Original paper

Aetiology and Management Practices of Pleural Effusions among Hospitalized Adult Patients at a Referral Facility in Kenya: A 5-Year Retrospective Study

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Abstract

Background: Pleural Effusion (PE) is a condition associated with significant mortality and morbidity, with varying aetiologies influenced by geography, patient age, and time trends. The variations in aetiologies of PE according to time necessitate the need to investigate the current trends of causation, and management of pleural effusion in Kenya.
Objective: This study described the common practices of care of patients presenting with PE at Kenyatta National Hospital in Kenya.
Methodology: We utilized a retrospective cross-sectional design, involving 1234 patients admitted with PE at Kenyatta National Hospital (KNH) between January 2018 and December 2022. The data collected included information on aetiology, presentation, management practices, length of stay, and mortality associated with PE. SPSS version 25 was used for data analysis. Continuous data was described using means and standard deviation. Proportions were utilized in describing the categorical variables. Logistic regression model was applied on significant variables to assess for independent risk factors for mortality due to pleural effusion and results to be reported in odds ratios and the associated 95% confidence interval.
Results: The predominant presenting symptoms was dyspnea (80.1%). Exudative effusions were the most common (65.8%), with tuberculosis being the primary cause of infectious effusions. Among transudative effusions, heart failure (53.0%) was the most common cause. Intercostal chest drainage, with large bore tubes, was a common therapeutic intervention. The average length of hospital stay was 18.57 days, and the mortality rate was 12.4%.
Conclusions: Pleural effusions remain to be the most common with infectious aetiology as the predominant cause. There still remains a huge gap in unreported data and adoption of electronic data entry may be a solution to this challenge.

Key words: Pleural effusion, Aetiology, Management, Outcomes

Introduction

Pleural Effusion (PE) refers to the pathological accumulation of fluid in the space between the layers of the pleura. Broadly, PE can be categorized as either being transudative or exudative effusion (1). Transudative effusion results from a rise in the hydrostatic pressure or a drop in the plasma oncotic pressure whereas exudative effusion results from an increase in capillary permeability. The two are differentiated using Light's criteria which terms exudative effusion by the presence of either one or more of the following conditions: levels of protein in the pleural fluid or protein in the serum more than 60%, (2) Lactic Acid Dehydrogenase (LDH) in the pleural fluid or LDH levels in the serum more than 60%, or (3) LDH level in the pleural fluid more than 67% the upper reference range for the levels of LDH in serum(2). This differentiation is important in understanding the aetiologies of a particular PE.

For instance, the presence of a transudative PE points the aetiology to systemic factors which affect either hydrostatic or oncotic pressures while an exudative effusion points to local factors that affect the integrity of capillaries (2). Systemic conditions responsible for transudative effusion include congestive heart failure, cirrhosis and hypoalbuminemia. On the other hand, local factors such as neoplasia and infectious

diseases are responsible for exudative effusion (3). The most prevalent cause of pleural effusion in a set up varies depending on local epidemiologic profile of underlying causes. In the USA, pleural effusion is most commonly caused by Congestive Heart Failure (CHF). The other causes include pleural infection and malignancy (2). In developing countries however, complicated bacterial infection is the leading cause (4). In Africa, pleural effusion is a significant health concern, often associated with infectious diseases such as tuberculosis and HIV/AIDS. East Africa, including countries like Kenya, has a relatively high prevalence of pleural effusion due to the endemic nature of tuberculosis. It is estimated that TB is responsible for up to 50% of all pleural effusions in the region (5).The burden is further exacerbated by limited access to healthcare resources and diagnostic tools. In the Middle East, pleural effusion is seen in conjunction with a variety of aetiologies, including infections, malignancies, and cardiovascular diseases, in line with the region's epidemiological diversity (5,6). The epidemiology of pleural effusion is complex and constantly evolving. As the global burden of disease changes, so too does the distribution of the underlying causes of pleural effusion. There is limited current data on the aetiology of PE in developing countries thus the need for further studies. Improved health care system performance has been associated with a decreased incidence of PE over the last seven years (7). In order to minimize death and morbidity from PE, physicians need to be updated with the common aetiologies of PE. This will not only enable them choose the correct diagnostic test but also help them to accurately interpret them. (1).

Dyspnea may be the only presenting symptom in PE. On physical examination, dullness to percussion may increase the clinical index of suspicion (8). Imaging serves as a reliable tool in the evaluation of PE as it helps in suggesting the aetiology. Both chest X-ray and Thoracic Ultrasonography (TUS) are used, however, TUS is the imaging modality of choice as it is more sensitive. Furthermore, thoracic ultrasonography is able to distinguish fluid in the pleural space from consolidation within the pleura and pleural thickening (8). Further, TUS guided thoracentesis precedes pleural fluid analysis which is important in distinguishing between transudative and exudative effusions mentioned earlier (8). There exists a dearth of local published data on diagnostic methods for PE hence a need to document the experience of clinicians in handling this condition. Furthermore, there is no local guideline directed management of PE. This study aims at describing the common practices of care of patients presenting with PE at National Hospital in Kenya.

Materials and methods

This was a retrospective chart review of patients who presented with pleural effusion between January 2018 and December 2022 at the Kenyatta National Hospital. The study population comprised of patients aged 18 years and above and with a diagnosis of PE. Medical records for patients in medical, surgical, and oncology wards were retrieved from the hospital registry and abstracted into a data collection tool. All files of patients who presented with PE during the study period were retrieved. Files with missing data with incomplete information were noted and a report of missing, unreported or incomplete data was presented as part of the results. Sociodemographic information (age, sex, social class, smoking), clinical features (dyspnea, chest pain), aetiology, risk factors, comorbid conditions such as hypertension and diabetes mellitus, HIV, cancer, duration of hospital stay were extracted. Findings at admission (dyspnea, chest pain, cough), pleural fluid biochemistry (total protein, LDH, glucose), cytological, histopathological, and microbiological results were also obtained. Other blood biochemistries including liver function tests (albumin levels), imaging modalities, drugs used, tubes used (small or large bores) and surgery done were also documented. Length of stay as a measure of morbidity and mortalities was also reported.

The analysis of data was conducted using Microsoft Excel 2023 and SPPS version 25. To evaluate the normality of the data, histograms and probability plots, such as Quantile-Quantile (QQ) plots, were employed. Following this, parametric tests were applied to data that displays a normal distribution. Descriptive statistics were calculated, including proportions for categorical data and means for continuous data that followed a distribution that is normal. This included proportions for the different causes of exudative and transudative pleural effusions as well as the diagnostic and management interventions for the adult patient. The sociodemographic profile including sex, smoking history, and HIV status were described using proportions. Effusion sides was also describe using proportions. Mean was used to described the age. Frequencies were used to describe the occurrence of the various symptoms of PE. Logistic regression model was employed to identify the independent risk factor for mortality. Ethical approval was obtained from the Kenyatta National Hospital-University of Nairobi Ethics and Review Commission (REF: KNH-ERC/A/481).

Table 1: Sociodemographic profile of patients

Sex	Proportion
Male	622 (50.4%)
Female	612 (49.6%)
Age	Mean 46.72 ±18.33 years
Smoking history	
Smokers	65 (5.3%)
Non smokers	831 (67.3%)
Unreported	338 (27.4%)
HIV status	
Seropositive	68 (5.5%)
Seronegative	880 (71.3%)
Unreported	286 (23.2%)

Results

Sociodemographic characteristics of study participants: A total of 1234 files were retrieved. Of these, 622 (50.4%) were males while 612 (49.6%) were females as shown in Table 1. The mean age of the patients included in the study was 46.72 ± 18.33 years, with a range of 13 to 95 years. The summary of the sociodemographic characteristics of the patients is provided in Table 1.

Clinical presentation of patients with pleural effusion at KNH: Five hundred and eighty four (47.3%) of the cases were right sided effusions, 404 (32.7%) on the left, 201 (16.3%) bilateral while the rest 45 (20%) were unreported (Figure 1). The most common presenting symptoms was dyspnea in 988 (80.1%) of the patients, followed by cough in 884 (71.6%) and lastly chest pain in 837 (67.8%) (Figure 2). Thoracentesis was done in 1019 (82.6 %) out of the 1234 cases with biochemistry on the pleural fluid done on only 628 (61.6%) of them. Out of the 1234 cases, the most common type of pleural effusion was exudative accounting for 812 (65.8%) of the cases. Only 207 (16.8%) of the effusions were transudative while the rest constituting 215 (17.4%) of cases were unreported. Of the patients with TB, the average age was 37±15.7 years with 50% of them having HIV-TB co-infection.

Figure 1: Distribution according to the effusion side

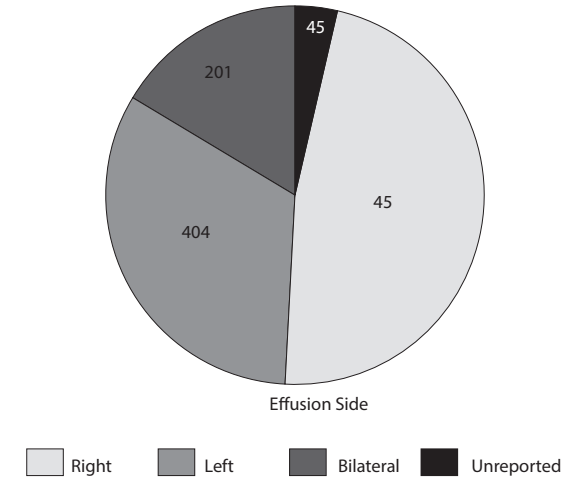
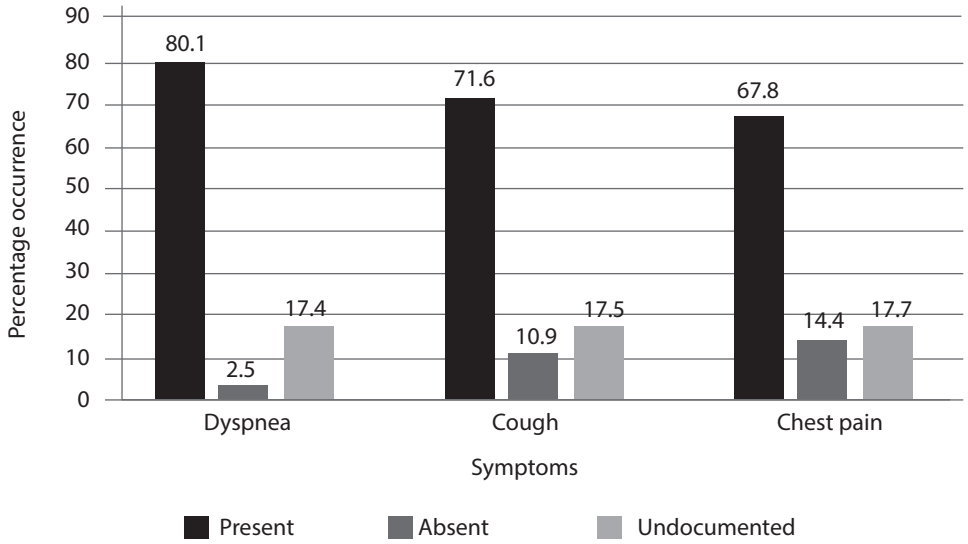
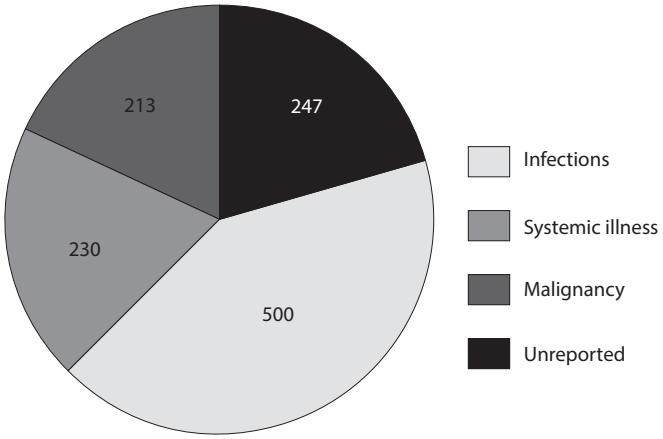


Figure 2: Commonly reported symptoms



Aetiology of pleural effusion: Infections were the major cause of PE accounting for 500 (42%) of the cases. Systemic conditions and malignancy accounted for 230 (19.3%) and 213 (17.9%) respectively as the causes of the PE while the rest of the 247 (20.7%) of cases were unreported (Figure 3).

Figure 3: Major causes of pleural effusions at KNH



Bacterial infections dominated with TB being the commonest cause of exudative effusions causing 318 (63.6%) of the infectious effusions followed by bacterial pneumonia and empyema with 131 (26.2%) and 37 (7.4 %) respectively. Viral cases were fewer with only 13 (2.6%) positive cases in which 11 were due to Covid-19. Only one (0.2%) case was as a result of parasitic infection (Figure 4).

Breast and lung cancers accounted for 99% of the effusions caused by malignancies with their absolute numbers as 122 and 88 cases respectively. Heart failure was the major cause of transudative effusions accounting for 110 (53%) of cases caused by systemic conditions. Renal and hepatic diseases accounted for 71 (34.3%) and 20 (10%) respectively. Other systemic conditions with variable positivity included Connective Tissue Disease (CTD), hypothyroidism and pulmonary embolism (Figure 5).

Figure 4: Infectious causes of pleural effusion

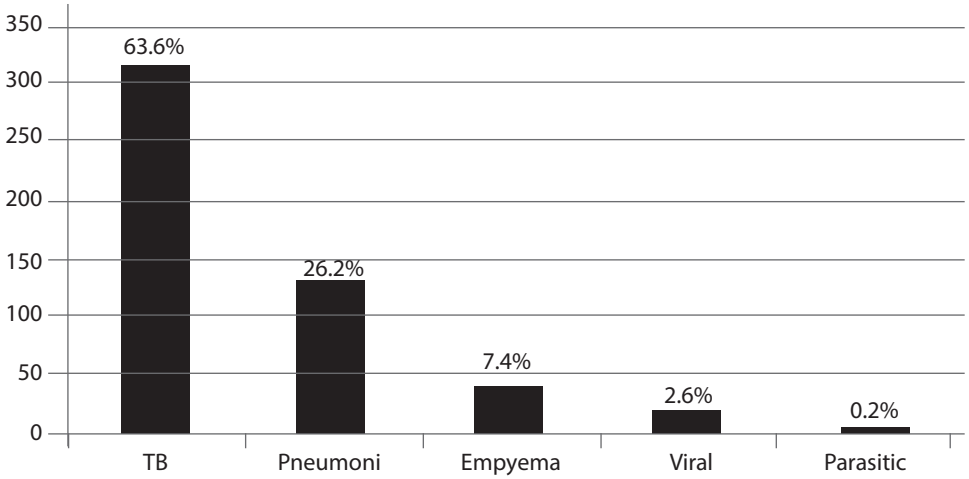
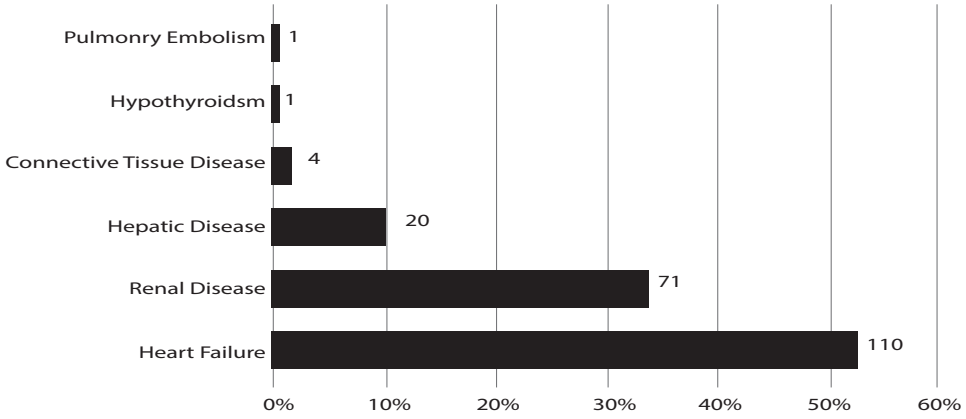


Figure 5: Systemic causes of pleural effusion at KNH

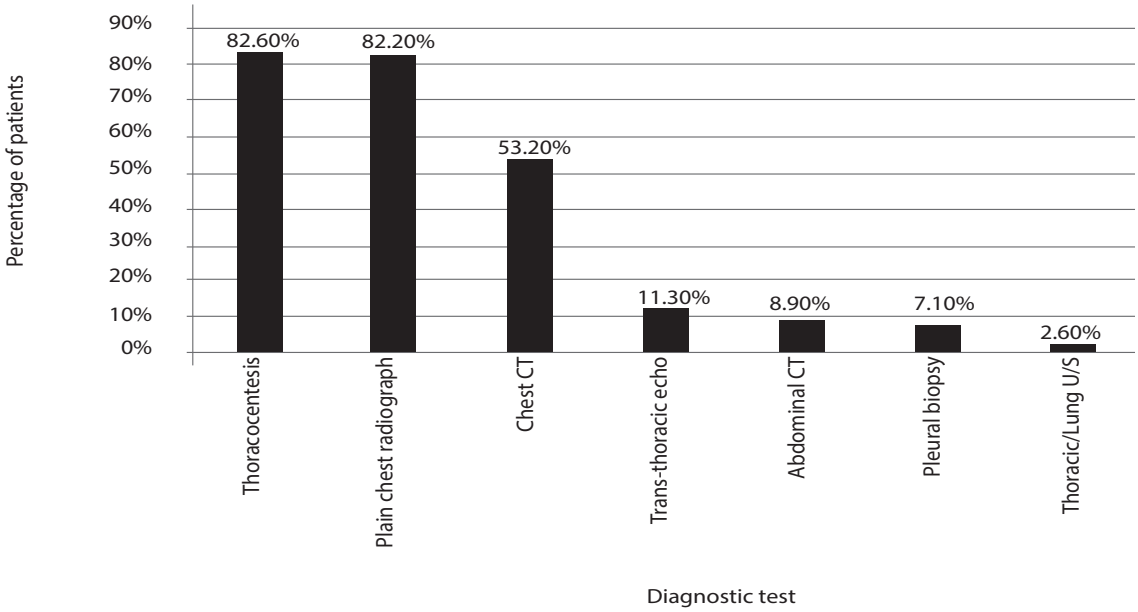


Diagnostic interventions among adult patients

Of the infectious causes of pleural effusion identified as TB (318), only 38 (11.9%) were confirmed either via Gene expert or pleural biopsy. Diagnostic thoracentesis was done in 1019 (82.6%) of the patients. Plain chest radiography was done in 1014 (82.2%) of the patients, CT scan of the chest in 657 (53.2%), CT abdomen in 110 (8.9%), Transthoracic-echocardiography in 139 (11.3%) and a thoracic/lung ultrasound in 32 (2.6%) (Figure 6).

A pleural biopsy was performed in 87 (7.1%) cases and histopathological findings documented. Two cases were reported as pulmonary adenocarcinoma, one as pleural adenocarcinoma, one as gastric adenocarcinoma while the rest of the 11 cases of adenocarcinomas were unspecified. Two cases had atypical metastatic mesothelial cells, 23 cases showed features of chronic inflammation, eight cases were acute inflammation while metastatic carcinomas were confirmed in 17 cases. Of the carcinomas, eight were lung carcinomas and nine were pleural.

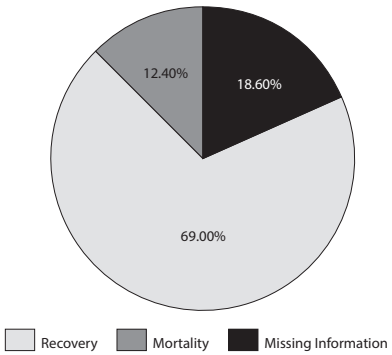
Figure 6: Distribution of diagnostic tests



Management of pleural effusion at KNH: Drainage of fluid was done in 1014 (82.2%) of the cases. A large pore tube was used in 736 (72.6%) patients while 97 (9.6%) were done using small pore tubes and unspecified in the remaining 181 (17.8%). Antibiotics alone were administered in 642 (52%) of the patients while diuretics alone were administered in 139 (11.3%) of the patients. Definitive management using both antibiotics and diuretics were administered to 116 (9.4%) of the patients. Pleurodesis was done in 86 (40.4%) of the patients with malignant effusions. Chemical pleurodesis was performed in 77 (89.5%) of these, no patient underwent mechanical pleurodesis while the type of pleurodesis done was not specified in 9 (10.5%) patients. The most commonly used agent was bleomycin. Other agents included; Doxycycline, iodine, iodine with normal saline and betadine.

Pleurodesis was reported successful in 76 (88.3%) of the 86 patients and unsuccessful only in 1 (1.2%) patient. The rest of the 9 (10.5%) patients had missing information on the success of the procedure. Recovery was recorded in 852 (69.0%) of the patients while 153 (12.4%) patients died. Mortality was observed in 137 (15.7%) of patients with exudative effusions and 16 (10.6%) in transudative effusions. The rest of the files had missing information on the outcome (Figure 7). The mean recovery time was 18.57±31.8 days, 19.9±15.7 days in exudative effusions and 24.4±81.7 days in transudative effusions.

Figure 7: Outcomes of patients treated for pleural effusions at KNH



Pleural effusions caused by TB, pneumonia and Covid-19 were associated with significantly increased risk of mortality (OR 0.457, 0.453 and 5.625 respectively) (Table 2).

Table 2: Logistic regression for independent risk factor for mortality

Risk factor	Adjusted Odds Ration	P-value
Tuberculosis	0.457	0.008
Pneumonia	0.453	0.030
Empyema	2.201	0.060
Parasitic	0.609	0.814
Covid-19	5.625	0.007
Other viral infections	0.0.655	0.842
Breast cancer	0.857	0.420
Lung cancer	1.215	0.303
Heart failure	1.300	0.668
Renal disease	0.818	0.713
Hepatic disease	1.147	0.862
Connective tissue disease	0.001	0.886
Chylothorax	0.145	0.880
Hypothyroidism	0.000	0.939
Pulmonary embolism	0.000	0.938
Age	0.996	0.444
Sex	1.109	0.601

Discussion

This study sought to document the aetiology, diagnostic and management interventions of pleural effusions of adult patients presenting at KNH. The study also determined the outcomes of adult patients treated for PE at KNH. TB and heart failure were the commonest causes of exudative and transudative PE respectively. On the other hand, diagnostic thoracentesis was the most utilized method to diagnose patients in line with the British Thoracic Society guidelines. The most utilized management interventions were drainage and antibiotics alone. The mean recovery time was 18.57 days with a mortality of 12.4%.

Socio demographic characteristics: The mean age of patients in this study was 46.72 years, which aligns with previous findings that pleural effusion is most commonly diagnosed in middle-aged and older individuals (9). Occurrence of pleural effusions was more significant among males compared to females, consistent with findings by Ibrahim *et al* (1). Interestingly, only 5.3% of patients had a positive smoking history. However, a substantial number of patients did not report their smoking and HIV status (27.4% and 23.2% respectively), indicating potential underreporting of crucial information. This underreporting could be due to cultural or societal factors, emphasizing the need for patient education

and awareness campaigns and development of a standardized tool to collect data routinely.

Clinical presentation of patients with PE at KNH: The clinical presentation of PE was characterized by specific symptoms. Dyspnea was the most common, reported by 80.1% of patients, followed by cough (71.6%) and chest pain (67.8%). These findings are consistent with previous studies, which have also identified dyspnea as a common symptom of PE(10). Notably, these symptoms are non-specific, and their presence should prompt clinicians to consider PE as a potential diagnosis. We however, did not investigate the predictive accuracy of these symptoms and this can form the foundation for further studies.

The distribution of PE was: right (47.3%), left (32.7%), and bilateral effusions were present in 16.3% of cases. These have been replicated in similar studies. Nonetheless, a conclusive explanation of the predilection of effusions on the right side has not been provided. Follow-up tests on pleural fluid and biochemistry were not conducted in all patients, which may affect the completeness of diagnostic information and treatment guidance. This may be attributed to economic reasons as opposed to resource availability as the center has the capacity to conduct the additional tests. This could also be due to a lack of knowledge on their necessity in the diagnostic formulations and also due to a lack of local guidelines for the same.

Interestingly, the prevalence of exudative effusions (65.8%) in this study was notably higher than that of transudative effusions (16.8%). This distribution differs from those reported in developed countries like the US in which transudative effusions dominate (7). The reasons behind this difference may relate to the specific aetiological factors contributing to PE in the Kenyan patient population. TB is a prevalent and endemic disease in the country and this could explain the predominance of exudative effusions in our set up. The most encountered TB in Kenya is secondary owing to the reactivation of the infection and is seen mostly in the marginalized setups such as the suburb middle aged population as reported in our study.

Aetiology of PE at KNH: The aetiological factors identified in this study shed light on the causes of PE at KNH and provide valuable insights for clinical practice. Infections were the most common cause, accounting for 42% of cases. Within the infectious category, tuberculosis (TB) was the dominant cause of exudative effusions (63.6%), followed by bacterial pneumonia and empyema. This observation is consistent with studies done in LMIC. Adeoye *et al* (10) reported that TB was the leading cause of exudative effusions in Nigeria accounting for 32.9% of the causes.. A similar study in Kenya by Owino *et al* (5) reported that TB caused approximately 79% of all exudative effusions. These higher figures may be explained by the virtue that this particular study focused on HIV patients in whom the effects of TB may be compounded. Nonetheless, as the disease is endemic in Kenya, it is crucial to revamp campaign against the spread of TB infections. Prevention of TB transmission and prompt and intensive treatment of this condition can help mitigate incidences of TB related PE.

Viral infections were less common, with Covid-19 accounting for a notable portion of these cases. The emergence of Covid-19 as a cause of pleural effusion is a recent development, and the high prevalence in this study warrants further investigation and highlights the evolving nature of pleural diseases. Malignancies were another substantial contributor to PE, with breast and lung cancers accounting for the majority of cases (99%). These proportions were higher than those reported in similar studies in Africa highlighting the burden of the cancers in sub-Saharan Africa. The prevalence of malignancy-related PE underscores the need for vigilant surveillance and early detection in cancer patients to help improve the treatment outcomes.

In the case of transudative effusions, heart failure was the major contributor, consistent with findings from other studies. Renal and hepatic diseases played a significant role as well, emphasizing the importance of addressing the underlying systemic conditions when managing transudative PE. The diverse range of aetiological factors, including connective tissue diseases, hypothyroidism, and pulmonary embolism, emphasizes the need for a comprehensive diagnostic approach to identify the underlying cause. Targeted intensive interventions of systemic conditions is crucial in lowering the rates of transudative pleural effusions.

Comparing these results to existing literature, it is clear that the aetiological landscape of PE varies by region and population. The dominance of TB as an infectious cause aligns with the high TB burden in Kenya. However, the prominence of Covid-19 as a cause is unique and reflects the impact of the global pandemic on local healthcare systems.

Diagnostic interventions among adult patients: The diagnostic approach to PE at KNH primarily involved diagnostic thoracentesis, with a high rate of performance (82.6%). This aligns with the standard procedure for diagnosing PE (2). The finding that 65.8% yielded exudates underscore the importance of conducting this procedure to differentiate between exudative and transudative effusions. Radiological investigations played a significant role in the diagnostic process. Plain chest radiography was performed in 82.2% of patients, while chest CT scans were conducted in 53.2%. These diagnostic methods are in line with international guidelines and are essential for assessing the extent and characteristics

of PE. There are three easily recognizable radiological patterns which aid differential diagnosis. These are the bilateral, massive and loculated PE. Heart failure constitutes the most common cause of bilateral PE (12).Other radiological findings in heart failure include but not limited to: cephalization or vascular redistribution, interstitial or alveolar edema, and increased size of the cardiac silhouette. The increase in size of the cardiac silhouette is of utmost importance because only a relatively small proportion (20%–30%) of patients with heart failure lack the finding (13).

The use of echocardiography (11.3%) and thoracic ultrasound (2.6%) in the diagnostic process was relatively low but valuable, especially in the evaluation of transudative effusions. These methods can provide real-time information on cardiac and pleural abnormalities, aiding in differential diagnosis. Additionally, the presence of a portable ultra sound equipment facilitates diagnosis and management PE at the POC (14). It is also more sensitive in recognizing fluid in the pleural cavity than radiographs of the chest (15). It can also be used to differentiate fluid in the pleural space from thickening of the pleura and from consolidation of the pleura. Presence of nodules in the pleura and its thickening can also point to a malignant cause which can be identified by thoracic ultrasonography.

Pleural biopsy was performed in a small proportion of cases (7.1%), with documented histopathological findings. The findings were diverse, with lung, pleural and gastric adenocarcinomas and metastatic carcinomas identified in a subset of cases, highlighting the importance of histopathology in confirming malignancy-related PE. Overall, the diagnostic interventions used at KNH are in line with established guidelines, but the lower utilization of echocardiography and ultrasound suggests potential areas for improvement. Additionally, the relatively low rate of pleural biopsies underscores the need for further exploration of tissue-based diagnostics in specific cases.

Management of PE at KNH: The management of PE at KNH involves various interventions, including drainage, antibiotics, diuretics, and pleurodesis. Drainage was performed in a significant majority of cases (82.2%), primarily using large bore tubes (72.6%). This aligns with common clinical practice and is essential for relieving symptoms and enabling further evaluation (7).

Antibiotics alone were administered in over half of the patients (52%). In cases where infection is the underlying cause, such as TB or bacterial pneumonia, antibiotics are a vital component of treatment. Diuretics alone were administered in 11.3% of cases, particularly for transudative effusions related to heart failure. Notably, a small but essential subset of patients received both antibiotics and diuretics as definitive management (9.4%). This approach is consistent with treating patients with complex aetiologies, such as heart failure with superimposed infection

Pleurodesis, performed in 40.4% of patients with malignant effusions, is a valuable intervention for preventing recurrence of PE. Chemical pleurodesis was used in most of these patients (89.5%), while mechanical pleurodesis was not done at all. The lack of utilization of mechanical pleurodesis may be attributed to resource constraints or the preference for other techniques (1). The success rate of pleurodesis in this study was 88.3%, and further research is needed to investigate the factors influencing the outcomes of this procedure. Successful pleurodesis is associated with a reduced risk of recurrence (16). The overall recovery rate in this study was 69.0%, with an average length of stay of 18.57 days. However, 12.4% of patients succumbed to death with mortality rates slightly higher among patients with exudative effusions, emphasizing the significance of PE as a life-threatening condition. These findings mirror previous literature which shows transudative effusion to be associated with significantly longer median overall survival, relative to exudative effusion (17). Of note, transudative effusions were associated with a slightly longer recovery period compared to exudative effusions possibly influenced by the natural history of the underlying cause of effusion. Further research should focus on identifying factors associated with successful recovery and reducing mortality.

The results of the multiple regression analysis indicate that PE caused by TB, pneumonia, and Covid-19 were associated with significantly increased risks of mortality. This finding underscores the importance of early diagnosis and appropriate management in cases with these aetiologies in an attempt to improve patient outcomes.

In conclusion, the aetiology and management of PE at KNH are characterized by unique regional and population-specific factors. The prominence of TB and Covid-19 as causes of PE, along with the relatively high success rate of pleurodesis, have implications for local healthcare policies and guidelines. Additionally, the high mortality risk associated with specific aetiologies highlights the need for targeted interventions and preventive measures. As the healthcare landscape continues to evolve, it is essential to adapt diagnostic and therapeutic strategies to optimize patient outcomes and reduce the burden of PE-related morbidity and mortality

Study limitations

Unrecorded data and missing information may have impacted the findings of the study. However, multiple sources and meticulous retrieval of information were carried out including retrieval of both digital and physical files. If complete information was not achieved, the specific files were excluded from analysis.

Conclusions

Exudative PE remains the most common with infectious causes predominating, particularly secondary to tuberculosis. There still remains a huge gap in unreported data due to poor documentation of procedures done and the outcomes. Quality assurance measures should be taken to ensure patient data is well documented to avoid missing records. Creation of a dedicated pleural service team would be essential to reduce length of stay and mortality in hospitalized patients with PE. Robustevidence is further required on diagnosis and management of PE by adoption of thoracic ultrasonography for diagnosis and plural biopsy to ensure patient safety and increase diagnostic yield.

Funding: None.

Conflict of interest: The authors have nothing to declare.

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