Original Article

Analysis of Risk Factors for Loculated Pleural Effusion in Patients with Tuberculous Pleural Effusion at dr. Zainoel Abidin Hospital

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Abstract

Background: Loculated pleural effusion is an effusion that has a lenticular configuration with smooth borders and is relatively homogeneous and can cause atelectasis in the surrounding lung tissue and is a result of excessive inflammation. Tuberculous pleural effusion is characterized by chronic accumulation of fluid and inflammatory cells in the pleural cavity. If not treated appropriately, a loculated pleural effusion can be life-threatening. This study aims to assess risk factors for loculated pleural effusion in TB pleural effusion patients.

Method: This is an observational, analytical research with a cross-sectional design. The research sample was taken based on a consecutive sampling technique from TB pleural effusion patients treated at dr. Zainoel Abidin Hospital, Banda Aceh, from January 2024 to April 2024.

Results: This study shows a relationship between age, kidney failure and diabetes mellitus on the incidence of loculated pleural effusion in TB pleural effusion patients (P<0.05). Age ≥46 years old has a 12.57 times risk, kidney failure 5.50 times and DM 14.5 times against the incidence of loculated pleural effusion. Gender, anemia, human immunodeficiency virus (HIV), pleural fluid analysis results and positive culture did not correlate with loculated pleural effusion (P>0.05).

Conclusion: Age, kidney failure and diabetes mellitus are risk factors for loculated pleural effusion. The increase in age-related risk is associated with chronic inflammation, called inflammaging. Increasing age is also associated with changes in the composition and function of lung cells, making the clearance of pathogens difficult. Intense inflammation and difficulty in clearing pathogens also contribute to the association of kidney failure and diabetes mellitus with loculated pleural effusion.

Keywords: age, diabetes mellitus, kidney failure, loculated pleural effusion, tuberculous

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Submitted: April 25th, 2024
Accepted: September 30th, 2025
Published: October 30th, 2025

J Respirol Indones. 2025
Vol. 45 No. 4: 258-66
https://doi.org/10.36497/jri.v45i4.822

INTRODUCTION

Tuberculosis (TB) is a leading global cause of mortality, with *Mycobacterium tuberculosis* (M.tb) being the causative agent of the infectious illness TB. TB frequently affects the lungs, known as pulmonary TB, but it can also spread to other organs, referred to as extra-pulmonary TB.[1] In underdeveloped nations, TB is a pressing concern and a significant health challenge, accounting for 95% of all TB-related deaths. Based on a WHO survey, Indonesia accounts for a third of the total TB cases in the world, with an incidence is 351,936 cases.[2]

Among extrapulmonary tuberculosis, the pleura ranks as the second most prevalent, following glandular TB.[3] Pleural effusion refers to the buildup of fluid in the space located between the visceral and parietal pleura, whereas tuberculous pleural effusion is defined as the persistent buildup of fluid and inflammatory cells in the pleural cavity.[4]

In non-endemic countries, the occurrence of TB pleural effusion is estimated to be 3–5%. However, in endemic countries, the incidence of TB pleural effusion is significantly higher, reaching 30%. This elevated prevalence is mostly attributed to the large number of persons with HIV, which is the primary source of lymphocytic effusion.[5] However, data also indicate that 80% of pleural effusion instances are attributed to tuberculosis, with cancer being the subsequent cause.[6]

Pleural effusion is known can disrupt the functioning of the cardiorespiratory system. The most prevalent symptom is dyspnea, which is characterized by irregularities in gas exchange, respiratory mechanics, muscle function, and hemodynamics.[6] Pleural effusion alters the equilibrium volume of the lungs and chest wall, resulting in the constriction of airflow, expansion of the chest wall, and compromise of respiratory muscle performance.[7]

Besides, there is a loculated pleural effusion, defined as a condition characterized by a smooth, bordered and rather uniform effusion that might lead to atelectasis in the adjacent lung tissue. Loculation caused by direct infection with M.tb, which consequently triggers an immunological response characterized by delayed hypersensitivity.[8] The presence of loculated pleural effusions can further complicate the process of draining via a chest tube, thereby requiring surgical intervention.[9]

Risk factor of loculated pleural effusions has not much research has been well studied to date. The study conducted by Li Wang et al in 2021 in China has specifically investigated the risk factors for loculated pleural effusion and found that risk factors for loculated pleural effusion in children with pleural TB were shown to be male gender, empyema, and peripheral monocyte count ≤0.46x10^9/L.[11] Another study by Ampow et al in Manado reveals that the most prevalent comorbidities associated with TB pleural effusion are kidney failure, diabetes mellitus (DM), and human immunodeficiency virus (HIV).[12]

Between 2020 and 2023, there were 150 cases of TB pleural effusion treated in specialized TB rooms in dr. Zainoel Abidin Hospital. But there are no studies that identify risk factors for loculated TB effusion. So, this research was conducted for the analysis of risk factors for loculated pleural effusion in patients with tuberculous pleural effusion in dr. Zainoel Abidin Hospital.

METHODS

This research is an observational study with a cross-sectional design, which was conducted at dr. Zainoel Abidin Hospital, Banda Aceh, and approved by the Health Research Ethics Committee of dr. Zainoel Abidin Hospital, Banda Aceh, with number 276/ETIK-RSUDZA/2023.

The inclusion criteria in this research were patients diagnosed with TB pleural effusion based on the Adenosine Deaminase (ADA) test from pleural fluids, complete clinical data, and patients willing to participate in the study (sign informed consent). Meanwhile, the exclusion criteria were patients with ADA levels <40 IU/L and who had cancer, congestive heart disease, pneumonia, or pulmonary embolism.

In this study, used low-frequency 3–5 MHz convex probe ultra-sonography because it has deep penetration, but poor resolution for detecting the presence or absence of localized pleural effusion. So, subjects of the study, who were diagnosed with pleural effusion, underwent thoracic ultrasound to determine the loculation of the effusion. This was followed by pleural fluid sampling via thoracocentesis and analysis of the pleural fluid.

Risk factors included in this study were age, gender, body mass index (BMI), comorbidities such as diabetes mellitus, HIV, and kidney failure, as well as anemia. Additionally, pleural fluid parameter analysis and culture results were also considered. Data was analyzed using SPSS 24.0. Univariate analysis was performed on the frequency distribution and variable proportions. Bivariate analysis was performed to assess the relation of each risk factor to the localized pleural effusion. The Spearman test was used in the bivariate analysis in this study, with $P<0.05$ indicating a relationship between the two variables.

RESULTS

In this study, there were 36 samples that met the criteria. The majority of patients with pleural effusion treated were male (52.8%), young adults (52.8%), from Aceh Besar (41.7%), and working as housewives (27.8%), with a high school education (61.1%). The most common comorbidities were anemia (55.6%), followed by diabetes mellitus (19.4%) and kidney failure (8.3%).

Table 1. Characteristics of the research subjects (n= 36)

Characteristics	n	%
Gender		
Man	19	52.8
Woman	17	47.2
Age	1	3.3
Young Adult (19–39 years)	19	52.8
Middle-aged adults (40–59 years)	13	36.1
Elderly (≥60 years)	4	11.1
Body Mass Index		
Malnutrition	28	77.8
Normal	8	22.2
Employment		
Housewife	10	27.8
Student	7	19.4
Retired	1	2.8
Farmer	1	2.8
Civil servants	8	22.2
Private	9	25.0
Education		
Elementary school	4	11.1
Junior high school	3	8.3
High School	22	61.1
Bachelor	7	19.4
District of Origin		
West Aceh	1	2.8
Southwest Aceh	1	2.8
Aceh Besar	15	41.7
Aceh Jaya	3	8.3
Aceh Tamiang	1	2.8
East Aceh	1	2.8
North Aceh	1	2.8
Biereun	1	2.8
Gayo Lues	1	2.8
Banda Aceh City	8	22.2
Langsa City	1	2.8
Lhokseumawe City	1	2.8
Pidie	1	2.8
Kidney failure		
Yes	3	8.3
No	33	91.7
Anemia		
Yes	20	55.6
No	16	44.4
Diabetes Mellitus		
Yes	7	19.4
No	29	80.6
HIV		
Yes	1	2.8
No	35	97.2
Loculated Tuberculous Pleural Effusion		
Yes	9	25.0
No	27	75.0
Pleural Fluid Culture		
Yes	15	41.7
No	21	58.3

Note: HIV=human immunodeficiency virus

. Pleural fluid analysis showed 41.7% positive culture, mean ADA test value 53.50±16.60, mean PMN cells value of 14.50±13.46, MN cells value of 88.00±13.45, total protein of 5.05±9.17, Albumin of 3.00±1.91, and glucose of 72.08±27.08.

Table 2. Characteristics of research

Characteristics	Mean±Standard Deviation
Age	39.75±15.76
BMI	18.06±0.77
ADA test	53.50±16.60
PMN cells	14.50±13.46
MN cells	88.00±13.45
Total Protein	5.05±9.17
Albumin	3.00±1.91
Glucose	72.08±27.08

Bivariate analysis using Spearman's correlation test showed a statistically significant relationship with moderate strength between age and loculated TB pleural effusion (r=0.500; *P*=0.002). This was tested using the Receiver Operating Characteristic (ROC) curve, which shows the area under the curve (AUC) value, indicating that localized pleural effusion occurred more frequently in the older population. Based on multivariate analysis, age has a significant effect on localized pleural effusion (*P*=0.001).

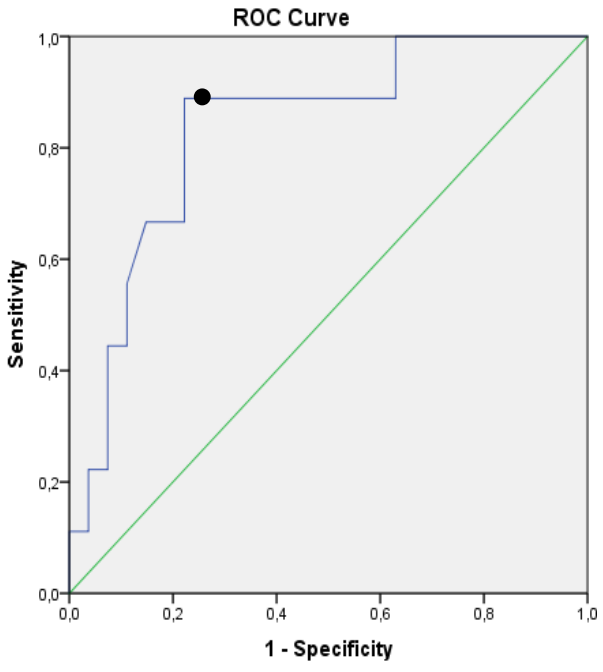

Figure 1. ROC curve analysis of Age on Loculated Pleural Effusion

Table 3. Risk Factor analysis of loculated pleural effusion

Risk Factors	Loculated Pleural Effusion			OR (95% CI)	*r*	*P*
	Yes	No	Total			
Age						
≥46 years old	8 (57.1%)	6 (42.9%)	14 (100.0%)	12.57 (1.757–89.957)	0.500	0.002*
<46 years old	1 (4.5%)	21 (95.5%)	22 (100.0%)			
Gender						
Woman	3 (17.6%)	14 (82.4%)	17 (100.0%)	0.55 (0.165–1.896)	---	0.335
Man	6 (31.6%)	13 (68.4%)	19 (100.0%)			
Body Mass Index						
Malnutrition	7 (25.0%)	21 (75.0%)	28 (100.0%)	1.00 (0.256–3.90)	-0.069	0.690
Normal	2 (25.0%)	6 (75.0%)	8 (100.0%)			
Kidney failure						
Yes	3 (100.0%)	0 (0.0%)	3 (100.0%)	5.50 (2.667–11.342)	0.522	0.001*
No	6 (18.2%)	27 (81.8%)	33 (100.0%)			
Diabetes Mellitus						
Yes	7 (100.0%)	0 (0.0%)	7 (100.0%)	14.50 (3.807–55.225)	0.851	0.0001*
No	2 (6.9%)	27 (93.1%)	29 (100.0%)			
HIV						
Yes	1 (100.0%)	0 (0.0%)	1 (100.0%)	4.37 (2.380–8.041)	0.293	0.083
No	8 (22.9%)	27 (77.1%)	35 (100.0%)			
Anemia						
Yes	7 (35.0%)	13 (65.0%)	20 (100.0%)	2.80 (0.672–11.669)	0.258	0.128
No	2 (12.5%)	14 (87.5%)	16 (100.0%)			
Microorganism Culture Results						
Positive	5 (33.3%)	10 (66.7%)	15 (100.0%)	1.75 (0.562–5.448)	0.163	0.343
Negative	4 (19.0%)	17 (81.0%)	21 (100.0%)			

Note: *statistically significant with *P*<0.05; HIV=human immunodeficiency virus; OR=odds ratio

The results of the ROC curve analysis found that the AUC for age-related incidence of localized pleural effusion was 83.3 (high accuracy). Next, the cut-off point that maximizes the sensitivity and specificity values (black circle) was determined to be 46 (sensitivity, 88.9%; specificity, 22.2%). An odds ratio (OR) analysis was performed, which showed that individuals aged ≥46 years had a risk of 12.57 times greater of developing localized pleural effusion (95% CI=1.757–89.957; P=0.002).

Based on Table 3, a significant risk factor of loculated pleural effusion in this study is kidney failure and diabetes mellitus (*P*<0,05). Patients with kidney failure had a 5.50-fold risk of loculated pleural effusion. Diabetes mellitus had a 14.5-fold risk factor for loculated pleural effusion.

This study revealed incidence of loculated TB pleural effusion yielded a value *P*>0.05, indicating that there was no statistically significant relationship between the PMN cell variables, total protein, albumin, and glucose, nor between the MN cell variables and the ADA test (Table 4).

Table 4. Correlation of Pleural Fluid Analysis Results to the Occurrence of Loculated Pleural Effusion

Pleural Fluid Analysis Results	Loculated Pleural Effusion		*r*	*P*
	Yes	No		
PMN cells	20.0±12.11	13.0±13.94	0.189	0.270
MN cells	80.0±13.44	92.0±13.04	-0.322	0.056
Total Protein	5.4±1.35	2.7±4.9	0.124	0.472
Albumin	4.0±2.55	3.0±1.61	0.197	0.250
Glucose	72.00±33.21	75.0±24.40	-0.189	0.271
ADA test	64.33±17.88	57.66±16.16	0.220	0.198

DISCUSSION

The present study demonstrates a moderate positive correlation between age and the incidence of pleural effusion loculation (r=0.500; *P*=0.002). This finding suggests that age was identified as a risk factor for loculated pleural effusion, where loculated pleural effusion was observed more frequently in the older population. Patients with tuberculous pleural effusion who were aged ≥46 years exhibited a risk of loculated pleural effusion that was up to 12.57 times as high as that of patients aged <46 years (95% CI=1.757–89.957). This finding is not in line with research conducted by Ko et al demonstrates that

age does not correlate with loculation in patients diagnosed with TB pleural effusion (*P*=0.139).[13]

As individuals age, they exhibit heightened basal inflammation, which results in persistent low-grade chronic inflammation, occasionally termed inflammaging. The presence of pathogenic cytokines, such as TNF and IL-6, has been demonstrated to be associated with an increased vulnerability to specific infectious diseases.[14] Furthermore, the process of aging is associated with a series of immune system disruptions that are facilitated by T cells. Consequently, this can lead to a reduction in the body's ability to regulate M. tuberculosis infection.[15]

The present study found no association between gender and loculated pleural effusion (*P*=0.335). The results obtained in this study are consistent with those previously reported by Ko et al.[13] Males and females differ in their immunological responses to antigens. While certain immune variations based on sex manifest throughout an individual's lifetime, others are only observed after puberty and before reproductive senescence.

This study has no association between body mass index and loculated pleural effusion (*P*=0.690). The presence of body weight below the normal range (underweight) may suggest nutritional insufficiency. Malnutrition, characterized by insufficient protein and calorie intake, reduces the effectiveness of the cellular immune system and many innate host defensive mechanisms that can be employed to protect against M.Tb. Protein-calorie malnutrition leads to a secondary immunodeficiency condition that heightens the susceptibility to TB infection. The research conducted by Cho et al demonstrates that the occurrence of TB rises in correlation with the severity of underweight, suggesting that deteriorating dietary conditions worsen immunological deficiencies.[16]

The present study established a correlation between kidney failure and the incidence of loculated pleural effusion. The relationship between kidney failure and loculated TB pleural effusion is moderate in strength and exhibits a positive direction (r=0.522; *P*=0.001) with an odds ratio of 5.50 (95% CI=2.667–11.342). This finding indicates that patients with kidney failure exhibit a 5.50-fold increased risk of developing TB pleural effusion. Immunodeficiency is a concomitant of kidney failure, which in turn renders patients more susceptible to TB reactivation or new infections.[12]

End-stage kidney failure has been demonstrated to be associated with a number of changes in the immune system, which have been shown to result in increased levels of anti-inflammatory cytokines, such as IL-10, and pro-inflammatory cytokines, such as TNF-α and IL-6. Cytokine accumulation is a detrimental consequence of the clearance of the kidneys and increased production. Altered immunity has been demonstrated to be associated with uremic toxins, oxidative stress, volume overload, and other comorbidities.[17]

The present study has demonstrated a strong positive relationship between DM with loculated tuberculous pleural effusion. The correlation coefficient (r) for this relationship is 0.851 and *P*=0.0001. The odds ratio demonstrated that patients with DM exhibited a 14.50-fold elevated risk of loculated tuberculous pleural effusion (95% CI=3.807–55.225).

Diabetes mellitus has been demonstrated to be a contributing factor to the heightened susceptibility to TB infection. It is estimated that approximately one-third of individuals diagnosed with DM also carry TB infection. It has been demonstrated that individuals suffering from DM on a long-term basis are exposed to a 2–3-fold elevated risk of contracting tuberculosis in comparison with those not afflicted by this chronic condition.[18]

Glucotoxicity in DM has been demonstrated to result in a decrease in immune system function and an increase in tissue vulnerability to damage. Glucotoxicity is defined as the process of damage that arises from the adverse effects of chronic hyperglycemia. The disruption of activity and the weakening of cellular immune function can impede the capacity of immune cells to obstruct and phagocytose M.tb germs that infect the body. Consequently, the proliferation of these germs perpetuates the progression of TB disease within the individual.[18]

The present investigation found no statistically significant association between HIV and loculated pleural effusion (*P*=0.083; OR=4.37). This may be attributed to the limited selection of samples containing HIV-positive individuals, namely, only one sample. In this study, the single sample exhibited a picture of loculated TB pleural effusion (Figure 2). The odds ratio also demonstrated a 4.37-fold increase in the incidence of loculated TB pleural effusion in HIV patients.

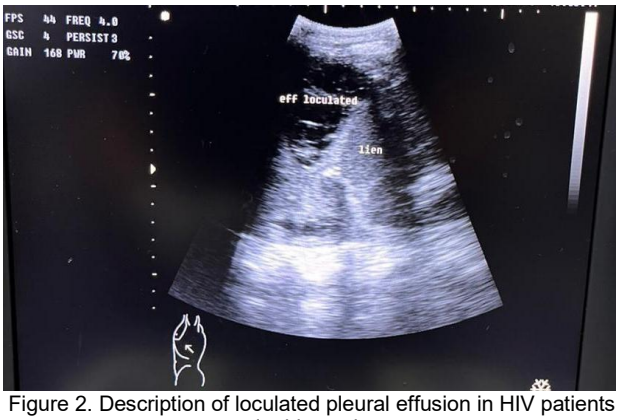

Figure 2. Description of loculated pleural effusion in HIV patients in this study

In patients with an inadequate immune system, for example, those with HIV, this can result in the manifestation of atypical signs and symptoms. In patients with both tuberculosis and HIV, the presence of cavitations is typically not detected on chest radiographs. Despite the absence of significant tissue damage due to the host's immune response in TB-HIV patients, the diminished immune response renders these patients more susceptible to TB bacterial proliferation and dissemination. This can be observed in the chest X-ray of a patient with TB miliary, a condition that is frequently observed in patients with both TB and HIV.[12,20]

Heller et al stated that pathological findings in tuberculous pleural effusion in patients with HIV showed an anechoic appearance, and there was black fluid at the costophrenic angle. This finding is a pleural effusion, which is generally completely free of echoes but may contain internal echoes such as strings or smoke caused by fibrinous structures or cells in the effusion. Pleural effusion in an HIV-positive patient is highly suggestive of a sign of TB, especially if unilateral.[21]

In the present study, the incidence of loculated pleural effusion was not found to be associated with anemia (*P*=0.128; OR=2.80). The OR indicates that patients diagnosed with anemia are 2.80 times more likely to develop pleural effusion with loculated tuberculosis. Empirical data from recent decades are conclusive that iron is an essential element for the proper maturation of the immune system.[22]

An essential function of iron in the immune system is to facilitate the growth of immune cells, particularly lymphocytes, which are involved in developing a targeted response to infections. The impact of iron deficiency on humoral immunity is less pronounced in comparison to that of cellular immunity. Monocyte/macrophage differentiation is dependent on iron, with macrophages relying on iron as a cofactor to execute crucial antimicrobial effector processes, such as nicotinamide adenine dinucleotide phosphate hydrogen.[22]

The anemia observed in this study may be attributable to the tuberculosis infection itself. Increased inflammation in patients with TB has been shown to result in impaired hemoglobin synthesis, leading to anemia of chronic disease. Severe anemia has been observed to increase susceptibility to bacteremia. Severe anemia heightens the susceptibility to invasive germs through several mechanisms, including enhanced intestinal permeability, compromised immunological response, and heightened iron/heme availability to combat pathogenic bacteria.[23]

The investigation of the pleural fluid revealed the following mean values: PMN cells were 14.50±13.46, for MN cells 88.00±13.45, for total protein 5.05±5.17, for albumin 3.00±1.91, and for glucose 72.08±27.08. In this study, it was found that there were no significant differences between the results of pleural fluid analysis, both PMN cells, MN cells, total protein, albumin, glucose and ADA test, in patients with loculated and without loculated pleural effusion (P>0.05). This result is different from Ko et al, who found that glucose levels were significantly related to loculated pleural effusion, with higher glucose levels found in loculated patients (82.0 vs. 96.0), and other analysis results, such as pH, protein,

albumin, LDH, ADA and CRP, were not related to loculated TB pleural effusion[13]

The present study examined a cohort of individuals diagnosed with tuberculous pleural effusion, whereby it was observed that all samples of pleural fluid contained exudates. It is widely accepted that pleural fluid can be categorized as either transudate or exudate. Transudate is derived from membrane ultrafiltration and contains low protein, while exudate is formed from active secretion or membrane leakage and contains high protein. The presence of transudate effusion indicates a non-inflammatory process caused by disturbances in hydrostatic pressure or colloid osmotic pressure, without involvement of pleural disease. Meanwhile, exudate fluid is indicative of the involvement of the pleura in an inflammatory or malignant process, which in turn causes increased capillary permeability.[24]

Levels of pulmonary fluid proteins are elevated to a significantly greater degree in cases of tuberculosis than in cases resulting from malignancies or non-tuberculous infections. The levels of proteins in pleural fluid are significantly elevated in cases of tuberculosis in comparison to other pathological conditions. The assessment of pleural fluid protein levels has been demonstrated to facilitate the diagnosis of tuberculous pleural effusion.[25]

The results of microorganism culture from pleural fluid samples were not related to the incidence of loculated pleural effusion in this study (r=0.163; *P*=0.343). The majority of patients with positive and negative culture results did not show loculated pleural effusion. Patients with positive microorganism culture results have been shown to have a 1.75 times greater risk of loculated TB pleural effusion.

This result is in line with Ko et al, who indicated an association between positive culture results and the incidence of loculated pleural effusion, with a 26.87-fold increase in positive culture results in loculated TB pleural effusion compared with the population devoid of loculation (OR=26.878; 95% CI=12.209–59.172; *P*<0.001).[13]

In this study, the positive microorganism culture results obtained in this study indicated the possibility of coinfection by additional pathogens other than M.tb. Furthermore, patients with tuberculosis frequently experience bacterial coinfections, which have been linked to a higher likelihood of death. Coinfection has been demonstrated to result in an elevated bacterial load and intense inflammation of the lungs. The underlying cause of loculated pleural effusion is chronic inflammation.

Furthermore, coinfection with other infections has been demonstrated to increase the susceptibility of tuberculosis to more severe pulmonary manifestations. The immunological response of the host may exert a significant influence on the extent of lung injury. One potential explanation for this phenomenon is the presence of heightened inflammation and elevated levels of lung matrix-degrading proteases that arise during infection.

Tuberculosis co-infection with other bacterial infections, such as *Klebsiella* and *Pseudomonas*, has been demonstrated to exacerbate the severity of TB and increase the likelihood of encountering complications. Furthermore, there is an increasing recognition of mixed infection TB with *Aspergillus* and non-tuberculous mycobacteria (NTM) in cases of lung infections. Concurrent infections can result in more severe pulmonary tissue injury and an extended period of therapy.[27]

An investigation conducted in Cambodia revealed that 33% of 40 patients who tested positive for TB in their sputum also had co-infection with other microorganisms. The most prevalent microorganisms isolated are Gram-negative bacilli, specifically *Klebsiella* and *Pseudomonas spp*. Approximately 11% of patients suspected of having pulmonary tuberculosis had isolated growth of NTM in sputum culture, according to the findings of another study.[27]

The presence of pleural effusion in cases of tuberculosis is more likely to be the result of type IV hypersensitivity than direct infection with M.tb of the pleural cavity. As time elapses, the difficulty of obtaining positive culture results decreases. That is

due to the effusion becoming increasingly lymphocyte-dominant and mycobacterial, indicating viable contamination. This may be the underlying reason for the absence of a relationship between positive culture results and loculated TB pleural effusion.

LIMITATIONS

In this study, there are several limitations to the research, namely that this study was conducted by assessing all the risk factors that allow loculated pleural effusion to occur, so that the role of each risk factor may overlap in causing loculated tuberculous pleural effusion. This research can be developed by assessing each risk factor in depth with inclusion and exclusion criteria that can minimize bias due to other risk factors.

CONCLUSION

This study found that factors age, kidney failure and diabetes mellitus are significant for the incidence of loculated pleural effusion in tuberculous pleural effusion patients.

ACKNOWLEDGEMENT

The authors would like to thank Prodia and colleagues who assisted the author in collecting data for this research.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

FUNDING

The authors funded this research.

REFERENCES

1. Raviglione M, Sulis G. Tuberculosis 2015: Burden, challenges and strategy for control and elimination. Infect Dis Rep. 2016;8(2):6570.
2. Dinas Kesehatan Aceh. Laporan kinerja Dinas Kesehatan Aceh tahun 2023. Banda Aceh; 2023.
3. Lo Cascio CM, Kaul V, Dhooria S, Agrawal A, Chaddha U. Diagnosis of tuberculous pleural effusions: A review. Respir Med. 2021;188:106607.
4. Zhai K, Lu Y, Shi H zhong. Tuberculous pleural effusion. J Thorac Dis. 2016;8(7):E486–94.
5. Shaw JA, Diacon AH, Koegelenberg CFN. Tuberculous pleural effusion. Respirology. 2019;24(10):962–71.
6. Thomas R, Jenkins S, Eastwood PR. Physiology of breathlessness associated with pleural effusions. 2015;21(4):338–45.
7. Mitrouska I, Klimathianaki M, Mitrouska I, Klimathianaki M. Effects of pleural effusion on respiratory function. Can Respir J. 2004;11(7):499–503.
8. Tucker TA, Idell S. Update on novel targeted therapy for pleural organization and fibrosis. Int J Mol Sci. 2022;23(3):1587.
9. Esmadi M, Lone N, Ahmad DS, Onofrio J, Brush RG. Multiloculated pleural effusion detected by ultrasound only in a critically-ill patient. American Journal of Case Reports. 2013;14:63–6.
10. Kennedy F. Beyond “prevention is better than cure”: Understanding prevention and early intervention as an approach to public policy. Policy Design and Practice. 2020;3(4):351–69.
11. Wang JL, Zhou M, Zhang YA, Wang MS. Loculations and associated risk factors of childhood pleural tuberculosis. Front Pediatr. 2021;9:781042.
12. Ampow AT, Timban JFJ, Rondo AGEY. Gambaran foto toraks pasien tuberkulosis paru dengan efusi pleura di RSUP Prof. Dr. R. D. Kandou periode Januari – Juni 2022. Medical Scope Journal. 2023;5(1):57–63.
13. Ko Y, Kim C, Chang B, Lee SY, Park SY, Mo EK, et al. Loculated tuberculous pleural effusion: Easily identifiable and clinically useful predictor of positive mycobacterial culture from pleural fluid. Tuberc Respir Dis (Seoul). 2017;80(1):35–44.

14. Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626–38.
15. Orme IM, Griffin JP, Roberts AD, Ernst DN. Evidence for a defective accumulation of protective T cells in old mice infected with mycobacterium tuberculosis. Cell Immunol. 1993;147(1):222–9.
16. Cho SH, Lee H, Kwon H, Shin DW, Joh HK, Han K, et al. Association of underweight status with the risk of tuberculosis: A nationwide population-based cohort study. Sci Rep. 2022;12:16207.
17. Ganmaa D, Uyanga B, Zhou X, Gantsetseg G, Delgerekh B, Enkhmaa D, et al. Vitamin D supplements for prevention of tuberculosis infection and disease. New England Journal of Medicine. 2020;383(4):359–68.
18. Ashenafi S, Bekele A, Aseffa G, Amogne W, Kassa E, Aderaye G, et al. Anemia is a strong predictor of aasting, disease severity, and progression, in clinical tuberculosis (TB). Nutrients. 2022;14(16):3318.
19. Hof A, Geißen S, Singgih K, Mollenhauer M, Winkels H, Benzing T, et al. Myeloid leukocytes' diverse effects on cardiovascular and systemic inflammation in chronic kidney disease. Basic Res Cardiol. 2022;117(1):38.
20. Paul K, Kretzschmar D, Yilmaz A, Bärthlein B, Titze S, Wolf G, et al. Circulating dendritic cell precursors in chronic kidney disease: A cross-sectional study. BMC Nephrol. 2013;14(1):274.
21. Heller T, Mtemang'ombe EA, Huson MAM, Heuvelings CC, Bélard S, Janssen S, et al. Ultrasound for patients in a high HIV/tuberculosis prevalence setting: A needs assessment and review of focused applications for Sub-Saharan Africa. International Journal of Infectious Diseases. 2017;56:229–36.
22. Muchtar NH, Herman D, Yulistini Y. Gambaran faktor risiko timbulnya tuberkulosis paru pada pasien yang berkunjung ke unit DOTS RSUP Dr. M. Djamil Padang tahun 2015. Jurnal Kesehatan Andalas. 2018;7(1):80–7.
23. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 diabetes and its impact on the immune system. Curr Diabetes Rev. 2019;16(5):442–9.
24. Andrade C. Sample size and its importance in research. Indian J Psychol Med. 2020;42(1):102–3.
25. DeRiemer K, Kawamura LM, Hopewell PC, Daley CL. Quantitative impact of human immunodeficiency virus infection on tuberculosis dynamics. Am J Respir Crit Care Med. 2007;176(9):936–44.
26. Mohamad WMW, Ab Rahman WSW, Al-Salih SAA, Hussin CMC. Immunological and haematological changes in HIV infection. In: Trends in Basic and Therapeutic Options in HIV Infection - Towards a Functional Cure. InTech; 2015.
27. Abuga KM, Nairz M, MacLennan CA, Atkinson SH. Severe anaemia, iron deficiency, and susceptibility to invasive bacterial infections. Wellcome Open Res. 2023;8:48.