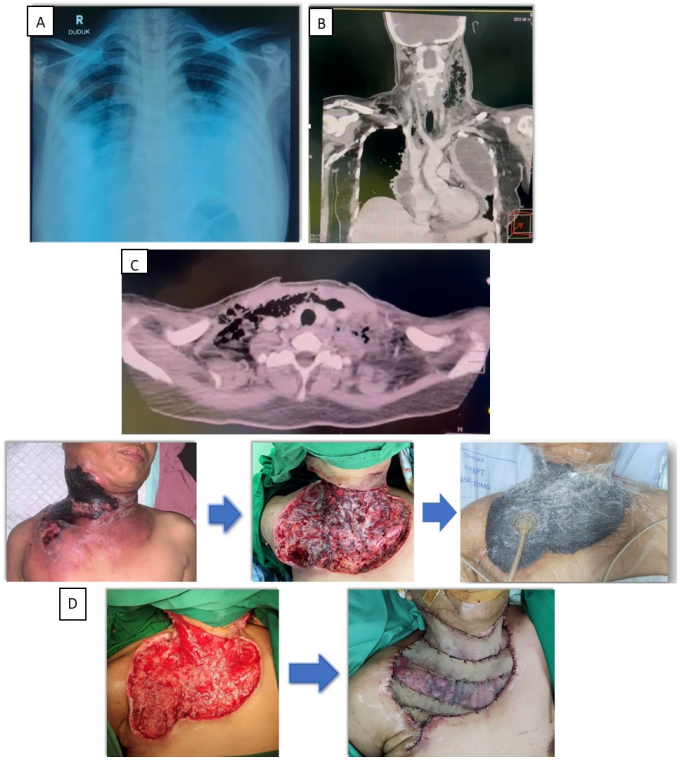

Figure 2. (A) X-ray show widening of mediastinum and bilateral pleural effusion. (B) Show DNM spreading from neck into thoracic cavity resulting loculated empyema. (C) DNM spreading into anterior mediastinum. (D) Surgical debridement has vital role in management of DNM, debridement necrotic tissue and combination with modern wound therapy vacuum dressing and followed by split thickness skin graft to cover wide defect after debridement

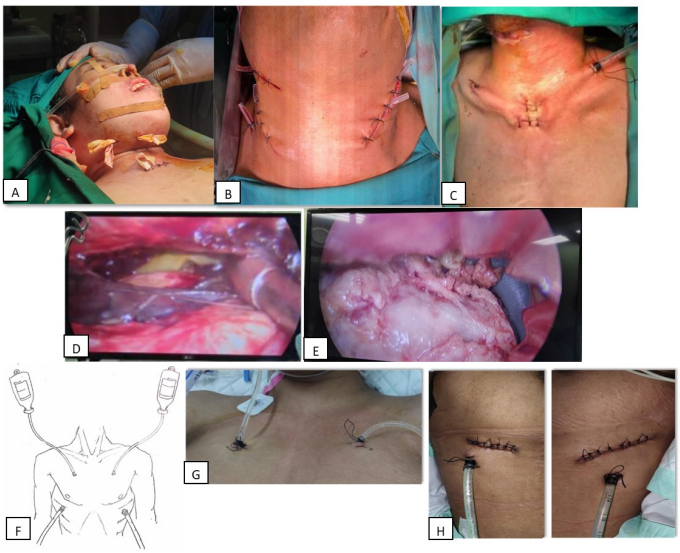

Figure 3. (A) Cervicotomy open the involved cervical space to facilitate drainage of pus**. (B)** Cervicotomy followed by penrose drain to facilate drainage. **(C)** Insertion of mediastinal drain to facilate drainage DNM with spreading into anterior mediastinum or retrosternal involvement. **(D)** VATS decortication and drainage into pleural cavity to ensure effective and minimal invasive medical management. **(E)** VATS facilitate exploration of thoracic cavity show located empyema. **(F)** Thoracic instillation drainage in combination with insertion of thoracic drain, continuous irrigation using normal saline show effective drainage intrathoracic washing. **(G)** Intrathoracic instillation washing to 2nd intercostal space. **(H)** Thoracic instilation in combination with insertion of thoracic drain

patients, found even longer ICU stays of 34.4 days and hospital stays of up to 113 days, although they reported a mortality rate of 0% (0/5) (Uwa et al., 2010). The shorter length of stay in our study could be attributed to several factors, including the presence of a large number of our subjects who unfortunately succumbed to the disease. This can be seen where in the bivariate analysis, the group that died had a significantly reduced length of hospital stay compared to the group that survived (p=0.000). Furthermore, within the deceased group, it was noted that the overall length of hospital stay was equivalent to the length of stay in the ICU. This finding suggests that all subjects in the deceased group died while receiving care in the ICU.

In this study, the other variables examined did not demonstrate statistical significance in predicting mortality. Similarly, in the study conducted by Deu-Martínez et al., which involved a sample size of 43 patients, they also explored possible predictors of mortality, such as diabetes mellitus and other comorbidities. However, their findings indicated that septic shock was the only independent predictor of mortality in their study cohort (Deu-Martín et al., 2010). Meanwhile, other literature has stated that comorbidities, especially DM, were linked to higher mortality rates in DNM cases (Mazzella et al., 2016).

Conclusion

In conclusion, this study highlights the clinical characteristics and predictors of mortality in patients with descending necrotizing mediastinitis (DNM) at Dr. Soetomo Hospital, Surabaya. Odontogenic infections were the primary source of DNM, with a predominance in male patients around the mean age of 46 years. A substantial portion of patients required cervicotomy substernal drainage, emphasizing its role in managing this severe infection. The study underscores the critical importance of early diagnosis and aggressive surgical intervention, as demonstrated by the high mortality rate of 48.6%. Effective management should involve broad-spectrum antibiotics tailored to microbial sensitivity and timely surgical drainage. The findings align with existing literature on the disease's epidemiology, clinical presentation, and treatment, providing valuable insights into DNM management. However, further research is needed to establish standardized guidelines and explore additional therapeutic strategies to improve patient outcomes in similar settings.

Author contributions

K.A.A.A., D.J., and M.R. conceived and designed the study, collected the data, analyzed and interpreted the results, and prepared the manuscript.

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Competing financial interests

The authors have no conflict of interest.

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