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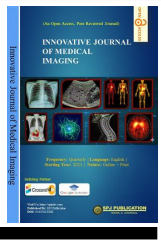

Original Article

Radiographic Assessment of Common Thoracic Disorders Using Chest X-Ray Imaging

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ABSTRACT

Background: Chest X-ray (CXR) remains one of the most widely used imaging modalities for the evaluation of thoracic diseases because of its rapid availability, affordability, low radiation exposure, and diagnostic effectiveness. It plays a crucial role in the early detection and assessment of various pulmonary and cardiovascular conditions, particularly in resource-limited healthcare settings.
Aim: To evaluate the diagnostic utility of chest radiography in the assessment of common thoracic disorders and to analyze their prevalence, radiographic characteristics, and diagnostic performance in a hospital-based population.
Methods: A retrospective observational study was conducted on 109 patients who underwent chest radiography at a tertiary care teaching hospital. Standard posteroanterior and anteroposterior chest radiographs were reviewed for the presence of cardiomegaly, pneumonia, pleural effusion, and pulmonary tuberculosis. Diagnostic performance was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. Descriptive statistics and Chi-square analysis were used for demographic evaluation.
Results: Among the 109 patients, 75 (68.8%) demonstrated at least one thoracic abnormality on chest X-ray. Pleural effusion was the most prevalent condition (26.6%), followed by pneumonia (22.0%), cardiomegaly (14.7%), and pulmonary tuberculosis (5.5%). Costophrenic angle blunting was the most common associated radiographic finding, observed in 67.9% of patients. The estimated mean age was 42.8 years, and no significant association was found between gender and age-group distribution ($\chi^2 = 1.485$, $p = 0.686$). Diagnostic accuracy ranged from 94.5% to 98.2%, with cardiomegaly showing the highest sensitivity (93.8%) and pulmonary tuberculosis demonstrating the highest specificity (99.0%).
Conclusion: Chest radiography is a reliable, accessible, and cost-effective diagnostic tool for the evaluation of common thoracic disorders. Its high diagnostic performance supports its continued role as a first-line imaging modality in routine clinical practice.

Keywords: Chest X-Ray, Thoracic Disorders, Cardiomegaly, Pneumonia, Pleural Effusion, Pulmonary Tuberculosis, Diagnostic Accuracy, Sensitivity

INTRODUCTION

Chest radiography, commonly referred to as chest X-ray (CXR), remains one of the most frequently performed and indispensable diagnostic imaging examinations in modern healthcare. Despite the rapid advancement of imaging technologies such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography, chest X-ray continues to serve as the primary imaging modality for the initial assessment of thoracic diseases due to its simplicity, rapid acquisition, cost-effectiveness, wide accessibility, and relatively low radiation dose exposure. [1] It provides a comprehensive overview of thoracic structures, including the lungs, pleura, mediastinum, diaphragm, and cardiovascular system, thereby facilitating the early detection and evaluation of a broad range of pathological conditions. Thoracic disorders contribute significantly to global morbidity and mortality, particularly in low- and middle-income countries where access to advanced imaging modalities may be limited. [2] Conditions such as cardiomegaly, pneumonia, pleural effusion, and pulmonary tuberculosis remain major public health concerns because of their high prevalence and substantial impact on patient health outcomes. Early diagnosis and timely management of these diseases are essential to reduce complications, improve prognosis, and decrease healthcare burden. In this regard, chest radiography serves as a valuable frontline diagnostic tool, enabling clinicians to identify characteristic

radiographic findings that guide further investigation and treatment. Cardiomegaly is a common radiographic finding associated with various cardiovascular disorders, including hypertension, cardiomyopathy, valvular heart disease, and congestive heart failure. On a standard posteroanterior chest radiograph, cardiac enlargement is commonly assessed using the cardiothoracic ratio (CTR), where a ratio greater than 0.50 is generally considered indicative of cardiomegaly in adults. [3] Recognition of an enlarged cardiac silhouette on chest X-ray often prompts further cardiac evaluation and plays a crucial role in the early identification of underlying cardiovascular disease. Pneumonia is an inflammatory condition of the lung parenchyma caused by bacterial, viral, fungal, or other infectious agents. It remains one of the leading causes of hospitalization and mortality worldwide, particularly among children, elderly individuals, and immunocompromised patients. [4] Chest radiography is considered the standard initial imaging investigation for suspected pneumonia and provides valuable information regarding the location, extent, and pattern of pulmonary involvement. Typical radiographic findings include focal or diffuse consolidation, air bronchograms, interstitial infiltrates, and multilobar opacities, which assist clinicians in diagnosis and disease monitoring. [5]

Pleural effusion, defined as the abnormal accumulation of fluid within the pleural cavity, may occur secondary to a variety of conditions including heart failure, infection, malignancy, renal disease, and liver cirrhosis. [6] Chest X-ray remains a highly effective method for detecting pleural fluid, particularly when moderate to large volumes are present. Characteristic radiographic features include blunting of the costophrenic angles, meniscus sign, and homogeneous opacification of the lower hemithorax. The identification of pleural effusion on radiographs provides important diagnostic clues regarding the underlying pathology and assists in determining the need for further diagnostic procedures such as thoracentesis. [7] Pulmonary tuberculosis (TB), caused by *Mycobacterium tuberculosis*, continues to represent a major global health challenge, particularly in developing nations. India accounts for a substantial proportion of the worldwide tuberculosis burden, making early detection and diagnosis a public health priority. [8] Chest radiography plays a pivotal role in TB screening and diagnosis, especially in resource-limited settings. Common radiographic manifestations include upper lobe infiltrates, cavitary lesions, fibrotic changes, nodular opacities, and hilar or mediastinal lymphadenopathy. Although chest X-ray alone cannot definitively diagnose tuberculosis, it remains an essential tool for identifying suspicious cases that require microbiological confirmation [9] The diagnostic performance of chest radiography has been extensively evaluated across various thoracic conditions. While the sensitivity and specificity of chest X-ray may vary depending on disease type and severity, it continues to demonstrate substantial clinical utility as an initial screening and diagnostic modality [10] Quantitative measures such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy are commonly employed to assess its effectiveness in clinical practice. These statistical parameters provide objective evidence regarding the reliability of chest radiography in detecting thoracic abnormalities and support evidence-based decision-making [11] Therefore, the present study was undertaken to evaluate the prevalence and radiographic characteristics of common thoracic conditions, namely cardiomegaly, pneumonia, pleural effusion, and pulmonary tuberculosis, among a hospital-based population of 109 patients. Furthermore, the study aims to assess the diagnostic performance of chest X-ray by determining key statistical indicators including sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. The findings of this study are expected to contribute to a better understanding of the clinical utility of chest radiography and reinforce its role as a fundamental imaging modality in the diagnosis and management of thoracic diseases. The primary aim of this study was to investigate the diagnostic utility of chest radiography in the evaluation of common thoracic conditions, namely cardiomegaly, pneumonia, pleural effusion, and pulmonary tuberculosis. The study further aimed to analyse the characteristic radiographic manifestations of these conditions, determine their prevalence within the study population, and assess the diagnostic performance of chest X-ray using established statistical parameters.

MATERILS AND METHODS

Study Design: This retrospective observational study was conducted in the Department of Radiology of a tertiary care teaching hospital affiliated with Jamia Hamdard University. The study involved the review and analysis of chest X-ray examinations performed during the study period. Ethical approval was obtained from the Institutional Ethics Committee prior to data collection.

Study Population: A total of 109 patients who underwent chest radiography were included in the study. Participants were selected using systematic random sampling from available radiographic records. Patients of both genders and various age groups were included. Radiographs with poor image quality, technical errors, or incomplete clinical information were excluded from the analysis.

Radiographic Technique: Chest radiographs were acquired using standard posteroanterior (PA) and anteroposterior (AP) projections according to patient

condition and clinical requirements. PA projections were preferred for ambulatory patients, whereas AP projections were utilized for bedridden or critically ill patients. All images were interpreted by qualified radiology professionals following standardized radiographic assessment protocols.

Diagnostic Criteria: The diagnosis of thoracic conditions was established based on characteristic radiographic findings:

- **Cardiomegaly:** Cardiothoracic ratio (CTR) greater than 50% on PA chest radiograph.
- **Pneumonia:** Presence of pulmonary consolidation, air bronchograms, patchy opacities, or interstitial infiltrates.
- **Pleural Effusion:** Blunting of the costophrenic angle, meniscus sign, or homogeneous pleural opacity.
- **Pulmonary Tuberculosis:** Upper lobe infiltrates, cavitary lesions, fibrosis, nodular opacities, or hilar/mediastinal lymphadenopathy.

Statistical Analysis: Data were entered and analyzed using appropriate statistical methods. Descriptive statistics, including frequencies and percentages, were used to summarize demographic and radiographic findings. Diagnostic performance of chest X-ray was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy using 2 × 2 contingency tables. The Chi-square (χ^2) test was applied to evaluate associations between demographic variables and disease distribution. A p-value of less than 0.05 was considered statistically significant. Mean age was estimated using the midpoint values of the respective age-group intervals.

RESULTS

Among the 109 patients included in the study, 75 patients (68.8%) demonstrated at least one radiographically detectable thoracic abnormality on chest X-ray. Pleural effusion was the most frequently observed condition, identified in 29 patients (26.6%), followed by pneumonia in 24 patients (22.0%), cardiomegaly in 16 patients (14.7%), and pulmonary tuberculosis in 6 patients (5.5%). In addition to these primary findings, blunting of the costophrenic (CP) angle was the most common associated radiographic feature, observed in 74 patients (67.9%).

These findings indicate that pleural and pulmonary pathologies constituted the majority of thoracic abnormalities within the study population, highlighting the important role of chest radiography in the detection and evaluation of common thoracic diseases.

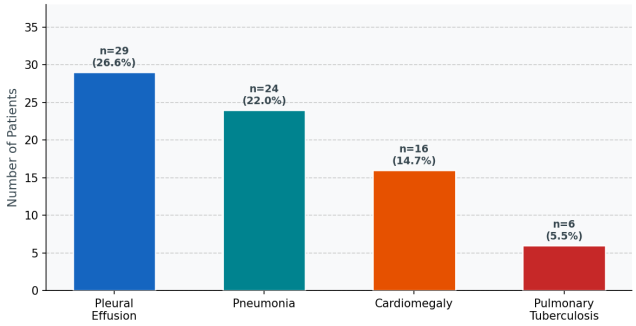

Figure 1: Bar Chart Showing Prevalence of Thoracic Conditions (N=109)

Age and Gender Distribution: A total of 109 patients were included in the study. Of these, 55 (50.5%) were males and 58 (53.2%) were females. The gender-stratified analysis yielded 113 entries because four patients presented with multiple thoracic conditions and were therefore counted separately for condition-specific gender distribution. The estimated mean age of the study population was 42.8 years, calculated using the midpoint method. The highest proportion of patients belonged to the 21–40 years age group (n = 42, 38.5%), indicating that young and middle-aged adults constituted the majority of the study population. In contrast, the 5–20 years age group represented the smallest proportion of participants (n = 13, 11.9%). These findings demonstrate a predominance of thoracic conditions among adults in the economically productive age groups.

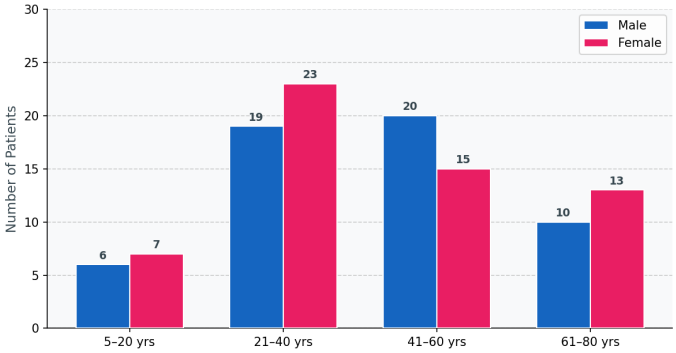

Figure 2: Grouped Bar Chart of Age and Gender Distribution

Chi-Square Analysis of Gender and Age Group Distribution: A chi-square test of independence was conducted to assess the association between gender and age group among the study participants. The analysis revealed no statistically significant relationship between these variables ($\chi^2 = 1.485$, df = 3, p = 0.686). Since the calculated chi-square value was substantially lower than the critical value of 7.815 at a significance level of 0.05, the null hypothesis was retained. These findings indicate that the distribution of males and females was comparable across the different age groups, suggesting

that age distribution was independent of gender within the study population.

Table 1: Chi-Square Analysis of Gender Distribution Across Age Groups

Age Group (Years)	Observed Male (n)	Observed Female (n)	Row Total (n)	Expected Male	Expected Female	χ^2 Contribution
5–20	6	7	13	5.85	6.15	0.003
21–40	19	23	42	18.90	19.86	0.058
41–60	20	15	35	17.08	17.96	0.970
61–80	10	13	23	10.35	10.88	0.148
Total	**55**	**58**	**113**	—	—	**$\chi^2 = 1.485$**

Statistical Parameters: $\chi^2 = 1.485$, df = 3, p = 0.686

The chi-square test demonstrated no statistically significant association between gender and age group distribution (p = 0.686). The observed frequencies were comparable to the expected frequencies across all age categories, indicating a relatively uniform distribution of males and females within the study population.

Distribution of Conditions by Age Group: Cardiomegaly showed the strongest age-related concentration, with 43.8% of cases in the 41–60 years group and 37.5% in the 61–80 years' group. Pleural effusion and pneumonia were distributed across all age groups but peaked in the 41–60 years bracket. Tuberculosis showed a relatively even distribution, with a slight predilection for the 21–40 years age group consistent with the known epidemiology of the disease.

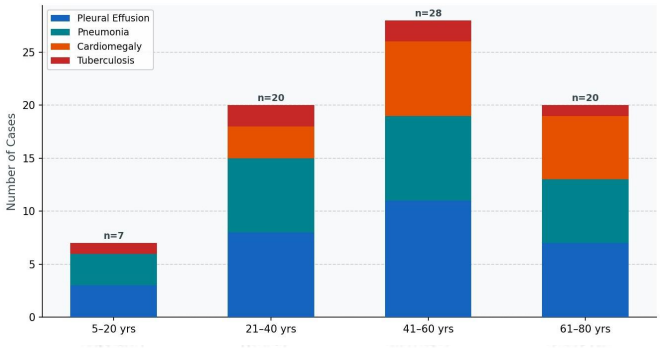

Figure 3: Stacked Bar Chart Showing Distribution of Conditions by Age Group

Diagnostic Performance of Chest X-Ray: The diagnostic performance of chest X-ray for the detection of common thoracic conditions was evaluated using 2×2 contingency tables comprising true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN). Performance was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. The results demonstrated that chest radiography provided high diagnostic reliability across all evaluated conditions, with overall accuracy values exceeding 94% for each pathology. Among the conditions studied, cardiomegaly assessed using the cardiothoracic ratio (CTR) exhibited the highest diagnostic performance, achieving a sensitivity of 93.8%, specificity of 98.9%, PPV of 93.8%, NPV of 98.9%, and an overall accuracy of 98.2%. These findings indicate that chest X-ray is highly effective in identifying cardiac enlargement and differentiating normal from abnormal cardiac silhouettes. For pleural effusion, chest radiography demonstrated a sensitivity of 89.7% and specificity of 96.3%, with corresponding PPV and NPV values of 89.7% and 96.3%, respectively. The overall diagnostic accuracy was 94.5%, confirming the effectiveness of chest X-ray in detecting pleural fluid accumulation through characteristic findings such as costophrenic angle blunting and the meniscus sign. Similarly, pneumonia showed strong diagnostic performance, with a sensitivity of 87.5% and specificity of 96.5%. The PPV and NPV were 87.5% and 96.5%, respectively, while the overall accuracy reached 94.5%. These results support the continued role of chest radiography as a primary imaging modality for identifying pulmonary consolidation and other radiographic features associated with pneumonia. Pulmonary tuberculosis demonstrated the highest specificity among the pulmonary conditions, reaching 99.0%, with an NPV of 99.0% and an overall accuracy of 98.2%. However, its sensitivity was comparatively lower at 83.3%, reflecting the known limitations of chest radiography in detecting early or subtle tuberculous lesions. Despite this limitation, the high specificity suggests that positive radiographic findings strongly correlate with the presence of disease. The findings indicate that chest X-ray provides excellent diagnostic performance for the evaluation of common thoracic conditions. The high sensitivity, specificity, predictive values, and accuracy observed across all disease categories underscore its value as a reliable first-line imaging investigation in routine clinical practice.

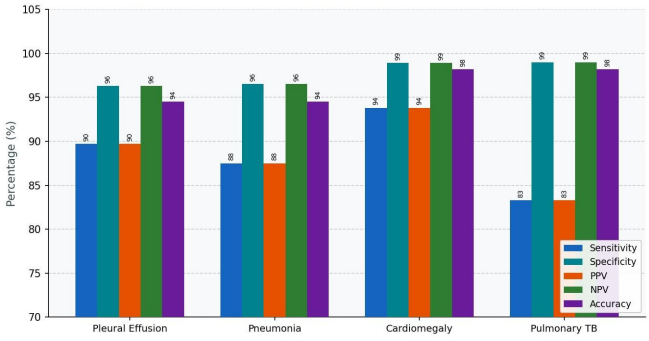

Figure 4: Grouped Bar Chart of Diagnostic Performance Metrics per Condition

The grouped bar chart **(Figure 4)** further illustrates the comparative diagnostic metrics for each condition, while

the receiver operating characteristic (ROC) curves presented in **Figure 5** demonstrate the strong discriminatory ability of chest radiography, with high area under the curve (AUC) values observed across all evaluated pathologies.

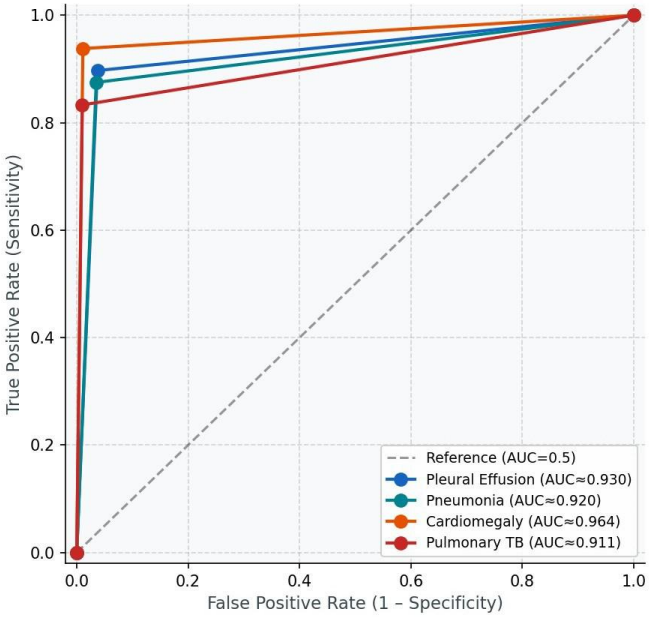

Figure 5: ROC Curves Showing Chest X-Ray Diagnostic Performance (AUC values shown per condition)

Table 2 summarizes the diagnostic performance metrics of chest X-ray for pleural effusion, pneumonia, cardiomegaly, and pulmonary tuberculosis, highlighting its overall effectiveness in thoracic disease detection and assessment.

Table 2: Diagnostic Performance Metrics of Chest X-Ray for Common Thoracic Conditions

Condition	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Pleural Effusion	26	3	3	77	89.7	96.3	89.7	96.3	94.5
Pneumonia	21	3	3	82	87.5	96.5	87.5	96.5	94.5
Cardiomegaly (CTR)	15	1	1	92	93.8	98.9	93.8	98.9	98.2
Pulmonary Tuberculosis	5	1	1	102	83.3	99.0	83.3	99.0	98.2

TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative; PPV = Positive Predictive Value; NPV = Negative Predictive Value; CTR = Cardiothoracic Ratio.

Cardiomegaly demonstrated the highest sensitivity (93.8%) among the evaluated conditions, while pulmonary tuberculosis exhibited the highest specificity (99.0%). Both cardiomegaly and pulmonary tuberculosis achieved the highest overall diagnostic accuracy (98.2%). Pleural effusion and pneumonia also showed excellent diagnostic performance, with accuracies of 94.5%. These findings indicate that chest radiography is a highly reliable diagnostic tool for the evaluation of common thoracic diseases.

DISCUSSION

The present study evaluated the prevalence, radiographic characteristics, and diagnostic performance of chest radiography in the assessment of common thoracic conditions among a hospital-based population of 109 patients. Chest X-ray remains one of the most accessible and cost-effective imaging modalities for the diagnosis of thoracic diseases, particularly in resource-constrained healthcare settings. The findings of this study demonstrate that chest radiography provides high diagnostic accuracy for the detection of pleural effusion, pneumonia, cardiomegaly, and pulmonary tuberculosis, thereby reinforcing its continued clinical relevance in routine practice. Pleural effusion was identified as the most common thoracic abnormality, accounting for 26.6% of all cases. This finding is consistent with previous studies reporting pleural effusion as a frequent manifestation of cardiovascular, infectious, malignant, and systemic disorders. The high prevalence observed in the present study may reflect the diverse spectrum of underlying diseases encountered in tertiary care hospitals. Costophrenic angle blunting was the most frequently observed associated radiographic sign and was present in 67.9% of patients, emphasizing its importance as an early indicator of pleural fluid accumulation. Chest radiography demonstrated excellent diagnostic performance for pleural effusion, with a sensitivity of 89.7%, specificity of 96.3%, and overall accuracy of 94.5%. These findings highlight the reliability of chest X-ray in detecting clinically significant pleural fluid collections. Nevertheless, radiographic detection becomes challenging in cases involving small-volume effusions, loculated fluid collections, or supine patients. Therefore, ultrasonography and computed tomography remain valuable adjunctive imaging modalities when radiographic findings are equivocal or clinical suspicion remains high.

Pneumonia was the second most prevalent thoracic condition, affecting 22.0% of the study population. Radiographic manifestations primarily included pulmonary consolidation, increased parenchymal opacities, and air bronchograms, which are well-established indicators of infectious involvement of the lung parenchyma. The observed prevalence underscores

the continuing burden of respiratory infections in the general population and their contribution to hospital admissions. The sensitivity and specificity of chest radiography for pneumonia were 87.5% and 96.5%, respectively, with an overall diagnostic accuracy of 94.5%. Although these values indicate strong diagnostic capability, certain limitations must be acknowledged. Early-stage pneumonia, atypical infections, dehydration, immunosuppression, and subtle interstitial involvement may produce inconspicuous radiographic findings, thereby reducing sensitivity. Despite these limitations, chest X-ray remains the preferred first-line imaging investigation owing to its rapid availability, affordability, and ability to guide clinical management.

Cardiomegaly was observed in 14.7% of patients and was predominantly identified among individuals in the middle-aged and elderly age groups. This observation is consistent with the increasing prevalence of cardiovascular disorders such as hypertension, ischemic heart disease, and cardiomyopathy with advancing age. Assessment of the cardiothoracic ratio (CTR) on posteroanterior chest radiographs remains a simple and widely accepted method for evaluating cardiac enlargement. Among all conditions studied, cardiomegaly demonstrated the highest sensitivity (93.8%) and one of the highest overall accuracies (98.2%). The specificity was also remarkably high at 98.9%, indicating excellent agreement between radiographic findings and final diagnosis. These results confirm the utility of chest radiography as an effective screening tool for cardiac enlargement. However, factors such as patient positioning, poor inspiratory effort, obesity, and the use of anteroposterior projections may artificially increase the apparent cardiac silhouette and should be considered during image interpretation.

Pulmonary tuberculosis accounted for 5.5% of all cases and represented the least prevalent condition in the study cohort. Despite its relatively low prevalence, tuberculosis remains a major public health concern, particularly in developing countries where disease burden remains substantial. Characteristic radiographic findings observed included upper lobe infiltrates, cavitary lesions, fibrotic changes, and nodular opacities, which are considered classic manifestations of post-primary pulmonary tuberculosis. Chest radiography demonstrated a specificity of 99.0% and an overall accuracy of 98.2%, indicating that characteristic radiographic abnormalities were highly predictive of disease presence. However, sensitivity was comparatively lower at 83.3%, reflecting the known limitations of chest X-ray in detecting early, minimal, or atypical tuberculosis. Consequently, chest radiography should be regarded as a screening and supportive diagnostic tool rather than a definitive diagnostic modality. Microbiological confirmation through sputum examination, culture techniques, or molecular methods such as GeneXpert remains essential for establishing a definitive diagnosis.

The demographic analysis revealed an estimated mean age of 42.8 years, with the majority of patients belonging to the 21–40 years age group. This finding suggests that thoracic diseases predominantly affect individuals within economically productive age groups, thereby potentially contributing to significant social and economic consequences. The distribution of thoracic conditions across age groups further indicates that disease burden increases with age, particularly for cardiomegaly and pleural effusion. Chi-square analysis demonstrated no statistically significant association between gender and age-group distribution ($\chi^2 = 1.485$, $df = 3$, $p = 0.686$). The absence of statistical significance indicates that the observed gender distribution was relatively uniform across all age categories, thereby supporting the representativeness of the study sample. Furthermore, receiver operating characteristic (ROC) analysis revealed satisfactory discriminatory performance for all evaluated conditions, with area under the curve (AUC) values indicating good overall diagnostic capability of chest radiography. The findings of this study demonstrate that chest X-ray possesses excellent diagnostic performance for the evaluation of common thoracic conditions and continues to play a pivotal role in the initial assessment of patients presenting with respiratory and cardiovascular symptoms.

CONCLUSION

The present study evaluated the role of chest radiography in the diagnosis and assessment of common thoracic conditions among a hospital-based population and demonstrated that chest X-ray remains a highly valuable imaging modality in contemporary clinical practice. Despite advances in cross-sectional imaging techniques, chest radiography continues to provide rapid, accessible, and cost-effective diagnostic information for a wide range of thoracic diseases. Among the evaluated conditions, pleural effusion emerged as the most prevalent abnormality, accounting for 26.6% of cases, followed by pneumonia (22.0%), cardiomegaly (14.7%), and pulmonary tuberculosis (5.5%). Costophrenic angle blunting was identified as the most common associated radiographic finding, emphasizing its significance as an important indicator of pleural pathology. The prevalence patterns observed in this study highlight the continuing burden of respiratory and cardiovascular diseases in routine clinical practice. The diagnostic performance analysis demonstrated that chest radiography achieved high levels of sensitivity, specificity, and overall accuracy across all evaluated conditions. Cardiomegaly

showed the highest sensitivity (93.8%), whereas pulmonary tuberculosis demonstrated the highest specificity (99.0%). Ddiagnostic accuracy ranged from 94.5% to 98.2%, confirming the reliability of chest X-ray as a first-line diagnostic investigation. These findings support the continued use of chest radiography as an effective screening and diagnostic tool for the assessment of thoracic abnormalities. The study also revealed that thoracic diseases were more frequently observed among adults and middle-aged individuals, with no statistically significant association between gender and age-group distribution. This suggests that the burden of thoracic pathology is influenced more by disease-specific risk factors and age-related physiological changes than by gender alone. Although chest radiography demonstrated excellent diagnostic performance, certain limitations must be acknowledged. Reduced sensitivity in early-stage disease, small pleural effusions, and atypical pulmonary infections may necessitate additional imaging or laboratory investigations. Therefore, chest X-ray should be interpreted within the context of clinical findings and supplemented by ultrasonography, computed tomography, echocardiography, or microbiological testing whenever appropriate.

DECLARATIONS

Ethics Approval and Consent to Participate: This retrospective observational study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of the affiliated institution prior to commencement of the study. As the study involved retrospective analysis of anonymized radiographic records, the requirement for individual informed consent was waived by the Ethics Committee.

Consent for Publication: Not applicable.

Availability of Data and Materials: The datasets analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional and ethical regulations.

Conflict of Interest: The authors declare that they have no competing interests related to this study.

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Authors' Contributions: All authors contributed substantially to the conception and design of the study. Data collection, radiographic evaluation, statistical analysis, interpretation of results, and manuscript preparation were performed collaboratively by the authors. All authors reviewed, revised, and approved the final manuscript and agree to be accountable for all aspects of the work.

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