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EDITORIAL

Resurgence of an Old Nemesis

Muhammad Shakhawath Hossain

[Chest Heart J. 2024; 48(1) : 1-2]

The COVID-19 pandemic has reshaped modern medicine. What began as a public health emergency rapidly evolved into a prolonged global challenge. The past few years have marked a period of both crisis and innovation. COVID-19 becomes a managed endemic threat rather than an acute catastrophe—the focus must shift toward evidence-based, scalable, and sustainable clinical strategies.

This transition demands a recalibration of how we define risk, allocate resources, and integrate COVID-19 care into broader healthcare delivery systems. Variants continue to emerge, patient presentations are evolving, and long-term sequelae remain a significant concern. The virus may no longer dominate headlines, but its presence in our wards and communities is far from over and our response must reflect that enduring reality.

We are still in search of a universally accepted guideline for managing COVID-19 patients. The Infectious Diseases Society of America (IDSA) has classified COVID-19 cases based on severity and setting of care, and has outlined management strategies accordingly.

Remdesevir: Ambulatory or hospitalized patients with mild-to-moderate COVID-19, at high risk for progression to severe disease, remdesivir should be initiated within seven days of symptom onset.

In patients on supplemental oxygen but not on mechanical ventilation or ECMO, treatment with five days of remdesivir rather than 10 days of remdesivir.

In hospitalized patients with severe COVID-19, remdesivir should be given.

In patients with COVID-19 on invasive ventilation and/or ECMO, no need to initiation of remdesivir.

Pemivibart: In moderately or severely immunocompromised individuals 12 years or older at risk for progression to severe COVID-19, pre-exposure prophylaxis with pemivibart is recommended when predominant regional variants are susceptible to the agent.

Nirmatrelvir/ritonavir: In ambulatory patients with mild-to-moderate COVID-19 at high risk for progression to severe disease, nirmatrelvir/ritonavir should be initiated within five days of symptom onset rather than no nirmatrelvir/ritonavir.

Molnupiravir: In ambulatory patients (≥18 years) with mild-to-moderate COVID-19 at high risk for progression to severe disease who have no other treatment options, molnupiravir initiated within five days of symptom onset.

Abatacept & Infliximab: In hospitalized adults receiving systemic glucocorticoids, who are experiencing severe, rapidly progressing COVID-19 or critical COVID-19, when baricitinib and tocilizumab are not available, abatacept or infliximab is recommended.

Tocilizumab: Among hospitalized adults with progressive severeor critical COVID-19 who have elevated markers of systemic inflammation, the IDSA guideline panel suggests tocilizumab in addition to standard of care (i.e., steroids) rather than standard of care alone.

When tocilizumab is not available for patients, sarilumab can be given in addition to standard of care (i.e., steroids).

Baricitinib: Among hospitalized adults with severe COVID-19, baricitinib with corticosteroids should be given. Patients who cannot receive a

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corticosteroid because of a contraindication, use of baricitinib with remdesivir is recommended.

Convalescent Plasma therapy (CPT): Not recommended in immunocompetent patient. Among immunocompromised patients hospitalized with COVID-19, the routine use of COVID-19 convalescent plasma is not recommended.

Among ambulatory patients with mild-to-moderate COVID-19, at high risk for progression to severe disease who have no other treatment options, FDA-qualified high-titer COVID-19 convalescent plasma within 8 days of symptom onset is recommended.

Corticosteroid: Among hospitalized patients with severe, but non-critical, COVID-19, dexamethasone is recommended.

Among hospitalized patients with mild-to-moderate COVID-19 without hypoxemia requiring supplemental oxygen, the use of glucocorticoids is not recommended.

Over time, new recommendations for antivirals and immunomodulators have emerged, many of which can be applied within the clinical context of our country as well.

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ORIGINAL ARTICLE

Diagnostic Performance of GeneXpert in clinically suspected Tubercular Lymphadenopathy

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Abstract:

Background: *Tubercular lymphadenopathy is the most common form of extra pulmonary tuberculosis. Accurate diagnosis and early treatment has the potential to reduce morbidity and mortality. But its diagnosis remains challenging. The routinely used methods have sub optimal sensitivity. Mycobacterial culture remains the gold standard but it is time consuming. For these limitations more rapid and reliable methods are needed. GeneXpert, a novel automated point of care real time nucleic acid amplification test that simultaneously detects Mycobacterium Tuberculosis complex and rifampicin resistance from clinical specimens within 2 hours have a sensitivity comparable to culture.*

Objective: *To assess the diagnostic performance of GeneXpert in clinically suspected tubercular lymphadenopathy.*

Materials & Methods: *This cross sectional observational study was conducted in the department of Respiratory medicine of NIDCH, Mohakhali, Dhaka from January 2020 to March 2021among 43 cases of clinically suspected tubercular lymphadenopathy. Fine needle aspirates from Lymph node done and specimens sent to the pathology and bacteriology laboratory for Cytology, GeneXpert & AFB culture.Pearson Chi square test was done. P value ≤0.05 was considered for claiming that the results are statistically significant.*

Results: *Among 43 patients , majority (60.47%) were female. Most of the patients (46.52%) were in age group of 21-30 years. Most of the patients (65.11%) presented with cervical lymphadenopathy. Cytology, GeneXpert & AFB Culture was positive in 83.72%, 53.48% and41.86% of patients respectively. The sensitivity, specificity and diagnostic accuracy of GeneXpert was 88.88%, 72.00%, and 79.06% respectively when compared to culture.*

Conclusion: *The high sensitivity and specificity coupled with its speed and simplicity make the GeneXpert the most useful and reliable tool in the rapid and accurate diagnosis of tubercular lymphadenopathy. In addition, GeneXpert offered rapid detection of rifampicin resistance and prompt initiation of the appropriate treatment.*

[Chest Heart J. 2024; 48(1) : 3-11]

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Introduction:

Tuberculosis (TB) is the oldest disease in the history of mankind and it is prevailing in the society perhaps for several million of years[1]. It is still the major health problem worldwide. In 2019, globally about 10 million people developed TB and 1.4 million died. Eight countries accounted for two thirds of the global total. Bangladesh ranks seventh in the list of the high TB burden countries. [2]

Tuberculosis remains major public health problem in Bangladesh. According to WHO In Bangladesh, the prevalence rate of TB is 404/100,000 and the incidence rate was 225/100,000. The estimated TB mortality is 45 per 100,000 population per year.[3] Over 95% of TB deaths occur in developing countries, and it is among the top 5 causes of death among women aged 15–44 years[2]

Primarily, TB is considered the pulmonary disease. However, it can affect almost any part of the body. Extrapulmonary tuberculosis continues to be one of the leading health problem in developing countries[4](Raja et al., 2021). Tubercular lymphadenopathy is the commonest form of extra pulmonary tuberculosis and accounts for 20–40% of extrapulmonary tubercular cases[5].

Tubercular lymphadenopathy is not always associated with the common constitutional symptoms of TB like fever, cough, weight loss, fatigue, and night sweats. Patients usually presents only with enlarged lymph nodes and they are prescribed an initial 2 weeks of antibiotic treatment. If the enlarged lymph nodes do not regress after treatment, there is suspicion of tubercular lymphadenopathy.

Accurate diagnosis and early treatment of TB has the potential to reduce morbidity and mortality associated with tubercular lymphadenopathy. However, the differential diagnosis of tubercular lymphadenopathy is broad and laboratory confirmation is of key importance for guiding appropriate therapy[6].But obtaining tissue specimens for microbilogical diagnosis is difficult and thus it remains challenging to diagnose & treat[7].

Fine needle aspiration cytology (FNAC) is rapid, simple and minimally invasive procedure for performing cytology, smear microscopy, mycobacterial culture and molecular tests on lymph node samples[8]. On cytology Chronic granulomatous inflammation supports the diagnosis of probable TB but it have low specificity because similar cytologic feature may found in other infectious and non-infectious conditions[9]. Conventional smear microscopy lacks sensitivity due to the paucibacillary nature of fine needle aspirates(FNA) [10]. Mycobacterial culture is the gold standard method for definitive diagnosis but its major limitations are it is quite time-consuming, takes 6-8 weeks on conventional Lowenstein-Jensen medium & not always available in resource poor settings.[11,12]. But for the disease such as tuberculosis, this is too long to wait for results of culture because it is necessary to start treatment at the earliest. Therefore, comparatively rapid diagnostic strategies need to be established for diagnosis of tubercular lymphadenopathy[13]

GeneXpert MTB/RIF is an automated, cartridge-based and isothermal nucleic acid amplification test (NAAT) for the detection of Mycobacterium tuberculosis complex and rifampicin resistance from sputum and other specimens, in less than 2 hrs, shows sensitivity comparable to culture [14,15]. In 2014, WHO has recommended GeneXpert, over the conventional tests (including conventional microscopy, culture or histopathology) for testing specific non respiratory specimens (lymph nodes and other tissues) from patients suspected of having Extra Pulmonary TB[16]. However, this was a conditional recommendation due to very low-quality evidence available. It shows impressive performance in case of gastric aspirate, urine, and stool[15]. Most of the studies conducted on sputum or aspirates but there are fewer evidence regarding the efficacy of this test on solid tissue such as lymph node specimens from high TB burden regions which is the main aim of this study.

Thus, we evaluated the performance of GeneXpert for the diagnosis of clinically suspected tubercular lymphadenopathy using routinely collected FNA material from lymph node and to compare it to conventional culture method.

Materials and Methods:

The purpose of the study was to assess the diagnostic performance of GeneXpert in clinically suspected tubercular lymphadenopathy. This was an cross sectional observational study done among 43 patients who fulfilled both inclusion and

exclusion criteria. Purposive sampling was done. A Structured questionnaire was used for data collection. The statistical analysis was carried out using SPSS version 23.0 for Windows. Ethical issue was addressed appropriately.

Inclusion Criteria:

In order to address the research question, the inclusion criteria for research participants include patients clinically suspected of having tubercular lymphadenopathy. Patients were >14 years of age with one or more superûcial lymph nodes persisting for more than 1 month.

Exclusion criteria:

The participants of the study excluded the patients unwilling to participate in the study. Patient previously diagnosed with TB and on anti tubercular treatment. Established malignant case.

This cross-sectional study was conducted in the NIDCH during the period from January 2020 to March 2021. Total 100 patients were screened. Among them 43 patients were finally enrolled who fulfilled inclusion and exclusion criteria.All of the study patients were counseled regarding the study's aim, objectives, and usefulness. Both verbal and written informed consent was collected from each patient. Prior to data collection informed written consent were taken from the respondents.

Demographic and clinical data were collected on a structured questionnaire. A baseline complete blood count with ESR, chest radiograph, MT, was performed.

Observations and Results:

This was a descriptive type of Cross-sectional study conducted in Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhaliamong43 patients of clinically suspected tubercular lymphadenopathy. The aim of this study was to evaluate the diagnostic performance of the GeneXpert for direct detection of Mycobacterium tuberculosis (MTB) and rifampicin resistance from lymph node specimens. Data were collected with structured face to face interview using data collection sheet.GeneXpert, Culture & cytology from FNA material done in all 43 patients. Diagnostic utility of the GeneXpert was assessed in the form of sensitivity & specificity by comparing to culture as the gold standard. Analysis was done by statistical software SPSS 23. The results are presented in this section.

Demographic profile of the study population

Table-I

Distribution of the study population according to Gender (n=43)

Gender	Frequency	Percentage
Male	17	39.53
Female	26	60.47

Table I shows that in this study out of 43 study population, 26 were females and 17 were males. Majority (60.47%) were female. Male female ratio was 1:1.5.

Table-II

Distribution of the study population according to Age (n=43)

Age groups	Frequency	Percentage
<20	8	18.60
21-30	20	46.52
31-40	9	20.93
41-50	4	9.30
>50	2	4.65
Mean ± SD (Years)	29.27 ± 12.68	

Table II shows that most of the study population 20 (46.52%) were in age group of 21-30 years and the second most common age group was 31-40 years constituting 9 (20.93%) of the patients. The mean age was 29.27 ± 12.68 years.

Table-III

Distribution of the study population according to occupation (n=43)

Occupation	Frequency	Percentage
Student	20	46.51
House wife	8	18.60
Worker	7	16.27
Service	5	11.62
Others	3	6.97

Table III shows that majority 20 (46.51%) of the study population were student by occupation, followed by House wife being the second most common reported occupation 8 (18.60%).

Clinical feature of the study population

Table-IV

Distribution of the study population according to clinical features (n=43).

Clinical features	Frequency	Percentage
Fever	26	(60.47)
Weight loss	22	(51.16)
Night sweating	26	(60.47)
Anorexia	23	(53.49)
Cough	11	(25.58)

Table IV shows that among the 43 study population 26 (60.47%) had both fever and night sweat, Whereas 23 (53.49%) had anorexia and 22 (51.16%) had weight loss.

Lymph node group involvement of the study population

Table-V

Distribution of the study population according to lymph node group involvement (n=43)

Name of the group	Frequency (%)	Percentage (%)
Cervical	28	65.11
Supraclavicular	6	13.95
Axillary	5	11.62
Submandibular	2	4.65
Pre auricular	1	2.33
Post auricular	1	2.33

Table V shows that the cervical lymph nodes were most commonly involved site 28 (65.11%). Next most common site of involvement was supraclavicular nodes 6 (13.95%).

Cytomorphological diagnosis of the study population

Table-VI

Distribution of study population according to Cytomorphological diagnosis (n=43)

Cytomorphological feature	Frequency	Percentage
Suggestive of tubercular lymphadenopathy		
Epithelioid granuloma with necrosis	18	41.86
Epithelioid granuloma without necrosis	10	23.25
Necrosis without epithelioid granuloma	8	18.60
Reactive	5	11.62
Others	2	4.65

Table VI shows that regarding Cytomorphological diagnosis Epithelioid granuloma with necrosis was the most common finding 18 (41.86%) followed by Epithelioid granuloma without necrosis was next common 10 (23.25%).

Screening test results of the study population

Table-VII

Distribution of study population according to Screening test results (n=43).

Screening test	Frequency	Percentage
CXR PA View		
Pulmonary TB present	6	13.95
Pulmonary TB absent	25	58.13
Not done	12	27.90
Sputum for AFB		
Present	1	2.32
Absent	12	27.90
Not done	30	69.76
MT test		
Positive	12	27.90
Negative	4	9.30
Not done	27	62.69

Table VII shows that MT was the most positive screening test, 12 (27.59%) followed by CXR PA view 6 (13.95%).

Cytology, GeneXpert & AFB culture result of study population

Table-VIII

Distribution of study population according to result of Cytology, GeneXpert& AFB culture (n=43)

Test	Positive	Percentage (%)	Negative	Percentage (%)
Cytology	36	83.72	7	16.27
AFB Culture	18	41.86	25	58.13
GeneXpert	23	53.48	20	46.51

Table VIII shows thatout of 43 study population tubercular lymphadenopathy was diagnosed by Cytology in 36 (83.72%) of cases, followed by GeneXpert 23 (53.48%) & AFB culture 18 (41.86%) of cases.

Association between Culture and GeneXpert result of study population

Table-IX

Association between the results of culture and GeneXpert test

	Culture					
	Positive		Negative		Total	
	n	%	n	%	n	%
Gene Xpert Positive	16	37.20	7	16.27	23	53.47
Gene Xpert Negative	2	4.65	18	41.86	20	46.51
Total	18	41.86	25	58.13	43	100

n= number

Pearson Chi-square statistics are significant at p ≤0.0002

Table IX shows that in this study 16 (37.20%) patients had true positive results & 18 (41.86%) patients had true negative results. The Pearson ÷2 test was highly significant at p d" 0.0002, suggesting a strong relationship between culture and GeneXpert result.

Performance indices of GeneXpert

Table-X

Performance indices of GeneXpert

Indices	Values %	95% CI
Sensitivity	88.88	(65.29% to 98.62%)
Specificity	72.00	(50.61% to 87.93%)
PPV	69.56	(54.42% to 81.40%)
NPV	90.00	(70.43% to 97.14%)
Accuracy	79.06	(63.96% to 89.96%)

Table X shows that in this study the sensitivity, specificity, PPV, NPV, Overall diagnostic accuracy, was 88.88%, 72.00%, 69.56%%, 90.00% and 79.06% respectively.

Rifampicin resistance on GeneXpert of study population

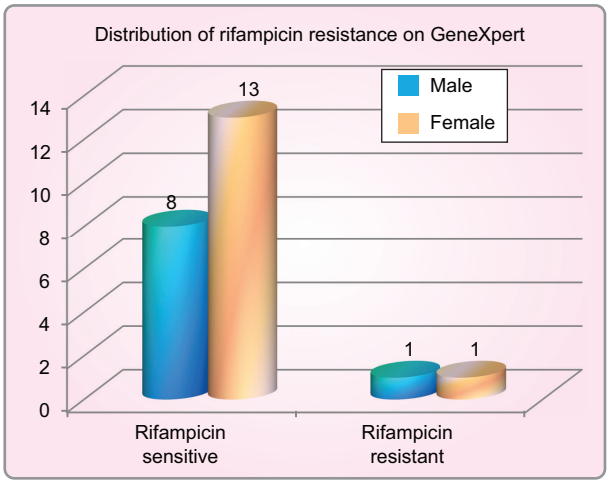

Figure 1 *shows rifampicin resistance was found in one male (2.33%) and one (2.33%) female patients.*

Discussion

TB is a worldwide disease having varied presentation. Extra pulmonary TB is a significant health problem worldwide. Tubercular lymphadenopathy is the most common form of extra pulmonary TB. The diagnosis of tubercular lymphadenopathy remains challenging. The routinely used methods have sub-optimal sensitivity. Recently, WHO recommends GeneXpert to be used as the initial diagnostic test in patients suspected of having extra-pulmonary tuberculosis. However, this was a conditional recommendation. In this context this study proposed to evaluate the performance of GeneXpert for the diagnosis of tubercular lymphadenopathy on concentrated fine needle aspirates (FNA)

This descriptive cross-sectional study was conducted in the Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka from January 2020 to March 2021. The aim of this study was to know the sensitivity and specificity of GeneXpert in the diagnosis of clinically suspected tubercular lymphadenopathy. In this study 43 patients of suspected tubercular lymphadenopathy were included according to inclusion and exclusion criteria.

In this study female predominance was seen which was similar to other studies. Male to female ratio was 1:1.5. Fontanilla et al had found in their study the same ratio [17] Similarly, Purohit et al alsofound same male to female ratio[18]. The female predominance might be due to biological, hormonal, social and environmental differences

between men and women. Biologically, there is a fundamental difference between men and women and a hormonal influence on immunity can be the underlying cause for the different patterns of disease in women19. Socially, in developing countries lower access to healthcare and nutritional status of women can affect the immune response to disease[18].

In this study, most of the patients were at younger age group. The peak incidence was in age group of 20–30 years. Although previously it was considered a disease of childhood, lymphadenopathy has a peak age of onset of 20–40 years[20]. This studies also showed that majority of the patients (67.44%) were in the age group of 20–40 years. Patients of age <14 years were not included in our study.

Most of the patients had fever and night sweating 26(60.47%) whereas 23 (53.49%) had anorexia and 22 (51.16%) had weight loss. These are the common constitutional presentation of extra pulmonary TB. In a study done by Gautam et al which shows 75% of tubercular lymphadenitis cases displayed fever as major symptom[21]. General signs such as, weight loss, sweats, fever, and asthenia are common in 20%–50% patients of tubercular lymphadenopathy[22].

In this study the cervical group of lymph nodes is the predominant site of involvement with 65.11% that is similar to other studies reported internationally at 45%–70%[5,23,24,25]. Cervical lymphadenitis is the consequence of lympho-hematogenous spread of pulmonary tuberculosis[20]. Further it might be also due to hyper reactivity of lymph nodes against previous pulmonary tuberculosis26 (Singh et al 2013). The major pathway of dissemination of the tubercle bacilli to the cervical lymph nodes is from lung parenchyma as the lymphatics of the right lung and the lower lobe of the left lung drain into the right supraclavicular lymph nodes and then upwards to the right lower cervical chain[26]

In this study, FNAC was suggestive of tubercular lymphadenitis in

83.72of the cases. The cytomorphologicalpatterns in FNAC smears of diagnosed tubercular lymphadenopathy patients ranging from well defined granuloma with caseous necrosis, to fewer epithelioid and multinucleated histiocytes, to only the presence of caseous necrosis. Several studies [21,27,28,29] have classified the cytomorphological spectrum in tubercular lymphadenopathy into three types depending on the presence or absence of granuloma or necrosis, such as necrotizing granuloma, non-necrotizing granuloma, or necrosis only.

A few studies also classify them as Epitheloid granuloma with necrosis ,Epitheloid granuloma without necrosis, or necrosis [30] . This study observed Epitheloid granuloma with necrosis as the most common cytomorphological pattern (41.86%) of all cases, which is similar to published data [27,28]. Chronic granulomatous inflammation most confidently can supports a diagnosis of TB in endemic areas [29]. However it is not pathognomonic and may be seen in other infectious conditions [17,29,31]. Reactive cytology does not exclude tubercular lymphadenopathy. One cases in this study with a reactive cytology who had bacteriological evidence of TB 1(2.32%) were GeneXpert positive. It may be due to few discrete granulomas may be missed during needling.

In our study sensitivity, specificity, PPV, NPV and Overall accuracy of GeneXprt was 88.88%, 72%, 69.56%, 90% and 79.06% respectively. In the present study, the sensitivity of GeneXpert was 87.8%. A systematic review and meta-analyses conducted by Denkinger et al showed that GeneXpert against culture has a sensitivity ranging from 50% to 100% with pooled sensitivity of 83% [32]. More recently, Penz et al reviewed 36 studies in their meta-analyses and confirmed GeneXpert pooled sensitivity of 87% that is similar to our study[33]. However, the sensitivity of GeneXpert in the current study is lower than that was found in similar study by Ligthelm et al at sensitivity, 96.7% [34].

Vadwai et al. also found GeneXpert sensitivity on lymph node is 94.93% and 83%, respectively[10] . There were 2 culture-positive cases which were negative on GeneXpert . The reason for false-negative GeneXpert test results may be due to the limited number of bacilli in the FNA sample and may be due to technical failure to correctly operate GeneXpert.

In this study the specificity of GeneXpert is72 %whis is lower than previous studies reported by others (specificity,89–99%) [32,33,34] . But similar to

the study done by Biadigilegn et al at specificity 69.2%.[35]. Seven culture-negative cases were GeneXpert positive suggesting the presence of nonviable or scanty bacilli due to either the harsh decontamination process or the nature of the caseous lesion in the lymph node tissue which may have contained dead tubercle bacilli. [35]

GeneXpert offers rapid detection of rifampicin resistant strains directly from the clinical sample, an important advantage over cytology and smear microscopy. In the current study, rifampicin resistance was identified in 4.66 % of GeneXpert positive cases which is supported by other studies.[21]

As GeneXpert detects mycobacterium tuberculosis with high sensitivity and specificity on FNA material with superior performance as compared to culture it promises to be a very convenient technique that can be confidently used for the diagnosis of clinically suspected tubercular lymphadenopathy.

Conclusion:

The high sensitivity and specificity coupled with its speed and simplicity make the GeneXpert the most useful and reliable tool in the rapid and accurate diagnosis of tubercular lymphadenopathy. In addition, GeneXpert offered rapid detection of rifampicin resistance and prompt initiation of the appropriate treatment.

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ORIGINAL ARTICLE

Utility of the Fifteen Steps Climbing Exercise Oximetry Test in Assessing Disease Severity in Stable COPD Patients- A Cross Sectional Study

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Abstract

Background: *Forced Expiratory Volume in the first second (FEV_1) from spirometry is essential in diagnosing and managing COPD. Early detection of severe COPD in primary care is vital for timely referral and treatment. Spirometry is often underutilized in rural areas due to limited resources. The Fifteen Steps Climbing Exercise Oximetry Test (15SCT) offers an alternative for assessing COPD severity.*

Objective: *To evaluate the efficacy of 15SCT in determining disease severity in stable COPD patients.*

Methods: *This cross-sectional study was conducted at the National Institute of Diseases of the Chest and Hospital (NIDCH) from June 2022 to August 2023, involving 116 stable COPD patients. Spirometry confirmed COPD diagnosis and severity grading. Pulse, respiratory rate, and oxygen saturation (SpO_2) were measured pre- and post-15SCT. Data were analyzed using SPSS v.23, employing Paired t-test, Unpaired t-test, and ROC curve analysis.*

Results: *Patients (mean age 61.3±8.1 years; M:F = 22.2:1) showed moderate (50.0%), severe (43.1%), very severe (5.2%) and mild (1.7%) COPD. Most patients (52.6%) took 61-90 seconds for 15SCT. Post-15SCT SpO_2 significantly decreased from baseline (92.9±2.3% vs. 96.3±1.3%; $p<0.05$). Patients with FEV_1<50% had higher SpO_2 reduction (4.37±1.12%) than those with FEV_1 ≥50% (2.51±0.96%). ROC analysis identified a ≥3.5% SpO_2 drop as indicative of severe airflow limitation with good sensitivity (80.4%), specificity (90.0%) positive predictive value (88.2%), and negative predictive value (83.1%).*

Conclusion: *Significant exercise-induced desaturation correlated with COPD severity, supporting 15SCT as a useful tool for predicting severe airflow limitation in stable COPD patients.*

Keywords: *COPD, 15SCT, oximetry, step test.*

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of death globally, characterized by progressive airflow limitation due to chronic inflammation of the airways and lung tissue[1]. Prolonged exposure to noxious particles or gases, such as cigarette smoke or biomass fuel, leads to structural lung changes[2, 3]. In Bangladesh, it is a neglected public health issue, as about 12.5% of adults suffer from COPD, predominantly elderly, resulting in significant morbidity and mortality[4].

With genetic factors being important determinants, COPD encompasses chronic bronchitis, small airway disease, and emphysema, with significant systemic effects[5]. Destruction of alveoli, terminal bronchioles, and capillary vessels, along with airway fibrosis and secretion, compromises the respiratory membrane and reduces gas transfer capacity, leading to decreased inspiratory capacity and breathlessness on exertion with reduced exercise capacity[6]. Hypoxemia in COPD results from ventilation-perfusion (V/Q) mismatch, worsening with disease progression[7]. The systemic inflammation in COPD raises pro-inflammatory cytokines, causing a range of different extra-pulmonary manifestations like- excessive weight loss, skeletal muscle dysfunction, diminished muscle strength, lower limb muscle atrophy, hindering activities like- walking, stair climbing etc.[8, 9, 10, 11].

COPD severity is typically graded by Forced Expiratory Volume in the first second (FEV_1) via spirometry, which is a reproducible, non-invasive and gives an objectivemeasurement of airflow limitation,widely available in most resource abundant countries[1] (GOLD, 2022). However, in resource-limited settings, exercise tests, which capture the integrated and multisystem effects of COPD, are crucial in assessing disease severity and facilitating timely referral to higher centers[12]. Pulse oximetry, an inexpensive and non-invasive method, measures SpO_2 before and after exercise, may indicate COPD disease severity in terms of significant decrease in SpO_2 which correlates with severe airflow limitation and a positive smoking history[13].

Studies conducted by several authors have shown a strong association between severe airflow limitation (FEV_1<45%) and exercise-induced oxygen desaturation in the 6-minute walk test (6MWT) and 2-minute walk test (2MWT)[14, 15, 16]. Step tests, first studied in as early as 1985, are efficient in eliciting higher metabolic and ventilatory responses than 6MWT, as they recruit less frequently used muscle groups[17]. Various step tests have been used to evaluate pulmonary disease severity, though many lack consistent validation against gold standard cycle ergometry Cardio-PulmonaryExerciseTest (CPET)[18].

The Fifteen Steps Climbing Oximetry Test (15SCT) is a simple step test conducted on a standard staircase. Patients climb up and down as rapidly as they can without pacing. Studies have compared exercise-induced oxygen desaturation in 15SCT with 6MWT, 2MWT, and CPET in COPD patients[16, 19]. The 15SCT is easy to perform, requiring less time, patient familiarization, and space, making it feasible in various settings.

This study aims to evaluate the 15SCT's clinical utility in assessing disease severity in stable COPD patients by measuring post-exercise oxygen desaturation. We also seek to establish a statistical cut-off for severe to very severe COPD.

Materials and methods

This cross- sectional observational study was carried out in the Department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka between June 2022 and August 2023.

Inclusion criteria were:

1. Patients coming to NIDCH who are diagnosed as a case of COPD on the basis of GOLD guideline.
2. Patients with stable COPD for a minimum duration of 4 weeks.
3. Patient's age >40 years.
4. Patients willing to participate in this study.

Exclusion criteria were:

1. COPD patients on acute exacerbation
2. COPD patients with chronic respiratory failure or on longterm oxygentherapy
3. Presence of other lung disease like Asthma, Diffuse Parenchymal Lung Disease (DPLD) or bronchiectasis etc.

4. A recent acute coronary syndrome (unstable angina or myocardial infarction) and acute heart failure
5. Patientswith active malignancy, orthopedic or neurological diseases with walking difficulties.

A total of 116 patients with stable COPD, attending in the Outpatient Department of NIDCH were selected through convenient sampling method. Informed written consent was taken from all the patients in presence of witness, after proper explanation about the study protocol. Relevant clinical history was taken and physical examination was performed. All individuals were subjected to spirometry including the reversibility test. The best record from three attempts was selected and recorded to obtain the forced vital capacity (FVC), FEV_1 and FEV_1/FVC ratio. All the patients were categorized according to GOLD grading of severity into mild, moderate, severe and very severe on the basis of FEV_1. Baseline data (FEV_1, FEV_1/FVC, resting pulse, respiratory rate and SpO_2) wascollected and then all the patients were subjected to 15 Steps Climbing Exercise Oximetry Test(15SCT) on the same day, about 1 hour later, on a regular staircase having steps of standard height and a strong support railing without fixed pacing. Thenpertinentpost-exercisedata (pulse, respiratory rate, SpO_2 and exercise time) was collected.

Results

Out of the 116 patients, three fourth (75.0%) patients belonged to age group 56-70 years. The mean age was 60.4±7.2 years with a age from 42 to 75 years. Male patients significantly outnumbered females 111(95.7%) and most of the patients were service holders 50(43.1%). Mean BMI of the patients was found 21.2±3.5 kg/m^2. More than half 61(52.6%) patients were current smokers, 50(43.1%) were ex-smokers and 5(4.3%) were non-smokers, while 5(4.3%) patients had exposure to biomass fuel. 22(19.0%) patients had HTN, 18(15.5%) patients had DM, 8(1.7%) had IHD, 2(1.7%) had CKD and 1(0.9%) had CLD. Three (2.6%) patients had multiple co-morbidities. Most of the patients had mMRC grade 1 (32.8%) or grade 2 (31.0%) dyspnea.

In post bronchodilator spirometry,the mean FEV_1 was 51.3±13.5% with a range of 22.0-88.0%. Majority 58(50.0%) patients had moderate COPD, 50(43.1%) had severe, 6(5.2%) had very severe and 2(1.7%) had mild COPD. Mean SpO_2 was significantly reduced after 15SCT than baseline (92.9±2.3 vs 96.3±1.3%) with mean difference 3.4%, 95% CI (3.1 to 3.6%). Mean pulse was 91.2±5.7 beats/min and respiratory rate was 18.3±1.6 breath/min) after 15SCT. The mean exercise time was 71.5±17.0 seconds, where more than half (52.6%) patients took between 61-90 seconds to complete the exercise. Mean 15SCT time was significantly higher in COPD patients with FEV_1<50% (81.5±15.8 seconds) than in patients with FEV_1≥50% (62.2±12.1 seconds). In a similar fashion, mean oxygen saturation difference (between before and after 15SCT) was significantly higher in COPD patients

Table- I

Demographic Distribution of the study population (n=116)

Demographic characteristics	Number of patients	Percentage
Age (years)		
40-55	28	24.1
56-70	87	75
>70	1	0.9
Mean±SD	60.4	±7.2
Range (min-max)	42.0	-75.0
Male	111	95.7
Female	5	4.3
Occupational status		
Service holder	50	43.1
Cultivator	28	24.1
Day laborer	15	12.9
Businessman	11	9.5
Retired	7	6.0
House wife	5	4.3
BMI (kg/m^2)		
Underweight (<18.5)	36	31.0
Normal (18.5-22.9)	42	36.2
Overweight (23.0-24.9)	20	17.2
Obese (≥25.0)	18	15.5
Mean±SD	21.2	±3.5
Range (min-max)	15.2 - 29.7	

Table- II

Distribution of patients by their smoking status and history of exposure to biomass fuel (n=116)

Exposure to noxious agents	Number of Patients	Percentage
Smoking Status		
Current Smokers	61	52.6
Ex-Smokers	50	43.1
Non-Smokers	5	4.3
Exposure to biomass fuel		
Yes	5	4.3
No	111	95.7

having FEV_1<50% (4.37±1.12%) than in patients having FEV_1 ≥50% (2.51±0.96%).

Receiver operating characteristic (ROC) curve was constructed by using oxygen saturation differences

Table- III

Distribution of the study population according to co-morbidities (n=116)

Co-morbidities	Number of patients	Percentage
HTN	22	19.0
DM	18	15.5
IHD	8	6.9
CKD	2	1.7
CLD	1	0.9

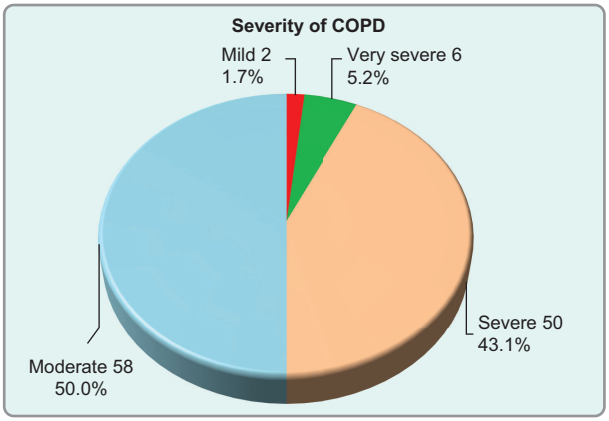

Figure 1: *Pie chart showing severity of airflow obstruction COPD according to post bronchodilator FEV_1 of the study population (n=116)*

Table-IV

SpO_2, pulse and RR at the beginning and after Fifteen Steps Climbing Oximetry Test (15SCT) (n=116)

	Baseline Mean±SD	After 15SCT Mean±SD	Mean difference (95% CI)	*P* value
SpO_2 (%)	96.3±1.3	92.9±2.3	3.4 (3.1 to 3.6)	0.001[s]
Pulse (beats/min)	85.6±6.2	91.2±5.7	5.6 (6.3 to 5.0)	0.001[s]
Respiratory rate (breaths/min)	16.3±0.9	18.3±1.6	2.0 (2.2 to 1.7)	0.001[s]

P value reached from paired t-test, s= significant

Table-V

Association between severity of airflow limitation of COPD and 15SCT time (n=116)

	Severity of COPD		F value	*P* value
	FEV_1 ≥50% (Mild +Moderate) (n=60) Mean±SD	FEV_1<50% (Severe+ Very severe) (n=56) Mean±SD		
15SCT time (seconds)	62.2±12.1	81.5±15.8	3.846	0.001[s]
Range (min-max)	30.0-90.0	50.0-130.0		

P value reached from unpaired t-test, s= significant

Table- VI

Association between severity of airflow limitation of COPD and oxygen saturation difference between before and after 15SCT (n=116)

	Severity of COPD		F value	*P* value
	FEV_1 ≥50% (Mild +Moderate) (n=60) Mean±SD	FEV_1<50% (Severe+ Very severe) (n=56) Mean±SD		
Oxygen saturation difference (%)	2.51±0.96	4.37±1.12	1.271	0.001[s]
Range (min-max)	0.0-6.0	2.0-8.0		

P value reached from unpaired t-test, s= significant

Table- VII

Valuation of oxygen saturation difference (ÄSpO$_2$) ≥3.5% against severe airflow limitation (FEV$_1$<50%) in stable COPD (n=116)

Oxygen Saturation difference ≥3.5%	Severe COPD according to GOLD 2022 grading	
	Positive (Severe+ Very severe) FEV$_1$<50% (n=56)	Negative (Mild +Moderate) (FEV$_1$ ≥50%) (n=60)
Positive (n=51)	45 (True positive)	6 (False positive)
Negative (n=65)	11 (False negative)	54 (True negative)

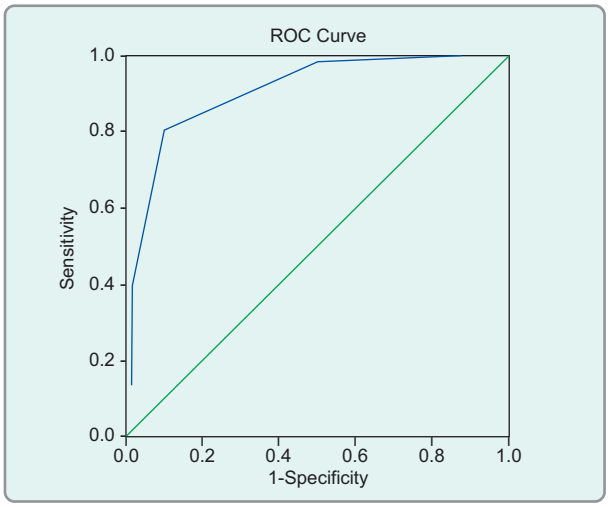

Figure- 2: *Receiver operating characteristic (ROC) curves of oxygen saturation (SpO$_2$) differences between baseline and after 15 steps climbing exercise oximetry test (n=116) gave a cut off value of ΔSpO$_2$ ≥3.5 percent with an area under curve 0.905.*

Table-VIII

Sensitivity, specificity, accuracy, positive and negative predictive values of the oxygen saturation difference (ΔSpO$_2$) ≥3.5%evaluation for prediction of severe airflow limitation (FEV$_1$ <50%) in stable COPD

Validity test	Percentage
Sensitivity	80.4
Specificity	90.0
Accuracy	85.3
Positive predictive value	88.2
Negative predictive value	83.1

(between before and after 15SCT), which gave a cut off value of ΔSpO$_2$ ≥3.5 percent, with 80.4% sensitivity and 90.0% specificity on validation against FEV$_1$<50% (severe and very severe grades of stable COPD).

Discussion:

This cross-sectional study aimed to evaluate the usefulness of the 15 Steps Climbing Test (15SCT) in assessing disease severity in patients with stable COPD, based on FEV$_1$ measurements. Conducted with 116 patients at NIDCH, the study provides valuable insights.

Most participants (75%) were aged 56-70, with a mean age of 60.4±7.2 years, reflecting the increased risk of COPD with advancing age. This finding aligns with previous studies by Ganju et al. (2011), Rusanov et al. (2008), and Starobin et al. (2006)[20, 21, 22]. The predominance of male patients (95.7%) underscores the higher prevalence of COPD in men, likely due to higher smoking rates, as 52.6% were current smokers and 43.1% were ex-smokers. These results are consistent with the findings of Islam et al. (2013) and other studies[23]. This study shows that 5(4.3%) patients had exposure to biomass fuel.

The mean BMI of 21.2±3.5 kg/m² indicates no particular BMI group being more prone to COPD, similar to findings by Gloeckl et al. (2016) and Ganju et al. (2011)[20, 24]. Comorbidities were common, with 19% of patients having hypertension and 15.5% having diabetes, reflecting the multi-system impact of COPD. Three (2.6%) patients had multiple co-morbidities.

Dyspnea grading showed that most patients had mMRC grade 1 (32.8%) or grade 2 (31.0%) dyspnea,

with no patients at grade 4. Post-bronchodilator spirometry revealed a mean FEV_1 of 51.3±13.5% of predicted value, with most patients having moderate (50%) or severe (43.1%) COPD. These findings are consistent with Rusanov et al. (2008) and Ganju et al. (2011)[20, 21]. An inference can be drawn that, at outdoor of tertiary care hospitals like NIDCH, mild cases are relatively less encountered, while very severe cases are too ill and attend the emergency department.

The 15SCT exercise time was higher in patients with FEV_1<50%, indicating greater disease severity. This is supported by Negm et al. (2012) and Starobin et al. (2006), who observed increased exercise time with higher COPD severity[19, 22]. The study also found a significant reduction in mean SpO_2 after the 15SCT, with a greater decrease in patients with FEV_1<50%. Mean SpO_2 was significantly reduced after 15SCT than baseline (92.9±2.3 vs 96.3±1.3%) with mean difference 3.4%, with 95% CI (3.1 to 3.6%). Mean oxygen saturation difference was significantly higher in COPD patients having FEV_1<50% (4.37±1.12%) than in patients having FEV_1 ≥50% (2.51±0.96%). These findings are in alignment with those studies done by Starobin et al. (2006) and Negm et al. (2012)[19, 22].

Using ROC curves, the study established a cut-off value of ΔSpO_2 ≥3.5% for predicting severe COPD, with 80.4% sensitivity, 90.0% specificity and 85.3% accuracy. This finding offers a valuable clinical tool for assessing disease severity in resource-limited settings.

Overall, the study demonstrates the efficacy of the 15SCT in evaluating COPD severity, providing a practical, low-cost alternative to spirometry in outpatient settings. This study also stablishes a post exercise cut off value for SpO_2 difference of e"3.5 percent with a good sensitivity and specificity for prediction of severe airflow limitation in case of stable COPD.

Conclusion:

This study demonstrated significant differences in oxygen saturation between mild to moderate and severe to very severe COPD patients before and after the 15 Steps Climbing Oximetry Test (15SCT). Using receiver operating characteristic curves, a cut-off value of ΔSpO_2 ≥3.5% was established, showing good sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for predicting severe airflow limitation (FEV_1<50%) in stable COPD patients. Therefore, the 15SCT is a useful, quick, simple, inexpensive, and convenient test for detecting severe airflow limitation in stable COPD patients. Farther study with larger sample size, including larger no. of mild cases, undergoing continuous oximetry during exercise is recommended.

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ORIGINAL ARTICLE

Usefulness of the PEARL Score to Predict 90-Day Post Discharge Outcome after Hospitalization among the Patients of Acute Exacerbation of COPD

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Abstract

Background: *Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) frequently leads to hospital admissions, with approximately one third of patients requiring readmission within 90 days. Early identification of this group of patients by a useful prognostic tool may ensure more aggressive treatment and lead to improved prognosis and reduced mortality.*

Objective: *To determine the usefulness of The PEARL score to predict 90-day post discharge outcome after hospitalization among the patients with AECOPD.*

Materials & Methods: *This prospective observational study was conducted in NIDCH, Mohakhali, Dhaka from May 2022 to September 2023. A total of 91 patients admitted with AECOPD, discharged after treatment were enrolled in this study. PEARL score & BODE index were calculated before discharge. On day 90 of discharge, they were followed up to assess & correlate the previously calculated score with the 90-day post discharge outcome as defined by need for readmission. Cut-off values of the PEARL score and BODE index were determined. The Statistical Package for Social Science (SPSS) v.23 was used for statistical analysis.*

Results: *Out of 91 patients admitted with AECOPD, 34 patients needed readmission within 90-day post discharge period. Mean PEARL score (5.5±1.5 vs 3.2±1.6) was significantly higher among the readmission group than non-readmission group in comparison to BODE index (5.4±1.4 vs 4.5±1.1). Receiver operating characteristic (ROC) curves showed PEARL score and BODE index cut-off values ofe"4.5 ande"5.5. Sensitivity and specificity of BODE indexwere 50.0% and 82.5%. While the sensitivity and specificity of PEARL score were 73.5% and 77.2%. The accuracy of BODE index and PEARL score were70.3% and 75.8%.Cohen's Kappa test determined Kappa value of 0.462 which reflectedmoderate agreement between BODE index and PEARL score.*

Conclusion: *The PEARL score is a valuable tool calculated by history taking and routinely available investigation, can predict the need for 90-day post discharge readmission in patients admitted with AECOPD.*

Keywords: *AECOPD, PEARL score, BODE index*

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is now one of the top three causes of death worldwide and 90% of these deaths occur in low and middle-income countries (LMICs)[1].Global burden will rise in future due toincreasing exposure to risk factors and aging of the population[1]. Though it is treatable and avoidable, the prevalence is rising, mostly in third worldcountries[2].

Acute exacerbation of COPD (AECOPD) is one of the most common causes for hospitalization and about one-third of patients need readmission within 90 days[3]. COPD is a grossly under diagnosed public health problem in Bangladeshi adults aged 40 years or older. Illiteracy, smoking & biomass fuel burning are modifiable risk factors of COPD[4].COPD is highly prevalent among Bangladeshi adults with an estimated prevalence of 12.5%[5]. Clinicians are not up to the mark to find out the patients who are at risk of readmission[6].

Chronic Obstructive Pulmonary disease is a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that causes persistent, often progressive airflow obstruction.COPD primarily consists of chronic bronchitis, small airway disease and parenchymal destruction (emphysema)[1]. COPD should be considered in any patient, usually age more than 40years, who has dyspnea, chronic cough or sputum production, history of recurrent lower respiratory tract infections and/or a history of exposure to risk factors for the disease.

Forced spirometry showing the presence of a post-bronchodilator FEV_1/FVCratio < 0.7 is required to establish the diagnosis of COPD[1]. Significant pathology such as chronic inflammation, increased inflammatory cells, and structural changes resulting in injury and lung repair are observed in COPD. COPD exacerbations are defined as an event characterized by increased dyspnea and/or cough &sputum that worsen over <14 days, often associated with increased local & systemic inflammation caused by airway infection pollution or other insults to the lung[7]. Exacerbations of COPD are important events in the management of COPD as they negatively impact health status, rates of hospitalization, readmission and progressive decline of lung function[8].

There is a lack of accuracy among physicians to identify particular risk factors for patients getting readmitted[6]. Care after discharge is directed by clinical judgement alone, which is not up to the mark[9].

Different scores have been designed to predict readmission or death in patients with COPD like BODE index, ADO index, PEARL score[10]. BODE index has shown potential to predict the future exacerbation in COPD patients of India[11]. Baseline BODE index could predict both survival and readmission for COPD[12]. PEARL score also has shown potential to predict readmission[9], but it has shown c-statistics of 0.703[10] and 0.70[9]. So, these findings need to be validated by further studies.

At present there is no gold standard scoring to predict readmission in COPD patients. Hence, a simple and accurate prognostic tool is required to identify these risk factors, that would benefit the patients from additional management and care, which will lead to improved prognosis and reduced mortality[10].

The aim of this study was to establish the usefulness of the PEARL score to predict the post discharge outcome after hospitalization among the patients of AECOPD in comparison to BODE index, that could have a significant impact on clinical decision making.

Materials and methods

This prospective observational study was conducted in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka from May 2022 to September 2023.

Inclusion criteria:

1. Patients admitted to NIDCH with acute exacerbation of COPD who were discharged after treatment.
2. Patients willing to participate in the study.

Exclusion criteria:

1. Medical history or clinical signs of asthma, asthma COPD overlap.
2. Inability to perform spirometry or six-minute walk test or both.
3. Recent myocardial infarction, unstable angina, decompensated heart failure.
4. Patients havinguncontrolled co-morbidities that could likely cause death within 2 years.
5. Patients having active malignancy.

Purposive sampling method was applied in this study. Ethical approval was taken from the Ethical Review Committee of NIDCH. A total of 91 acute exacerbation of COPD patients who were admittedto NIDCH, Mohakhali,Dhaka&discharged after management were enrolledfulfilling the inclusion and exclusion criteria. Informed written consent was obtained from all the patients and their attendants after proper explanation about the study protocol. Enrolled patients were evaluated in detail, including present and past clinical history, physical examination. Both PEARL score & BODE index of the individual patient were calculated. They were followed up physically or over telephone 90 days after discharge to assess & correlate the previously calculated scores with the 90-day post discharge outcome as defined by need for readmission. Sensitivity, specificity, positive and negative predictive values, accuracy of the PEARL score and BODE index were determined. Cut-off values of the PEARL score and BODE index for prediction of the requirement of readmission were also determined by plotting on ROC curves.As none of these scores is gold standard, agreement between the scores was assessed by Cohen's Kappa test.

Results

Out of 91 patients, majority (38.5%) belonged to age group 61-70 years and the mean age was 62.2±8.5 years. Male patients were predominant (96.7%), male to female ratio was 29.3:1. Majority 31(34.1%) patients were cultivator. Fifty patients had normal BMI, 4 were underweight, the mean BMI was 22.0±2.2 kg/m^2.Majority (68.1%) patients were current smokers,28.6% were ex-smokers and3.3%were never-smoker. Exposure to biomass fuel was found in 3 patients.NIV was required in 24 patients (26.4%) during index admission. Majority (38.5%) needed admissions e"2 times in past year. The mean duration of hospital stay during index admission was 6.6±2.0 days.Right heart failure was found in 21(23.1%) and left heart failure in only 2(2.2%) patients. Moderate airflow obstruction- was found in 36 patients, severe in 46 and very severe in 9 patients. The mean FEV_1 was 45.0±10.2. More than half (50.5%) had intermediate-risk, 41.8% had high-risk and only 7 patients had low-risk of PEARL score. Mean PEARL score was 4.0±1.9 with range from 0.0 to 8.0. Forty-one patients(45.0%) had BODE index quartile-3 (5-6), 44.0% had quartile-2 (3-4) and11.0% had quartile-4 (7-10). The mean BODE index was 4.9±1.3 with range from 3 to 8.

Among 91 patients 34 needed readmission representing 37.4% of study population, the mean time elapsed for readmission was 50.8±19.1 days. One patient died which is 1.1% of total study population. Mean PEARL score (5.5±1.5 vs 3.2±1.6) was significantly higher among readmission group than non-readmission group of patients in comparison to BODE index (5.4±1.4 vs 4.5±1.1). Mean duration of hospital stay was significantly longer in high risk of PEARL score than low &intermediate risk of PEARL score group (7.8±2.0 and 5.8±1.5 days).Based on the ROC curves, PEARL score had better area under curve (0.837) than BODE index (0.679).ROC curve gave the PEARL score a cut-off value of e 4.5& BODE index cut-off value of e 5.5. BODE index showed Sensitivity of 50.0%, specificity 82.5%, accuracy 70.3%, positive predictive value 63.0% andnegative predictive value 73.4%. The PEARL score showed sensitivity of 73.5%, specificity 77.2%, accuracy 75.8%, positive predictive value 65.8%and negative predictive value 83.0%.

Observed agreement was 74.7%. Kappa value was 0.462. This measure of agreement is statistically significant with moderate agreement between BODE index and PEARL score.

Table I

Distribution of the study population by demographic profile (n=91)

Demographic profile	Number of patients	Percentage
Age (years)		
41-50	13	14.3
51-60	31	34.1
61-70	35	38.5
71-80	10	11.0
>80	2	2.2
Mean ±SD	62.2	±8.5
Range (min-max)	43.0	-85.0
Sex		
Male	88	96.7
Female	3	3.3
Occupational status		
Cultivator	31	34.1
Businessman	18	19.8
Unemployed	14	15.4
Day laborer	6	6.6
Service holder	6	6.6
Housewife	3	3.3
Tobacco industry worker	2	2.2
Brick field worker	4	4.4
Others	7	7.7

Table II

Distribution of the study population according to clinical information (n=91)

Clinical information	Number of patients	Percentage
H/O Chronic cough	81	89.0
H/O Chronic sputum production	73	80.2
Need for NIV (During index admission)	24	26.4
History of previous admissions		
≥2 times in past year	35	38.5
<2 time in past year	32	35.2
No admission in past year	24	26.4
Mean duration of hospital-stay (days)	6.6	±2.0
Range (min-max)	3.0	-11.0

Table-III

Distribution of the study population according to clinical parameters (n=91)

Clinical parameters	Number of patients	Percentage
eMRCD score		
1-3	2	2.2
4	14	15.4
5a	22	24.2
5b	53	58.2
Right heart failure		
Yes	21	23.1
No	70	76.9
Left heart failure		
Yes	2	2.2
No	89	97.8
Severity of airflow obstruction(FEV_1% predicted)		
Moderate (50% to <80% predicted)	36	39.6
Severe (30% to <50% predicted)	46	50.5
Very severe (<30% predicted)	9	9.9
Mean±SD	45.0	±10.2
6 min walk distance (meters)		
150-249	6	6.6
250-349	46	50.6
≥350	39	42.9

Table-IV

Distribution of the study population according to outcome at 90-day after discharge (n=91)

Outcome at 90-day after discharge	Number of patients	Percentage
Need for readmission		
Yes	34	37.4
No	57	62.6
Time elapsed for readmission (Days)	50.8	±19.1
Range (min-max)	15.0	-81.0
Death		
Yes	1	1.1
No	90	98.9

Table-V

Relation between PEARL score and BODE index with 90-day post discharge outcome (n=91)

	No need for readmission (n=57) Mean ±SD	Need for readmission (n=34) Mean ±SD	t value	df	P value
PEARL score	3.2±1.6	5.5±1.5	6.665	89	0.001[s]
Range (min-max)	0.0-6.0	2.0-8.0			
BODE index	4.5±1.1	5.4±1.4	3.250	89	0.002[s]
Range (min-max)	3.0-7.0	3.0-8.0			

s= significant

P value reached from unpaired t-test

Table-VI

Receiver operating characteristic (ROC) curve of BODE index and PEARL score for prediction of need for readmission

	Cut-off value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI) Lower bound	Upper bound
BODE index	≥5.5	50.0	82.5	0.679	0.561	0.797
PEARL score	≥4.5	73.5	77.2	0.837	0.756	0.919

Table-VII

Association between BODE index and PEARL score evaluated by need for readmission (n=91)

BODE index	PEARL score ≥4.5 n=38	%	<4.5 n=53	%
≥5.5 (n=27)	21	55.3	6	11.3
<5.5 (n=64)	17	44.7	47	88.7

s=significant

Measures of agreement Kappa Value 0.462, p value 0.001[s]

Kappa value matches with moderate agreement.

Observed agreement = 74.7%

Kappa	Interpretation
< 0	Poor agreement
0.0 – 0.20	Slight agreement
0.21 – 0.40	Fair agreement
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 1.00	Almost perfect agreement

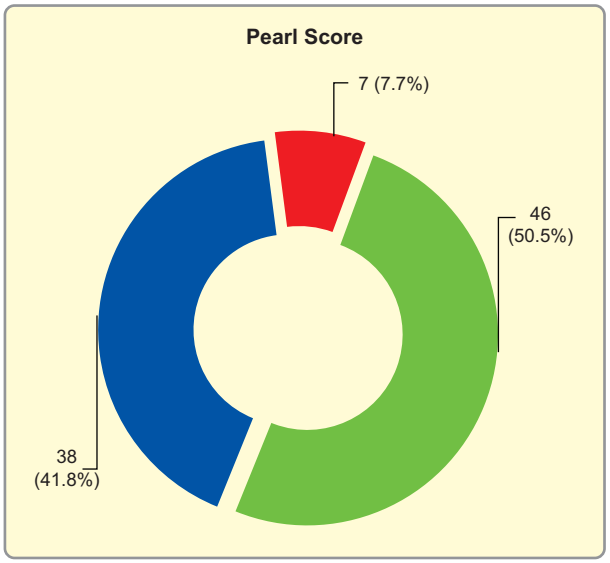

Figure 1: *Distribution of the study population according to PEARL score (n=91)*

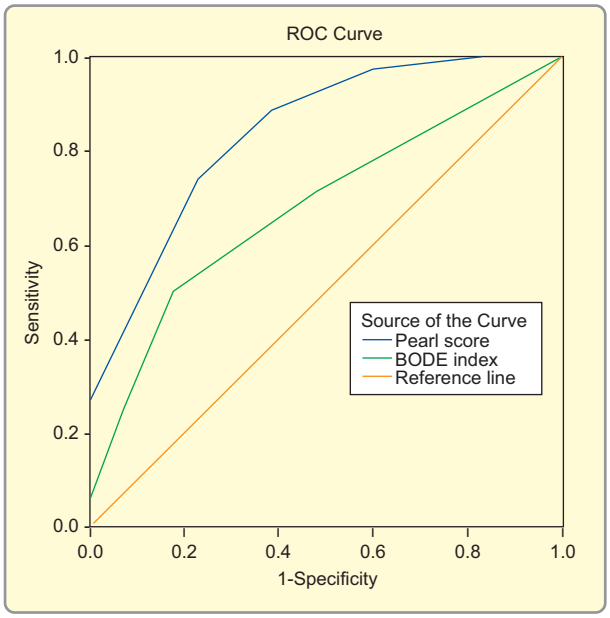

Figure 2: *Receiver operating characteristic (ROC) curves of BODE index and PEARL score.*

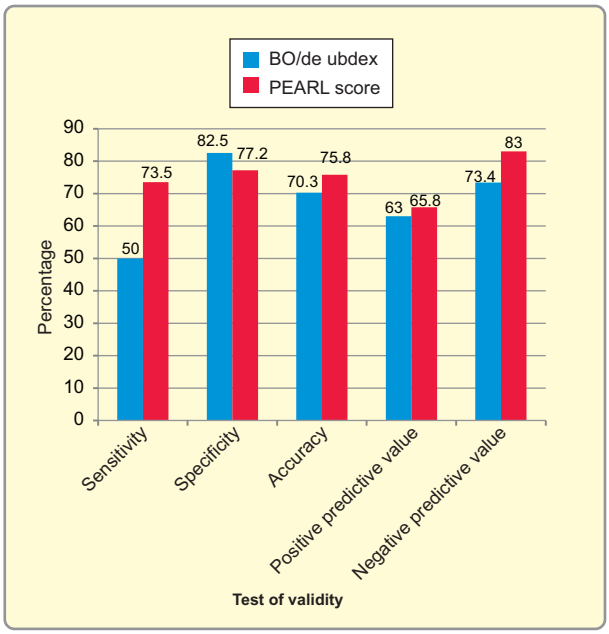

Figure 3: *Bar diagram showing sensitivity, specificity, accuracy, positive and negative predictive values of the PEARL score and BODE index for prediction of need for readmission*

Discussion

This prospective observational study was carried out with an aim to determine the usefulness of the PEARL score to predict 90-day post discharge outcome(need for re-admission) after hospitalization among patients withAECOPD.A total of 91 patients admitted to NIDCH, Mohakhali, Dhaka with AECOPD and discharged after treatment who fulfilled the inclusion and exclusion criteria during the period from May 2022to September 2023were included in this study. The present study findings were discussed and compared with previously published relevant studies.

In our study, majority 35(38.5%) patients belonged to age group of 61-70 years, the mean age was 62.2±8.5 years. In a study conducted by Joshi et al. (2021) reported that the mean age of the patients was 70.54 ± 10.85 years with range from 45 to 98 years[13]. A study done by Soler-Cataluña et al. (2019) found the mean age was 71±9 years[14]. Another study done by Praveen et al. (2009) found the mean age was 65.55±7.21 years[11]. So, most of the patients were from older age group which was almost similar to thisstudy.

Regarding clinical information, this study observed that NIV was needed in 24(26.4%) during index admission. Majority 35(38.5%) had history of previous admissions two or more times in past year. The mean duration of hospital stay was 6.6±2.0 days. Chen and Chen (2021) reported that,70.60% patients did not need readmission[15]. C. Echeverria et al. (2017) found need for NIV in 17.8% patients and mean length of hospital stay was 6(4-11) days in their derivation cohort[10]. These findings were also consistent with my study.

This study observed that, majority 53(58.2%) patients had eMRCD score 5b.Moderate airflow obstruction- was found in 36(39.6%), severe in 46(50.5%) and very severe in 9(9.9%) patients. The mean FEV_1 was 45.0±10.2. It was also found that 46(50.6%) patients had 6 min walk distance 250-349 m. Chen and Chen (2021) had observed that mMRC grade 2 was found in 43.87% and grade 3 in 29.72%[15]. The mean FEV_1% predicted 55.33±17.82%. Another study also done by Ko et al. (2011) showed the mean FEV_1% predicted 51.7±21.6%, mean 6 min walk distance was 262.3 ±99.0 m[12]. These findings were almost similar to this study.

Our study observed that, majority of the patients had intermediate risk of PEARL score 50.5%, while 41.8% had high risk and 7.7% had low risk of PEARL score. The mean PEARL score was 4.0±1.9.

In a study conducted by Joshi et al. (2021) obtained that the intermediate risk PEARL group had the highestnumber of patients (43.1%) followed by low-risk PEARLgroup with 40% of patients while high risk PEARL grouphad the least number of patients (17.6%)[13].Kishor et al. (2020) also showed that the mean PEARL score3.140±2.094[10]. There was minimum variation in mean PEARL score and distribution within risk groups among the studies.

Regarding outcome at 90-day after discharge, need for readmission was found in 34(37.4%), the mean time elapsed before readmission was 50.8±19.1 days. Only one (1.1%) patient died within 90 days of follow up. In a study conducted by Kishor et al. (2020) reported that of the 100 patients, 51(51%) patients were not admitted, 29(29%) patients were readmitted and 20(20%) patients died[10].Percentage of readmitted and not readmitted patients are almost similar to this study but number ofdeaths is less than other relevant studies.

In this present study it is observed that, mean PEARL score (5.5±1.5 vs 3.2±1.6) was significantly higher in those who needed readmission compared to BODE index (5.4±1.4 vs 4.5±1.1) ($p<0.05$). Kishor et al. (2020) described that the mean value of PEARL score in not admitted, readmitted, dead patients were 1.569±0.7281, 4.034±1.592, and 5.850±1.461 respectively[10]. The mean value of BODEX index was 6.294±1.238, 7.759±0.9876, 8.300±0.6569 respectively. It was evident that higher PEARL score was associated with increased probability of readmission.

This study observed that need for NIV was significantly higher in high risk of PEARL score than intermediate PEARL score (42.1% vs 17.4%). Similarly, a study conducted by Joshi et al. (2021) demonstrated that need for NIV was found in15.0% in low-risk group, 15.9% in intermediate group and 44.4% in high-risk group, which is consistent with our study.

ROC curve was constructed using BODE index showing sensitivity of 50.0%, specificity 82.5% with a cut-off value of e"5.5 and AUROC of 0.679. Kishor et al. (2020) described that the area under the curve (AUC) cure was 0.500 in BODE index. De Torres et al. (2014) also showed the BODE Index has the best predictive capacity of all of the single explored parameters with an AUC of 0.71 (95% CI 0.67 to 0.76, $p<0.001$). The abovementioned study findings werealmostsimilar to thisstudy.

Based on the ROC curves PEARL score had better area under curve (0.837). The ROC curve measured PEARL score cut off value of e"4.5, sensitivity of 73.5% and specificity of 77.2%.Echevarria et al. (2017) reported that the AUROC for the PEARL score for 90-day readmission/deathwithout readmission was: derivation=0.73(95% CI 0.70 to0.77); internal validation=0.68 (95% CI 0.64 to 0.72) andexternal validation=0.70 (95% CI 0.66 to 0.73). Kishor et al. (2020) obtained that the AUROC was 0.6250 forPEARL score. PEARL scorewas better at predicting readmission or death inpatients with AECOPD. These findings were also consistent with our study.

Conclusion

This study demonstrates that the PEARL score is a simple and valuable tool that uses routinely available and non-invasive investigation in risk stratification and prediction of 90-day post discharge outcome in patientsadmitted with acute exacerbation of COPD. The PEARL score is found to be a better predictor than BODE index. Hence, the PEARL score has the potential to reduce the burden of exacerbation, improve patient outcome and contribute to improved quality of life in this group of patients.

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ORIGINAL ARTICLE

Efficacy of Quinolone Based Newer Regimen in Retreatment of Smear Positive Pulmonary Tuberculosis

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Abstract

Background: *Tuberculosis (TB) continues to be a major public health problem in much of the developing countries. Even though effective anti-bacterial treatment for TB has been available for more than six decades, the long duration of treatment poses challenges to patients. Poor compliance facilitates development of drug resistance that further aggravates the problem. Moreover, no new drug specific for TB has been introduced since the late 1960s. Shortening the duration of treatment for TB is a global research priority. Clinical trials that studied the efficacy of 3 - 4 month regimens in the 1970s and 1980s had high relapse rates. Various studies showed that the quinolones could be advantageously used in shortening TB treatment duration. Levofloxacin is proposed as the Fluoroquinolone of first choice in the retreatment regimen for a number of reasons, like better safety profile, fewer known drug interactions.*

Materials & Methods: *This prospective, observational study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital, Dhaka, Bangladesh from April 2019 - March 2020 in collaboration with the Department of Pathology, Radiology and Respiratory Laboratory. A total of 139 cases of smear positive pulmonary tuberculosis were enrolled in this study for retreatment. Sputum conversion was observed by microscopy. Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-23).*

Results: *A total number of 139 cases of smear positive pulmonary tuberculosis patients were selected for retreatment who was receiving Quinolone based retreatment with Levofloxacin + 4FDC. MTB was detected in sputum by gene Xpert and RIF sensitive. Initially, 139 (100.0%) patients were found sputum for AFB positive. After 2 months, 129(92.8%) patients were found sputum for AFB negative. After 5 months, 133(95.7%) patients were found sputum for AFB negative. After 6 months, 134(97.1%) patients were found sputum for AFB negative.After 6 months follow up, 4(2.9%) patients were found smear positive, 134(96.4%) were smear negative and 1(0.7%) died.*

Conclusion: *It is observed; total 139 patients were treated by Quinolone based retreatment regimen (Levofloxacin + 4FDC) for 6 months. The cure rate was 96.4%. It is satisfactory. Besides, projected costs and rates of toxicity were less. So, Quinolone (Levofloxacin) based retreatment of smear positive PTB cases is observed to be effective, safe & well tolerated.*

Key words: *Smear positive pulmonary tuberculosis, Retreatment, Quinolone*

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Introduction:

Tuberculosis (TB) is a major public health problem in Bangladesh since long. Bangladesh Ranks 6th among the 22 high TB burden countries. According to WHO, the annual estimated incidence 225, prevalence 434 and TB mortality is 45 per 100,000 populations per year. So, effective treatment of TB is very important. Early treatment and cure of infectious cases of TB cut the chain of transmission of TB infection in the community. Therefore, quick identification of presumptive TB cases, rapid diagnosis, early initiation and successful completion of treatment are the most effective ways of preventing TB. Fixed dose combinations are used to treat TB. Several regimens are available. Cure rate (98%) is satisfactory with effective completion of Cat - I. Relapse is seen in only 2% cases, among them two third are seen in next 2 years. Relapsed cases need retreatment with Cat - II (2HRZES + 1HRZE / 5HRE). To accelerate global progress in the control of tuberculosis, newer drugs and shorter, easily usable regimens are needed to treat all forms of tuberculosis, including drug-resistant (DR TB). Tuberculosis (TB) continues to be a major public health problem in much of the developing countries. Even though effective anti-bacterial treatment for TB has been available for more than six decades, the long duration of treatment poses challenges to patients. Poor compliance facilitates development of drug resistance that further aggravates the problem. Moreover, no new drug specific for TB has been introduced since the late 1960s. Shortening the duration of treatment for TB is a global research priority. Clinical trials that studied the efficacy of 3- 4 month regimens in the 1970s and 1980s had high relapse rates. A randomized clinical trial by the National Institute for Research in TB (NIRT), Chennai, India showed that 4- or 5-month regimens containing Ofloxacin (O), Isoniazid (H), Rifampicin (R) and pyrazinamide (Z) daily for 3 months followed by H and R twice weekly for one or two months were very effective, with 99% of patients becoming sputum culture negative at the end of treatment and only 4% and 2% respectively suffering recurrence of TB over 24 months of follow-up. This study showed for the first time that the quinolones could be advantageously used in shortening TB treatment duration. Among the fluoroquinolones Levofloxacin, Moxifloxacin, and Gatifloxacin have the most activity against *M. tuberculosis*. On the basis of cumulative experience suggesting a good safety profile with long-term use of Levofloxacin, this drug is the preferred oral agent for treating drug-resistant tuberculosis caused by organisms known or presumed to be sensitive to this class of drugs, or when first-line agents cannot be used because of intolerance. The doses given are for levofloxacin, *Adults*: 500–1,000 mg daily.Levofloxacin is proposed as the Fluoroquinolone of first choice in the retreatment regimen for a number of reasons.

Firstly, this medicine has a better safety profile compared to other fluoroquinolones and was the one most frequently used in the studies reviewed for this guidance.Secondly, levofloxacin has fewer known drug interactions with other medications as compared to Moxifloxacin. The retreatment schedule used in recent past was more difficult to use, longer in duration and associated with more side effects. These resulted in poor compliance and less adherence of patients to the treatment. So, new easily usable, short and less toxic regimen is required to overcome the barriers in effective treatment of tuberculosis. For this reason, the efficacy of this newer Levofloxacin based regimen should be observed.WHO already recommended use of Levofloxacin based retreatment regimen in places of Cat - II, but more researches are required to observe the efficacy, side effects and long term outcomes. Moreover, no such study is conducted in our country, so it is very important to see the effect of retreatment with this new regimen.

Methods

This prospective observational study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from April 2019 - March 2020. Smear positive PTB patients, who require retreatment and attended in NIDCH both indoor & outdoor and who gave informed consent were enrolled in this study. Rifampicin resistance, intolerance or history of drug toxicity to any drug in the regimen, known or suspected risk of prolonged QT interval, patients who are already getting Cat – II, smear negative PTB cases, extra pulmonary TB, patients who refused to be part of study were excluded from the study. A total of 139 smear

positive pulmonary tuberculosis patients attending in the above mentioned hospital were included in this study. Among them 1 patient died and excluded from this study. Finally, 138 patients were enrolled in the study. Having obtained ethical clearance from the Ethical Committee and informed written consent from the patients, the data collection was commenced. All patients were subjected to detailed history taking, physical examination and necessary investigations. Investigations included complete blood count, random blood sugar, sputum for AFB, chest x-ray, S. creatinine, SGPT, Sputum for Gene Xpert and ECG. Patients were treated by Cat-1 anti TB treatment. At the end of 2^{nd},5^{th} and 6^{th}month of treatment all patients were followed up clinically and by investigating sputum for AFB. Microscopy was done to see the conversion of sputum.The collected data of each patient was recorded systematically. All data were analyzed by using computer based SPSS -23 (statistical package for social sciences). Data were presented in frequency, percentage and mean and standard deviation as applicable. Chi square test was used for categorical variables. Paired t-test was used for continuous variables. P value of less than 0.05 was considered as statistically significant.

Results

Table-I

Socio-demographic characteristics of the study patients (n=139)

Parameters	Number of patients	Percentage
Age (years)		
≤20	14	10.1
21-30	39	28.1
31-40	25	18.0
41-50	19	13.7
51-60	26	18.7
61-70	13	9.4
>70	3	2.2
Mean±SD	40.6	±16.1
Range (min-max)	13	-75

Table-II

Distribution of the study patients according to clinical history (n=139)

Medical history	Number of patients	Percentage
Cough		
≤3 weeks	10	7.2
>3 weeks	129	92.8
Sputum		
Present	139	100.0
Absent	0	0.0
Hemoptysis		
Present	21	15.1
Absent	118	84.9
Chest pain		
Present	10	7.2
Absent	129	92.8
Dyspnoea (modified MRC scale)		
0	87	62.6
I	22	15.8
II	13	9.4
III	11	7.9
IV	6	4.3
Duration of illness (weeks)	4.3	±0.6
Range (min-max)	3	-6

Table II shows that 129(92.8%) patients were found to have cough for >3 weeks, 139(100.0%) were sputum positive, 21(15.1%) had hemoptysis, 10(7.27%) had chest pain, 22(15.8%) had dyspnoea (mMRC Scale I) and mean duration of illness was found 4.3±0.6 weeks.

Table-III

Sputum for AFB in different follow up (n=139)

Sputum for AFB	Number of patients	Percentage
Initially		
Positive	139	100.0
Negative	0	0.0
After 2 month		
Positive	10	7.2
Negative	129	92.8
After 5 month		
Positive	6	4.3
Negative	133	95.7
*After 6 month	(n=138)	
Positive	4	2.9
Negative	134	97.1

*One patient dropout due to death

Initially, all (100.0%) patients were found sputum for AFB positive. After 2 months, 129(92.8%) patients were converted to sputum for AFB negative. After 5 months, 133(95.7%) patients and after 6 months, 134(97.1%) patients were found sputum for AFB negative.

Mean weight was found 53.7±7.2 kg in pretreatment group and 56.9±7.4 kg in post treatment group.The difference was statistically significant ($p<0.05$) between two groups.

Chest X-rays were found normal initially in 9(6.5%) patients of the study group and improved in 119(86.2%) after 6 months of treatment. The difference was statistically significant ($p<0.05$) between two groups.

After 6 month follow up, 4(2.9%) patients were found smear positive, 134(96.4%) were smear negative and 1(0.7%) was dead. Though sputum for AFB smear was observed here but the Gold standard test for this purpose is Sputum for AFB culture.

Table-IV

Body weight in different follow up (n=139)

	Initially (n=139)		*After 6 month (n=138)		P value
	Mean	±SD	Mean	±SD	
Weight (kg)	53.7	±7.2	56.9	±7.4	0.001[s]
Range (min-max)	35	-62	35.8	-66.5	

*One patient dropout due to death, s= significant, P value reached from paired t-test, here t = -39.08 with df= 137 and p value= 0.001

Table-V

Chest X-rayin different follow up (n=139)

Chest X-ray	Initially (n=139)		*After 6 month (n=138)		P value
	n	%	n	%	
Normal	9	6.5	119	86.2	
Patchy opacity	41	29.5	1	0.7	
Cavitary lesion	27	19.4	2	1.4	
Consolidation	4	2.9	0	0.0	
Diffuse	45	32.4	0	0.0	
Cavitary lesion + diffuse	9	6.5	0	0.0	0.001[s]
Nodular+ diffuse	2	1.4	0	0.0	
Fibrosis	0	0.0	15	10.9	
Cavitary lesion+ consolidation	1	0.7	0	0.0	
Cavitary lesion+ patchy	1	0.7	0	0.0	
Inhomogeneous nodular	0	0.0	1	0.7	

* One patient dropout due to death, s= significant, P value reached from chi square test, here $x^2= 232.2$ with df= 10 and p value= 0.001

Table-VI

Distribution of the study patients according to outcome (n=139)

Outcome	Number of patients	Percentage
Positive	4	2.9
Negative	134	96.4
Died	1	0.7

Discussion

This study was carried out with an aim to observe the efficacy of Levofloxacin based current regimen by sputum conversion. This study also suggests the validity of newer regimen with shorter duration and less hazardous administration technique by regular follow up. The present study findings were discussed and compared with previous relevant studies. In this study it was observed that majority (28.1%) of patients belonged to age 21-30 years. The mean age was found 40.6±16.1 years with range from 13 to 75 years. Almost similar study found that the mean age of the included patients was 37.8 years (Sobhy et al., 2012) and in another study it was 32.6 years (Hossam., 1999). Mean age was 34.9 years in newly diagnosed patients and the mean age to retreated cases was 36.5 years(Mohamed et al., 2002). The reason for this difference of age at presentation in various regions of the world may be due to genetic, geographic or ethnic influences. In this present study it was observed that 129(92.8%) patients had cough for >3 weeks, 139(100.0%) were sputum positive, 21(15.1%) had hemoptysis, 10(7.27%) had chest pain, 22(15.8%) had dyspnoea scale I and mean duration of illness was found 4.3±0.6 weeks. It was reported that cough was present in 26(63.4%), sputum in 17(41.5%), hemoptysis in 7(17.1%) and dyspnoea in 10(24.4%) patients (Kang et al., 2016). Their finding also supported this study. In this study it was documented that all the patients were Gene Xpert positive for MTB and RIF sensitive. Initially, all (100.0%) patients were found sputum for AFB positive. After 2 months 129(92.8%) patients, after 5 months 133(95.7%) patients and after 6 months, 134(97.1%) patients were found sputum for AFB negative. Individual-Patient Data (IPD) meta-analysis of isoniazid-resistant tuberculosis (UNDER REVIEW FOR PUBLICATION) presented that 245/251 (97.6%) patients were converted to negative after treatment with levofloxacin based new regimen compared to 1253/1350 (92.8%) patients with current regimen (WHO, 2018).In a study sputum AFB smear was positive in 28(68.0%) patients (Kang et al., 2016).It was documented that 1 to 2+ sputum AFB smear were 2(20.0%) and 3+ to 4+ were 8(80.0%) patients (Johnson et al., 2006). The proportion of sputum culture conversion to negative at 2 months is an important parameter for assessing the efficacy of a TB drug regimen (Fox et al., 1999). It was reported that 83% and 88% of patients treated with the Gatifloxacin and Moxifloxacin regimens respectively became sputum culture negative at 2 months compared to 78% of those treated with the control regimen (Jawahar et al., 2013). These culture conversion rates were significantly lower than the 92–94% culture negativity that was observed in the previous Ofloxacin study with daily dosing (Tuberculosis Research Centre 2002). Our results were consistent with these data, although the smear positive rate for PTB in our study (2.9%) was lower compared to previous studies, partly because all patients were documented drug-susceptible pulmonary TB. In this study it was observed that mean weight was found 53.7±7.2 kg in pre treatment group and 56.9±7.4 kg in post treatment group, which indicates that mean weight was significantly higher in post treatment group than before treatment. Mean weight was found 51.0 kg in a study (Yew et al., 2003) and 55.5 kg in another similar study (Johnson et al., 2006). In the present study, initially 9 (6.5%) patients had normal Chest X-ray and after 6 months of treatment 119(86.2%) patients had radiological improvement. It was significantly higher in after treatment group than before treatment.Cavitary lesion was found in 27(19.4%) patients before treatment and 2(1.4%) had cavities in after 6 months of treatment. Itwas observed that cavity was present in CXR in 15(34.5%) patients in Levofloxacin group (Yew et al., 2003) and in another study itwas present in 150 (25%) patients (van der Heijdenet al., 2012).

Regarding outcome in this study it was observed that after 6 month follow up, 4(2.9%) patients were found smear positive due to co-morbidities and more age. 134 (97.1%) patients were found smear negative and 1 died. Almost similar study conducted where the success rates for the Levofloxacin group was 90.0 % (Yew et al., 2003). Previously it was reported that drug resistance of PTB patients for Levofloxacin was 10.7% in new cases, 15% in retreated cases (Sobhy et al., 2012). These findings were identical to the results of the national Egyptian survey carried out and published in 2001, as regards Streptomycin resistance which was 18% in new cases, 48% in retreated cases, near to the INH resistance results which was 9.3% in

new cases, 43% in retreated cases. Far from Rifampicin resistance results which showed 3.6% in new cases, 46.3% in retreated cases and Ethambutol showed 2.1% in new cases, 25.8% in retreated cases. In Lebanon, one study showed INH resistance 12% in new cases 63% in retreated cases, Rifampicin 3% in new cases 59% in retreated cases, Streptomycin 12% in new cases 44% in retreated cases, Ethambutol 3% in new cases, 44% in retreated case (George et al., 2006). It is found that among the MDR patients in his study treatment failure represents 61.1%, defaulters 33.6%, but new cases only 4.4%.Other studies showed that proportions of cross resistance among Ofloxacin-resistant isolates were high for Levofloxacin (87%)(Zignol et al., 2016), and Moxifloxacin when tested at 0·5 ìg/mL (72%)(Abd El Fatah., 2008). It is reported that the response at the end of treatment was uniformly high in all 3 regimens, with 95% and 98% of the patients treated with a thrice-weekly 4-month Gatifloxacin and Moxifloxacin regimens respectively becoming culture negative at the end of treatment, compared to 97% in the control regimen(Jawahar et al., 2013). This is same with the previous experience at the NIRT when 99% of patients treated with the Ofloxacin containing 4-month regimen, with a daily intensive phase were culture negative at the end of treatment (Tuberculosis Research Centre 2002). The most striking finding of this study was that the recurrence rate of TB during 24 months of post-treatment follow-up was higher in the Gatifloxacin arm (16%) compared to the Moxifloxacin (10%) and control regimen arms (6%). The recurrence rates in both the quinolones regimens was much higher than the 4% recurrence in our previous study in which OHRZ was given daily for 3 months followed by RH twice weekly (Tuberculosis Research Centre 2002). Clearly, a thrice weekly 4-month regimen is inferior to a 4-month regimen with an initial daily phase in terms of recurrence of TB. However, even though the recurrence rate in the Moxifloxacin arm (10%) was higher than that in the control regimen arm (6%), the difference was not statistically significant. It is pertinent to point out that 90% of patients treated with the 4-month thrice-weekly Moxifloxacin regimen were recurrence free 24 months after treatment completion. It was documented that the main finding of the review is that the 4-month Moxifloxacin- or Gatifloxacin-containing regimens successfully treated 75–90% of pulmonary TB patients, but none of them demonstrated a favorable outcome after a follow-up period of at least 6 months, compared to the standard DS-TB regimen (Pranger et al., 2019). It was reported that Fluoroquinolone use was a significant predictor for an initial favorable outcome, which was increased 3-fold for users versus non-users odds ratio [OR] 3.11; 95% CI 1.21, 7.95; p = 0.02)(Park et al., 2004).

Conclusion:

In conclusion, smear positive pulmonary tuberculosis cases who were previously treated with Cat-1, this time they are treated with Quinolone based retreatment regimen (Lfx+4FDC) for 6 months. Provided all these patients were Rifampicin sensitive. Among them majority (97.1%) of patients were recovered successfully which is evident by sputum conversion. 80.6% patients had weight gain ≥3kg and 88.8% patients had radiological improvement on chest X-ray in post treatment sputum negative group. There were no significant side effects or intolerance. This regimen was less time consuming. So, patients were adherent to complete the treatment. Finally, it is observed that use of Fluroquinolone based newer retreatment regimen is effective, safe & well tolerated.

Conflict of Interest: The authors of this paper have declared that there is no conflict of interest to any of the authors.

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ORIGINAL ARTICLE

Postoperative Morbidity and Mortality after Ivor Lewis Esophagectomy with and without Feeding Jejunostomy: A Retrospective Analysis

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Abstract

Background: *Esophagectomy, particularly the Ivor Lewis procedure, remains a key surgical approach for esophageal carcinoma but is associated with significant postoperative risks. Feeding jejunostomy (FJ) is frequently used to ensure nutritional support; however, its routine placement is debated due to potential complications and unclear benefits.*

Methods: *A retrospective comparative cross-sectional study was conducted at a tertiary care center in Dhaka, Bangladesh, from January 2022 to June 2023. Seventy patients with histologically confirmed esophageal cancer undergoing Ivor Lewis esophagectomy were included. Patients were divided into two groups: Group A (n=30) without FJ and Group B (n=40) with FJ. Demographic, clinical, operative, and postoperative data were analyzed using SPSS v25, with a p-value d" 0.05 considered statistically significant.*

Results: *Baseline characteristics between the two groups were comparable. The operative time was significantly longer in Group B (336.25±40.11 minutes) compared to Group A (296.00±28.11 minutes; p=0.05). There were no significant differences in ICU stay, discharge weight, readmission rate, or mortality. Skin complications were noted exclusively in Group B (13.33%; p=0.04). No significant differences were observed in anastomotic leakage or mortality.*

Conclusions: *Routine placement of feeding jejunostomy during Ivor Lewis esophagectomy does not appear to significantly enhance postoperative outcomes and may lead to an increased risk of local complications, such as skin infections. Therefore, selective use of FJ based on the patient's nutritional status, comorbidities, and perioperative risk factors may be a more appropriate approach. Further prospective studies are warranted to validate these findings and guide clinical practice.*

Keywords: *Esophageal cancer, Ivor Lewis esophagectomy, feeding jejunostomy, postoperative morbidity, mortality, nutritional support.*

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Introduction

Esophageal cancer represents a major global health concern, ranking as the seventh most common malignancy and the sixth leading cause of cancer-related death worldwide [I]. According to GLOBOCAN 2020, approximately 604,100 new cases and 544,076 deaths were reported globally, reflecting a rising burden, especially in low- and middle-income countries [II]. The increasing incidence of esophageal cancer has been linked to multiple risk factors, including tobacco use, alcohol consumption, dietary deficiencies (such as low intake of fruits and vegetables), poor oral hygiene, and exposure to carcinogenic substances [III]. In Bangladesh, the impact is particularly significant, with esophageal cancer ranking as the third most common cancer among males and fifth among females. More than 6,000 new cases are diagnosed each year, and the burden continues to grow due to delays in diagnosis and limited access to specialized care [IV]. Despite advances in multimodal treatment including neoadjuvant chemoradiotherapy and targeted therapy, surgical resection remains the primary curative option for patients with resectable disease [V]. Among the available surgical techniques, the Ivor-Lewis esophagectomy is frequently utilized for tumors located in the middle thirds of the esophagus [VI]. This procedure combines a laparotomy and right thoracotomy to allow for subtotal esophagectomy and the creation of an intrathoracic esophagogastric anastomosis [VII]. It provides excellent oncologic outcomes and permits systematic lymphadenectomy. However, the extensive nature of the surgery and postoperative physiological stress contribute to a high incidence of complications [VIII]. Adequate nutritional support during the perioperative period is therefore essential to reduce postoperative morbidity, accelerate recovery, support immune function, and improve patient outcomes [IX]. Feeding jejunostomy is a commonly performed adjunct procedure during esophagectomy, facilitating early postoperative enteral nutrition [X]. Although this technique offers a reliable route for nutrient delivery, it is not without drawbacks. The procedure involves puncturing and fixing the jejunum to the abdominal wall, which can result in intestinal adhesions, bowel obstruction, leakage, and surgical site infections [XI]. Furthermore, local skin complications such as corrosion, ulceration, and necrosis due to backflow of digestive secretions are frequently observed [XII]. These risks have led some surgeons, especially in Asia, to favor total parenteral nutrition (TPN), which avoids enteral access but carries significant risks including catheter-related bloodstream infections, liver dysfunction, and increased healthcare costs [XIII]. In response to these challenges, a modified technique during Ivor-Lewis esophagectomy, which avoids the formal creation of a jejunostomy while still allowing for enteral feeding through a simpler, less invasive intraoperative tube placement [XIV]. This method has been routinely used at our institution for the past four years with promising outcomes. The aim of this retrospective study is to compare postoperative morbidity, mortality, and nutritional complications in patients undergoing Ivor-Lewis esophagectomy with versus without feeding jejunostomy, in order to evaluate the safety, efficacy, and clinical feasibility of this alternative nutritional strategy.

Methodology & Materials:

This retrospective comparative cross-sectional study was carried out in the Department of Thoracic Surgery at the National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka, Bangladesh, over a period spanning from January 2022 to June 2023. The study included 70 patients with histologically confirmed esophageal carcinoma who underwent Ivor Lewis esophagectomy. Participants were divided into two groups based on whether a feeding jejunostomy was performed during surgery:

Group A (n=30): Patients who underwent Ivor Lewis esophagectomy without feeding jejunostomy.

Group B (n=40): Patients who underwent Ivor Lewis esophagectomy with feeding jejunostomy.

Inclusion Criteria

- Patients undergoing Ivor Lewis esophagectomy for carcinoma of the esophagus.
- Individuals of any age and gender who provided written informed consent.

Exclusion Criteria

- Patients with pre-existing chronic kidney disease.

- Those diagnosed with other simultaneous malignancies.
- Individuals with a history of abdominal surgery.
- Patients unwilling to participate.

Ethical Considerations

The study adhered to the ethical principles set forth in the Declaration of Helsinki (2011). Prior to participation, all patients received full information about the study and provided written informed consent. Confidentiality was strictly preserved throughout the study. Ethical approval was obtained from the Institutional Review Board of NIDCH, along with administrative permissions from appropriate hospital departments.

Data Collection

Patient data were collected retrospectively from medical records using a structured proforma. Baseline characteristics such as age, sex, body mass index (BMI), and preoperative albumin levels were documented. Disease-related variables includingtumor pathology was also recorded.

All patients underwent a standardized Ivor Lewis esophagectomy, which consisted of a laparotomy in the supine position for gastric mobilization, followed by a right posterolateral thoracotomy in the lateral decubitus position to mobilize the esophagus and perform an intrathoracic esophagogastric anastomosis. In Group B, a feeding jejunostomy was created using the Witzel technique with a soft feeding tube. Group A did not receive feeding jejunostomy. Operative time and intraoperative findings were recorded. Following surgery, patients were kept nil per oral for 6 days. Group B patients began enteral nutrition via jejunostomy from postoperative day 3 or once bowel sounds returned, while Group A patients received parenteral nutrition. On postoperative day 7, a contrast swallow study was performed to assess anastomotic integrity prior to initiating oral feeding. Postoperative complications were documented. Other outcomes included operative duration, length of hospital stay, and intensive care unit (ICU) stay. Additionally, the 30-day readmission rate and body weight at the time of discharge were recorded. Furthermore, the study examined 30-day mortality and in-hospital mortality to assess short-term survival outcomes following Ivor Lewis esophagectomy with and without feeding jejunostomy.

Statistical Analysis

Data were analyzed using SPSS version 25. Continuous variables were presented as mean ± standard deviation (SD) and compared using independent sample t-tests. Categorical data were summarized as frequencies and percentages, with comparisons performed using the chi-square test. A p-value d" 0.05 was considered statistically significant.

Result

The study included a total of 70 patients, with 30 in Group A and 40 in Group B. As outlined in Table 1, the mean age was 55.7±10.4 years in Group A and 55.3±9.87 years in Group B. Male patients constituted 73.3% in Group A and 80.0% in Group B, while females accounted for 26.7% and 20.0%, respectively. The mean body mass index was 22.32±3.67 kg/m² in Group A and 22.21±4.54 kg/m² in Group B. Preoperative hypoalbuminemia (albumin <3.5 g/dL) was noted in 33.3% of Group A and 30.0% of Group B. Squamous-cell carcinoma was the predominant tumor type in both groups, seen in 86.67% of Group A and 90.00% of Group B, followed by adenocarcinoma in 13.33% and 10.00% (Table 2). The mean operation time was 296.00±28.11 minutes in Group A and 336.25±40.11 minutes in Group B. The mean duration of hospital stay was 13.87±3.19 days in Group A and 14.18±7.53 days in Group B. ICU stay was nearly similar in both groups. Readmission within 30 days was reported in 13.33% of Group A and 10.0% of Group B. The mean discharge weight was 44.2±7.53 kg in Group A and 46.5±9.27 kg in Group B (Table 3).Postoperative complications showed no significant differences between groups for anastomotic leakage, reflux esophagitis, or delayed gastric emptying. However, skin corrosion and ulceration were significantly higher in Group B ($p = 0.04$) (Table 4). As shown in Table 5, 30-day mortality was reported in 6.67% of Group A and 5.00% of Group B, while in-hospital mortality occurred in 10.00% and 5.00%, respectively.

Table-I

Baseline characteristics of the study population (N=70)

Variables	Group A (n=30)		Group B (n=40)		P-value
	n	%	n	%	
Age (years), Mean±SD	55.7±10.4		55.3±9.87		0.86
Gender					
Male	22	73.3	32	80.00	0.51
Female	8	26.7	8	20.00	
Body mass index (kg/m2)	22.32 ± 3.67	22.21 ± 4.54	0.05		
Preoperative Albumin <3.5	10	33.3	12	30.00	0.69

Cite as: Baseline demographic and nutritional status were comparable between groups (Table I).

Table-II

Disease characteristics of the study population (N=70)

Tumor Pathology	Group A (n=30)		Group B (n=40)		P-value
	n	%	n	%	
Squamous-cell carcinoma	26	86.67	36	90.00	0.09
Adenocarcinoma	4	13.33	4	10.00	

Cite as: The majority of patients in both groups had squamous-cell carcinoma (Table II).

Table-III

Comparison of postoperative parameters between Group A and Group B patients (N=70)

Variables	Group A (n=30), Mean±SD	Group B (n=40), Mean±SD	P-value
Operation time (minutes)	296.00±28.11	336.25±40.11	0.05
Hospital stay (days)	13.87±3.19	14.18±7.53	0.04
ICU stay (days)	3.0 ± 2.0	3.2 ± 1.9	0.59
30-day readmission (%)	4 (13.33%)	4 (10.0%)	0.76
Weight during discharge	44.2±7.53	46.5±9.27	0.31

Cite as: Group B had a significantly longer operation time and hospital stay compared to Group A, though ICU stay, readmission, and discharge weight were similar (Table III).

Table-IV

The incidence of post-operative complication among patients (N=70)

Variables	Group A (n=30)		Group B (n=40)		P-value
	n	%	n	%	
Anastomotic leakage	0	0.00	1	2.50	0.07
Reflux esophagitis	2	6.67	2	5.00	0.22
Functional delayed gastric emptying	1	3.33	0	0.00	0.08
Skin corrosion and ulceration	0	0.00	4	13.33	0.04

Cite as: Skin complications were observed only in the FJ group, reaching statistical significance (Table IV).

Table-V

Postoperative Mortality (30-day)

Mortality	Group A (n=30)		Group B (n=40)		P-value
	n	%	n	%	
30-day mortality	2	6.67	2	5.00	0.24
In-hospital mortality	3	10.00	2	5.00	0.28

Cite as: No statistically significant difference in 30-day or in-hospital mortality was observed between the groups (Table V).

Discussion

The Ivor Lewis esophagectomy remains a complex surgical procedure with significant risks of postoperative morbidity and mortality, which may be influenced by the use of feeding jejunostomy[15]. This retrospective analysis compared postoperative morbidity and mortality after Ivor Lewis esophagectomy with and without feeding jejunostomy (FJ) in well-matched groups, providing important insights into the role of routine FJ placement in esophageal cancer surgery.

Baseline demographic parameters, including age (55.7±10.4 vs 55.3±9.87 years; p=0.86), gender distribution (male predominance: 73.3% vs 80%; p=0.51), BMI (22.32±3.67 vs 22.21±4.54 kg/m²; p=0.05), and preoperative hypoalbuminemia rates (33.3% vs 30%; p=0.69), were statistically comparable between groups. These similarities confirm a balanced study population and eliminate baseline nutritional or physiological status as confounders—consistent with matching approaches used in previous studies[16,17]. Tumor-related parameters also showed no significant intergroup difference. Tumor pathology (predominantly squamous cell carcinoma: 86.7% vs 90%; p=0.09) was equivalent. These findings resemble the patient profiles described in the study by Markar et al., who also emphasized the necessity of balancing tumor burden when evaluating postoperative strategies [18].

While the operation time was notably longer in the FJ group (336.25±40.11 min vs 296.00±28.11 min; p=0.05), this aligns with previous findings where the jejunostomy procedure added operative complexity and time[19]. Despite the extended surgery, ICU stay duration (3.2 ± 1.9 vs 3.0 ± 2.0 days; p=0.59) and weight at discharge (46.5±9.27 vs 44.2±7.53 kg; p=0.31) were comparable. Interestingly, length of hospital stay was slightly longer in the FJ group (14.18±7.53 vs 13.87±3.19 days; p=0.04), possibly reflecting a more cautious postoperative approach due to the presence of enteral access devices.

Our study noted no statistically significant differences in 30-day readmission rates (13.33% vs 10%; p=0.76), again suggesting that FJ use did not improve short-term convalescence. These results correspond with previous reports by Al-Temimi et al., who showed no significant differences in mortality, serious morbidity, length of stay, readmission rates, or anastomotic leak rates between the FJ and non-FJ groups, despite a longer operative time and increased superficial wound infections in the FJ group[20].

However, one notable adverse event in the FJ group was skin corrosion and ulceration (13.33% vs 0%; p=0.04), which directly implicates jejunostomy tube-related complications. This finding mirrors those from Gong et al., who described tube-related skin issues in up to 10% of cases[21]. Other complications, including reflux esophagitis (6.67% vs 5%; p=0.22), delayed gastric emptying (3.33% vs 0%; p=0.08), and anastomotic leakage (0% vs 2.5%; p=0.07), were not significantly different between groups. While the incidence of anastomotic leak was low overall, our result supports findings from Lee et al., suggesting that jejunostomy does not significantly reduce leak rates[22].

The 30-day mortality was similar in both groups (6.67% vs 5%; p=0.24), and in-hospital mortality showed no significant difference (10% vs 5%; p=0.28). These mortality rates are consistent with contemporary surgical literature on Ivor Lewis esophagectomy, which reports 30-day mortality ranging between 3–10%[20]. Thus, FJ placement does not appear to offer a survival benefit in this surgical context.

Our results align with a growing body of literature that questions the routine use of feeding jejunostomy during Ivor Lewis esophagectomy. While FJ can provide nutritional security, particularly in high-risk or malnourished patients, its universal application may expose patients to device-specific complications without significant benefits in reducing leak rates, hospital stay, or mortality. In the present study, although the FJ group experienced slightly longer operations and unique complications (e.g., skin ulcers), overall outcomes including morbidity and mortality were equivalent to the non-FJ group[22].

Limitations of the study:

- The study duration was short, making it difficult to assess long-term complications, nutritional outcomes, or survival.
- Being retrospective in nature, potential selection and information biases could not be completely eliminated.

Conclusion and Recommendations

The findings of this study suggest that the use of feeding jejunostomy during Ivor Lewis esophagectomy does not confer significant benefits in terms of reducing morbidity or mortality. While jejunostomy provides a secure route for postoperative nutrition, it may be associated with specific complications such as skin ulceration. On the other hand, the absence of jejunostomy did not lead to increased anastomotic leak or mortality rates. Therefore, the decision to place a feeding jejunostomy should be individualized, reserving it for patients at high nutritional risk or anticipated prolonged recovery. Further multicenter, prospective studies with larger sample sizes and longer follow-up are needed to validate these findings.

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ORIGINAL ARTICLE

Prevalence of Non-tuberculous Mycobacteria Detection from Sputum and Bronchoalveolar Lavage among Patients with Chronic Cough and Chest X-ray Abnormality

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Abstract

Introduction: *Nontuberculous mycobacteria (NTM) infections, though less common than Mycobacterium tuberculosis (MTB), are an increasing clinical concern. NTM includes species outside the MTB complex, such as M. avium complex (MAC), and can affect individuals with pre-existing lung disease or immunodeficiency. Accurately distinguishing between MTB and NTM is crucial for appropriate treatment, especially in resource-limited settings where microscopy is commonly used. This study aims to assess the prevalence of NTM infections in patients with chronic cough and abnormal chest X-ray.*

Methodology: *A cross-sectional study was conducted at the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU) over one year. The study included 196 patients aged 18 and above with chronic cough and recent chest X-ray abnormalities. Consecutive sampling was used, and sputum or bronchoalveolar lavage (BAL) samples were collected and tested for NTM using Ziehl-Neelsenacid-fast bacilli (AFB) staining, GeneXpert and NTM DNA (Real time PCR).*

Results: *The prevalence of NTM infection was 5%, with the highest proportion of positive cases in the 31-60 years age group 6(66.6%). Male participants represented 6(66.6%) of NTM-positive cases. Clinical factors such as diabetes mellitus 3(33.3%) and a history of tuberculosis 1(11.1%) were observed in NTM-positive individuals, but none showed statistically significant associations with infection status. Radiologically, consolidation was the most common finding (58.16%), followed by cavitary lesions (28.57%) and nodules (13.27%). However, no significant association between radiological patterns and NTM positivity was found.*

Conclusion: *This study shows a low prevalence of NTM infections in patients with chronic cough and abnormal chest X-rays. While consolidation was the most common radiological finding, distinguishing NTM from MTB remains challenging. Further research is needed to improve diagnostics and identify key risk factors for NTM infections.*

Keywords: *Nontuberculous Mycobacteria, Chronic Cough, Radiological Patterns, GeneXpert, Acid-Fast Bacilli, Real time PCR.*

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Introduction

Infection with Mycobacterium tuberculosis (MTB), the causative agent of tuberculosis, is a leading global health issue, responsible for an estimated 1.67 million deaths worldwide in 2016 .[1]While MTB and closely related species, such as Mycobacterium bovis, are the primary pathogens of human pulmonary mycobacterial infections, infections with nontuberculous mycobacteria (NTM) are also of clinical concern globally.[2,3]NTM encompasses all Mycobacterium species that do not belong to the M. tuberculosis complex (MTBC), including M. leprae and M. ulcerans, and are typically considered rare pathogens in humans. However, NTM infections can occur in individuals with pre-existing lung disease or immunodeficiency, and certain species have been found to cause disease even in elderly women without underlying pulmonary disease or immunodeficiency.[4,5] NTM are ubiquitous in the environment, isolated from sources such as soil, water, dust, animals, and birds.[5]

Over 140 species of NTM have been reported, although most are rarely isolated from clinical samples.[6] The Mycobacterium avium complex (MAC), comprising M. intracellulare, M. avium, and M. chimaera, represents the most common group of clinically significant NTM. Other potentially pathogenic NTM species include M. chelonae, M. kansasii, M. xenopi, M. marinum, M. abscessus, and M. fortuitum.[7-9]The clinical management and treatment of infections caused by MTBC and NTM differ significantly, particularly as many NTM species exhibit resistance to drugs commonly used to treat MTBC infections. This necessitates a careful differential diagnosis. Human infections with NTM are primarily caused by species of the Mycobacterium avium complex (MAC), although other mycobacterial species, such as M. kansasii, M. fortuitum, M. xenopi, M. abscessus, and M. simiae, are also implicated.[10-14]

Nocardia species, which are closely related to mycobacteria and commonly found in the environment, can also cause tuberculosis-like disease in humans (Centers for Disease Control and Prevention USA, 2017). Differentiating between MTBC and NTM infections is crucial for appropriate treatment, but such distinctions can be challenging, particularly in low-resource settings where microscopy remains the primary method for diagnosing MTBC infections.[15]While microscopy for acid-fast bacilli (AFB) allows rapid identification of mycobacteria, it does not distinguish M. tuberculosis from NTM.A study conducted in Nigeria highlighted the challenges posed by this lack of differentiation. Pokam andAsuquo(2012) demonstrated that failure to identify NTM in AFB-positive lung infections led to misclassification and incorrect treatment as pulmonary tuberculosis, as all smear-positive patients were started on TB treatment.[16]To differentiate between MTBC and NTM, traditional cultural methods are often required, although they can take up to six weeks for results.[17]

In our country, there is a significant gap in understanding the burden of pulmonary disease caused by nontuberculous mycobacteria (NTM). Patients with respiratory samples positive for acid-fast bacilli (AFB) are often assumed to have tuberculosis (TB) and are treated with anti-tubercular chemotherapy. However, mycobacterial culture testing is infrequently performed, and the differentiation between MTBC and NTM remains poorly practiced.

The aim of this study is to determine the prevalence of NTM in sputum and bronchoalveolar lavage (BAL) samples among patients presenting with chronic cough and chest X-ray abnormalities. Additionally, this study seeks to highlight the challenges in distinguishing between MTBC and NTM infections in clinical settings, particularly in resource-limited environments, and to emphasize the need for improved diagnostic practices in the management of these infections.

Methodology

Study Design: This study is a cross-sectional design aimed at investigating the prevalence of nontuberculous mycobacteria (NTM) in patients with chronic cough and abnormal chest X-ray findings.

Study Place:The study was conducted at the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Study Period:The study period was one year, starting after approval from the Institutional Review Board (IRB) from March 2019 to February 2020.

Study Population: The study included both male and female patients aged 18 years and above, attending the inpatient and outpatient departments of the Respiratory Medicine unit at BSMMU, who had chronic cough lasting at least eight weeks, coupled with a recent abnormal chest X-ray (within the past 4 weeks). Patients with chronic cough without a recent chest X-ray were asked to perform a chest X-ray (P/A view), and those with abnormal findings were also included in the study.

Inclusion Criteria

- Male and female patients aged 18 years and above
- Unexplained Chronic cough present on most days of the week for at least eight weeks
- Chest X-ray abnormalities within the last four weeks

Exclusion Criteria

- Patients diagnosed with active pulmonary tuberculosis or currently undergoing treatment for pulmonary tuberculosis
- Patients diagnosed with lung cancer, diffuse parenchymal lung disease (DPLD) orany chronic lung disease.

Study Procedure: The study utilized consecutive sampling, a non-probability sampling method, to select participants who met the inclusion criteria. After obtaining informed written consent, basic demographic information was collected using a pre-structured questionnaire. Participants were then asked to provide two sputum samples-one collected on-site and the other the following morning-which were transported in cooler boxes to the laboratory for processing within 24 hours. For patients with dry cough and no sputum production, fiber-optic bronchoscopy was performed to collect bronchoalveolar lavage (BAL) fluid. Both sputum and BAL fluid samples underwent Ziehl-Neelsenacid-fast bacilli (AFB) staining, with smears considered positive if five or more bacilli were detected in at least 100 microscopic fields. Additionally, GeneXpert, NTM DNA(Real time PCR) testing was conducted on both sample types. All laboratory personnel were blinded to the clinical and radiological status of the participants to ensure impartiality in result interpretation. Strict infection control protocol was maintained.

Data Analysis : The sample size for the study was calculated using the formula:

$n = z^2pq/d^2$

Where n is the estimated sample size, z = 1.96 (the Z-value for a 95% confidence interval), p = 0.15 (frequency of NTM isolation from respiratory samples as per Chanda-Kapta et al. 2015)[18], q = 0.15 (1 - p), and d = 0.05 (marginal error). The calculation resulted in a minimum required sample size of 196 patients.

Data were reviewed for completeness and accuracy after collection. The information was entered into the Statistical Package for the Social Sciences (SPSS) version 23 for analysis. Descriptive statistics, such as means, frequencies, and standard deviations, were used to summarize the data. Chi-square tests were applied to analyze the relationships between qualitative variables. A p-value of less than 0.05 was considered statistically significant.

Ethical approval:Ethical approval for the study was granted by the Institutional Review Board (IRB) of the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU). Participants were fully informed about the study, and written informed consent was obtained. Confidentiality was maintained, and the study caused no physical, mental, or social harm to participants. It did not impose extra costs or interfere with their ongoing treatment.

Results

Table I presents the distribution of study subjects by age and sex in relation to NTM infection status. The mean age of NTM-positive patients was 40.4±16.1 years, while the mean age of negative cases was 40.6±13.9 years. The distribution of cases across different age groups is relatively even, with the highest proportion of positive cases observed in the 31-60 years age range (66.6%). The <20 and 61-70 years age groups showed the lowest number of positive cases (11.1% each). Regarding sex distribution, among the 9 NTM-positive individuals, 6 (66.6%) were male and 3 (33.3%) were female. Among the 187 NTM-negative individuals, 101 (54.0%) were male and 86 (46.0%) were female. The p-value of 0.303 indicates no statistically significant difference in NTM infection rates between males and females, suggesting that any observed differences could be due to chance.(Table I)

Table-I

Distribution of NTM Infection by Age Group and Sex (N=196)

Variables	NTM Infection		P-value
	Positive (n=9)	Negative (n=187)	
Age group (years)			
<20	1 (11.1%)	21 (11.2%)	0.666
21-30	1 (11.1%)	28 (15.0%)	
31-40	2 (22.2%)	49 (26.2%)	
41-50	2 (22.2%)	42 (22.5%)	
51-60	2 (22.2%)	30 (16.0%)	
61-70	1 (11.1%)	17 (9.1%)	
Mean±SD	40.4±16.1	40.6±13.9	
Sex			
Male	6 (66.6%)	101 (54.0%)	0.303
Female	3 (33.3%)	86 (46.0%)	

p-value obtained by Unpaired t-test, p<0.05 considered as a level of significance.

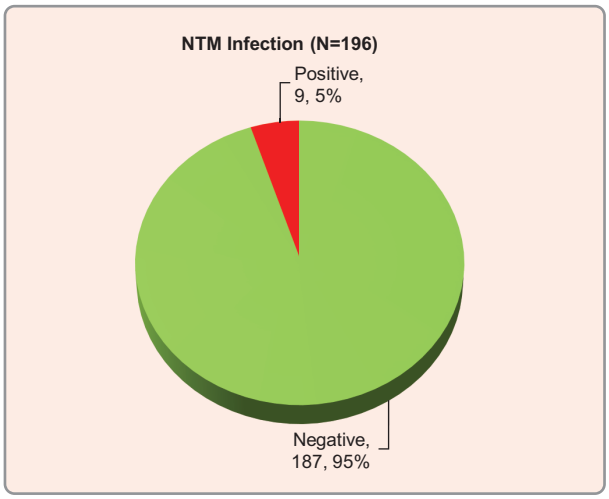

Figure-1: *Pie diagram showing the frequency of NTM infection among the study subjects.*

The pie chart illustrates the distribution of NTM infection status among the 196 study participants. The majority of participants (95%) were negative for NTM infection, while a smaller proportion (5%) tested positive. Although the positive cases constitute a minor fraction, they remain an important part of the analysis and contribute to the overall findings of the study.(Figure 1)

Table II shows the clinical characteristics of participants by NTM infection status. Among the 9 NTM-positive individuals, 33.3% had diabetes mellitus (DM), 11.1% had a history of tuberculosis (TB), and 11.1% were smokers. In contrast, 13.4%, 24.6%, and 7.0% of the 187 NTM-negative individuals had DM, a history of TB, and smoker, respectively. None of these factors showed a statistically significant association with NTM infection status (p-values > 0.05).(Table II)

Table-II

Distribution of Clinical Factors Among Study Participants by NTM Infection Status (N=196)

Clinical Factor	NTM Infection		P-value
	Positive (n=9)	Negative (n=187)	
DM	3 (33.3%)	25 (13.4%)	0.284
History of TB	1 (11.1%)	46 (24.6%)	0.563
Smoking	1 (11.1%)	13 (7.0%)	0.466

p-value obtained by fisher exact test, p<0.05 considered as a level of significant.

Table III presents the distribution of presenting complaints by NTM infection status. Among the 9 NTM-positive individuals, 4 (44.4%) had fever, compared to 112 (59.9%) of the 187 NTM-negative individuals. Cough was reported by 77.7% of NTM-positive and 77.0% of NTM-negative individuals. Shortness of breath (SOB) was observed in 44.4% of NTM-positive individuals and 39.6% of NTM-negative individuals. Chest pain was reported by 44.4% of NTM-positive and 26.2% of NTM-negative individuals. Anorexia was present in 44.4% of NTM-positive and 20.9% of NTM-negative individuals. Weight loss was reported by 23.0% of all participants, with no significant difference between the groups. None of the differences in presenting complaints between NTM-positive and NTM-negative individuals were statistically significant.(Table III)

Table-III

Distribution of the study participants by presenting complaints (N=196)

Variables	NTM Infection		Total (N=196)	P-value
	Positive (n=9)	Negative (n=187)		
Fever	4 (44.4%)	112 (59.9%)	116 (59.2%)	0.367
Cough	7 (77.7%)	144 (77.0%)	151 (77.1%)	0.722
SOB	4 (44.4%)	74 (39.6%)	78 (39.8%)	0.874
Chest Pain	4 (44.4%)	49 (26.2%)	53 (27.1%)	0.306
Anorexia	4 (44.4%)	39 (20.9%)	43 (21.9%)	0.174
Hemoptysis	1 (11.1%)	41 (21.9%)	42 (21.4%)	0.689
Weight Loss	2 (22.2%)	43 (23.0%)	45 (23.0%)	0.661

p-value obtained by fisher exact test, p<0.05 considered as a level of significance.

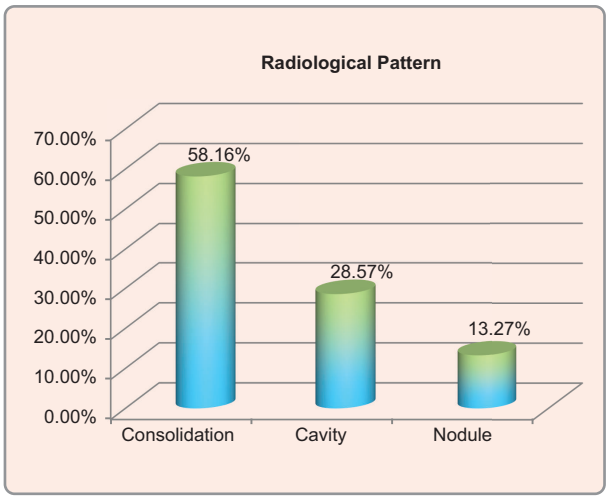

Figure-2: *Bar diagram showing radiological pattern in NTM positive subjects.*

Bar diagram presents the radiological patterns observed in NTM-positive subjects. The most common radiological finding was consolidation, observed in 58.16% of cases. Cavitary lesions were seen in 28.57% of the subjects, while nodules were present in 13.27% of cases. These findings highlight the predominant role of consolidation in the radiological presentation of NTM infection in this study.(Figure 2)

Table IV shows the distribution of NTM positivity based on radiological patterns. Among patients with consolidation, 2.55% were positive for NTM infection, while 1.53% of patients with cavitary lesions and 0.51% of patients with nodules tested positive for NTM infection.(Table IV)

Table-IV

NTM Positivity according to radiological pattern (N=196)

Radiological pattern	N (%)	NTM Infection		P-value
		Positive (n=9)	Negative (n=187)	
Consolidation	114 (58.16%)	5 (2.55%)	109 (55.61%)	0.194
Cavitary	56 (28.57%)	3 (1.53%)	53 (27.04%)	
Nodule	26 (13.27%)	1 (0.51%)	25 (12.76%)	
Total	196 (100%)	9 (4.59%)	187 (95.41%)	

p-value obtained by Chi-square test, p<0.05 considered as a level of significance.

Discussion

This study aimed to assess the prevalence of Nontuberculous Mycobacteria (NTM) infection in individuals with chronic cough and abnormal chest X-rays. The findings highlight several key clinical and radiological characteristics associated with NTM infection, although no significant associations were found between NTM positivity and factors such as age, sex, or clinical complaints.

The mean age of NTM-positive patients was 40.4±16.1 years, similar to the findings of previous studies, which report a higher prevalence of NTM infection among middle-aged adults.[19] In our study, the highest proportion of positive cases was observed in the 31-60 years age group (66.6%), consistent with the general age distribution for pulmonary NTM infection, which commonly affects individuals between the ages of 40 and 60.[20,13] Interestingly, the <20 and 61-70 years age groups showed lower proportions of positive cases, which may reflect the relatively lower incidence of NTM infections in younger and older populations.[21]

When examining sex distribution, 66.6% of NTM-positive patients were male, which is in line with other studies that have reported a higher prevalence of NTM infection in males.[3] However, the p-value of 0.303 indicates that the difference in NTM infection rates between males and females in this study was not statistically significant, suggesting that sex may not be a significant factor in NTM infection risk in this population. This is consistent with findings by Cassidy et al. (2009), who noted no significant sex-related difference in NTM infection rates in their cohort.[22]

Clinical factors such as diabetes mellitus (DM), smoking, and a history of tuberculosis (TB) were explored in relation to NTM infection status. Our findings indicated that 33.3% of NTM-positive patients had DM, compared to 13.4% of NTM-negative patients. While this suggests a potential link between DM and NTM infection, no significant association was found (p=0.284). Other studies have similarly suggested that patients with DM may be at an increased risk for NTM infections due to impaired immune function,[23,24] but further research is needed to confirm this association. Additionally, while a history of TB was present in 11.1% of NTM-positive patients, this was not significantly different from the 24.6% in NTM-negative individuals (p=0.563), suggesting that prior TB may not be a major risk factor for NTM infection in this cohort.

Regarding presenting complaints, the most commonly reported symptom was cough, which was observed in 77.7% of NTM-positive and 77.0% of NTM-negative individuals. This is consistent with the findings of other studies that have shown cough to be a prevalent symptom in patients with pulmonary NTM infection.[25,26] Interestingly, fever, which was reported in 44.4% of NTM-positive patients, was also common in NTM-negative individuals (59.9%). This lack of significant difference (p=0.367) suggests that fever may not be a distinguishing feature for NTM infection. Similarly, anorexia was reported by 44.4% of NTMpositive individuals, but no significant association was observed (p=0.174). These findings underscore the challenge of using presenting complaints alone to distinguish between NTM-positive and NTM-negative individuals.

Radiologically, consolidation was the most common pattern observed in NTM-positive patients, accounting for 58.16% of cases. This is consistent with prior studies, which have highlighted consolidation as a typical radiological finding in pulmonary NTM infections.[27,28] Cavitary lesions were seen in 28.57% of NTM-positive patients, in line with reports from previous research that suggest cavities are a frequent radiological feature of pulmonary NTM infection.[9] Nodule formation was the least common radiological pattern, observed in 13.27% of NTM-positive cases, which is consistent with findings by Chung et al. (2005), who reported that nodules are less frequently observed in NTM infections.[29] The absence of a statistically significant association between radiological patterns and NTM positivity (p>0.05) indicates that while radiological features are helpful, they may not be definitive in identifying NTM infection on their own.

Limitation of the study:The limitations of this study include the small sample size of NTM-positive cases (n=9), which may limit the generalizability of the findings. Additionally, the study was conducted at a single institution, which may not fully represent the broader population. The reliance on radiological patterns and clinical complaints for diagnosis, without the use of

advanced diagnostic methods like culture, may have led to misclassification. Lastly, the observational design limits the ability to establish causal relationships between risk factors and NTM infection.

Conclusion

In conclusion, this study provides valuable insights into the prevalence and clinical characteristics of Nontuberculous Mycobacteria (NTM) infections among patients with chronic cough and abnormal chest X-rays. Although the overall prevalence of NTM infection was low (5%), consolidation was the most common radiological finding, and certain clinical characteristics such as diabetes mellitus showed potential associations with NTM infection. However, no statistically significant differences were found between NTM-positive and NTM-negative cases in terms of age, sex, or clinical complaints. The study highlights the need for improved diagnostic methods and further research to better understand the risk factors associated with NTM infections.

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Informed Consent Statement

All patients provided written informed consent.

Conflict of interest

There are no conflicts of interest among authors.

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Bangabandhu Sheikh Mujib Medical University

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REVIEW ARTICLE

Pulmonary Hypertension in Chronic Respiratory Diseases: A Comprehensive Review of Pathogenesis, Diagnosis, and Treatment

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Abstract:

Pulmonary hypertension (PH) is a significant condition that gets worse over time. It frequently complicates several chronic respiratory diseases (CRDs), such as chronic obstructive pulmonary disease (COPD), interstitial lung diseases (ILDs), and obstructive sleep apnea (OSA). The presence of PH in conjunction with CRDs can severely impact patient outcomes. This results in increased rates of illness and mortality. This review discusses the causes, diagnostic approaches for PH, and the current treatment strategies for managing PH in individuals with CRDs. The aim is to promote early detection and tailored care.

Keywords: Pulmonary hypertension, chronic respiratory diseases, pathogenesis, diagnosis and treatment.

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Introduction

Pulmonary hypertension is defined hemodynamically by a mean pulmonary arterial pressure (mPAP) that exceeds 20 mmHg at rest, a condition assessed through right heart catheterization (RHC)[1]. In people with chronic lung diseases, pulmonary hypertension often develops due to pulmonary hypoxic vasoconstriction, vascular remodeling, and inflammation. This type of pulmonary hypertension, linked to chronic respiratory diseases, is classified as Group 3 in the WHO categorization of pulmonary hypertension[2]. Although it is typically mild to moderate in intensity, advanced pulmonary hypertension in these patients leads to a poor prognosis and complicates diagnosis and management.

Pathogenesis of pulmonary hypertension in chronic respiratory diseases

Hypoxic pulmonary vasoconstriction

Chronic hypoxia is an important characteristic of various long-term respiratory conditions. It triggers the constriction of blood vessels in the lungs to enhance the alignment of ventilation and perfusion. However, ongoing hypoxia results in continued vasoconstriction, damage to blood vessel linings, and thickening of smooth muscles. This results in elevated pressures within the lungs[3].

Vascular remodeling

The remodeling of the pulmonary arteries is facilitated by growth factor expression, oxidative stress, and inflammation. Medial hypertrophy,

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adventitial fibrosis, and intimal proliferation are caused by the upregulation of pro-inflammatory cytokines (like IL-6, TNF-á) and growth factors (like VEGF, PDGF)[4].

Loss of capillary bed

Vascular resistance rises in ILDs as a result of fibrosis obliterating the pulmonary capillary bed. Similar to this, the pulmonary vascular cross-sectional area is decreased in emphysema due to the destruction of alveolar-capillary units[5].

Epidemiology and risk factors

Prevalence of PH depending on the type of CRDs :

- COPD: Although typically mild, PH is present in 30–70% of patients with severe disease[6]. A meta-analysis encompassing 38 studies on patients with varying degrees of COPD severity revealed a prevalence of pulmonary hypertension (PH) at 39.2%. In individuals with severe COPD, according to GOLD criteria, nearly 90% exhibit a mean pulmonary artery pressure (mPAP) exceeding 20 mmHg, with most falling between 20 and 35 mmHg. The occurrence of PH in patients classified as GOLD 1 and 2 COPD is considerably lower, approximately 5%[7].
- ILD: Up to 40% of people with idiopathic pulmonary fibrosis (IPF) develop moderate to severe PH. In individuals with idiopathic pulmonary fibrosis (IPF), the occurrence of pulmonary hypertension (PH) is approximately 8% to 15% during the initial phases of the illness and increases significantly in advanced stages, exceeding 60% by the time patients are assessed for lung transplantation, and more than 80% in those with terminal IPF. Data from a tertiary care facility showed that 46% of patients with interstitial lung disease (ILD) had pulmonary hypertension (PH); this analysis included a total of 239 patients, comprising those with hypersensitivity pneumonitis (32%), autoimmune ILD (31%), idiopathic pulmonary fibrosis (IPF) (16%), sarcoidosis (13%), other forms of non-IPF idiopathic interstitial pneumonitis (2%), and various other types of ILD (6%). About 30% to 50% of people with both pulmonary fibrosis and emphysema also have PH[8,9].
- OSA: Up to 41% of patients may develop PH, which frequently coexists with obesity hypoventilation syndrome and left heart disease[10,11].

  Chronic hypoxemia, smoking, the severity of the underlying illness, and coexisting comorbidities like left heart dysfunction are risk factors.

Clinical presentation and diagnosis

Clinical features

Non-specific symtoms that often overlap with underlying lung diseases-

- Dyspnea on exertion
- Chest pain
- Fatigue
- Syncope (in severe cases)
- Peripheral edema and signs of right heart failure

Diagnostic tests

- Echocardiography: The first-line method for determining the size and function of the right heart and estimating pulmonary artery pressure[12].
- Pulmonary Function Tests: To assess the degree and pattern of lung disease.
- High-Resolution CT (HRCT): Assists in identifying parenchymal abnormalities such as emphysema or ILD.
- Ventilation-Perfusion (V/Q) Scan: To exclude chronic thromboembolic PH.
- Right Heart Catheterization: Gold standard test for diagnosis and classification of PH[13].

Management strategies

General management

General management should focus on the treatment of underlying lung diseses and supportive care:

- O_2 therapy: recommended for hypoxemic patients; enhances quality of life and survival in COPD patients[14].
- Smoking cessation and
- Pulmonary rehabilitation.

Pharmacological treatment

- Diuretics
- PH-specific treatment: Use in Group 3 PH is still debatable. Examples of such treatments include phosphodiesterase-5 inhibitors and endothelin receptor antagonists. There is some evidence to support its use in carefully chosen patients with mild lung disease and severe PH [15,16].The INCREASE trial and later analyses indicate that inhaled treprostinil could be very important in slowing disease progression and enhancing outcomes for individuals with PH-ILD[17,18].
- Immunosuppressive treatment: For ILDs associated with connective tissue disease.

Lung transplantation

Regarded to be in advanced illness that is not responsive to treatment, particularly in young individuals with COPD or ILD[19].

Prognosis

In CRDs, PH is linked to increased hospitalization rates, higher mortality, and decreased exercise tolerance. Even mild PH is a predictor of poor outcomes in COPD. In certain cohorts, the median survival is less than two years, indicating that severe PH considerably reduces survival in ILD [20].

Conclusion

Pulmonary hypertension (PH) is a prevalent and critical issue in chronic respiratory illnesses. Comprehending its intricate causes and identifying it promptly through appropriate diagnostic assessments is vital. The treatment primarily targets the underlying respiratory disease and includes supportive care. Recent findings regarding selective vasodilator therapy present possibilities for tailored management in specific patient populations. Future studies should aim to enhance diagnostic indicators and therapeutic approaches that are tailored to the unique pathophysiology of Group 3 PH.

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CASE REPORT

Superior vena cava (SVC) Syndrome due to an Uncommon Pathology– A Case Report

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Abstract:

Superior vena cava (SVC) syndrome, caused by obstruction of blood flow in the SVC, is relatively uncommon secondary to intravascular thrombosis in the context of malignancy. While external compression by tumors is the commonest etiology, we present an unusual case of SVC syndrome stemming from thrombosis secondary to non-Hodgkin's lymphoma (NHL).We present a 28-year-old woman who was admitted with a two-month history of high-grade fever, followed by progressive facial, neck, and upper chest swelling, along with exertional dyspnea for one month. She also reported right-sided neck pain and a palpable lump in her neck for nine months. Comprehensive evaluation confirmed SVC syndrome due to thrombosis caused by high-grade B-cell lymphoma, favoring diffuse large B-cell lymphoma (DLBCL), non-germinal center B-cell type. Prompt management led to symptomatic improvement and a reduction in SVC thrombus size. This case highlights an uncommon cause of SVC syndrome challenging the typical association with lung carcinoma. It underscores the critical importance of early recognition, accurate diagnosis, and timely management, especially when thrombosis complicates such an uncommon pathological entity.

Keywords: *Superior vena cava, Malignancy, Thrombosis, Non-Hodgkin's lymphoma*

[Chest Heart J. 2024; 48(1) : 54-59]

Introduction

Superior vena cava (SVC) syndrome, a potentially fatal condition, results from severe obstruction or blockage of the SVC[1-3]. Superior vena cava, the largest mediastinal vein, drains venous blood from the head, neck, upper extremities, and upper thorax[4]. Its primary tributary is the azygos vein, which, along with other small mediastinal veins, can become prominent in cases of SVC obstruction to compensate for impaired blood flow[5]

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Malignancies cause approximately 70% of SVC syndrome cases, with lung cancer being the most common (75%), followed by non-Hodgkin lymphoma (20%), and metastatic cancers like breast cancer [2, 3, 6, 7]. The incidence of device-related SVC syndrome, linked to central venous catheters and pacemaker/defibrillator leads, has increased[2,3]. While thrombotic occlusion is common with these devices, spontaneous thrombosis can also occur in hypercoagulable states, such as those associated with malignancy[4].

SVC syndrome can arise from external compression (e.g., by tumors or lymphadenopathy) or internal obstruction (e.g., thrombus formation or tumor infiltration)[4]. These mechanisms can coexist, though their overlapping clinical implications are not well understood[4].

Clinical presentation typically includes swelling of the face, neck, and upper extremities, with possible hoarseness, chest pain, dysphagia, headache, syncope, mental status changes, and periorbital edema. While onset is often gradual, acute, life-threatening presentations can occur[4].

Initial management focuses on identifying and treating the underlying cause. For malignancy-associated SVC syndrome, oncologic therapies like chemotherapy or radiation therapy (RT) are prioritized[2]. Historically, RT was the primary treatment, especially for airway obstruction. However, endovascular stent placement is now preferred for life-threatening symptoms or refractory disease[8]. Anticoagulation is routinely recommended for SVC stenting and in cases of thrombotic occlusion linked to intravascular devices[9]. Some clinicians advocate for extended anticoagulation for primary and secondary thrombosis prevention in malignancy-related SVC syndrome, though evidence is limited[10].

Case Report

A 28-year-old lady presented with two-month history of high-grade intermittent fever, followed by one month of progressive facial, neck, and upper chest swelling with exertional dyspnea. She also reported right-sided, non-radiating neck pain and a palpable right neck lump for nine months.

Clinical examination revealed an ill, anxious, plethoric patient with facial and neck swelling and congested eyes. Prominent, visible veins on the upper chest showed downward blood flow. An enlarged, rubbery, non-tender, mobile right anterior cervical lymph node measured approximately 2x2 cm. Her pulse rate was 108/min, BP 110/80 mmHg (no postural drop), and SpO2 98% on room air.

Initial blood tests showed: hemoglobin 11.7 g/dL, TLC 12.80 × 10y /L (neutrophils 65%, lymphocytes 25%, monocytes 8%, eosinophils 2%), ESR 23, and elevated platelet count 441 × 10y /L. Liver function tests revealed elevated SGPT (123 IU/L) with normal bilirubin. Serum LDH was markedly elevated at 789.38 U/L. Electrolytes report was normal.

Chest X-ray showed mediastinal widening, suggestive of bilateral paratracheal and right hilar lymphadenopathy [Figure 1]. USG of the whole abdomen was unremarkable except for Grade II fatty liver [Figure 2A]. Neck ultrasonography revealed bilateral cervical lymphadenopathy, with the largest one measuring 27.9 × 24.6 mm [Figure 2B].

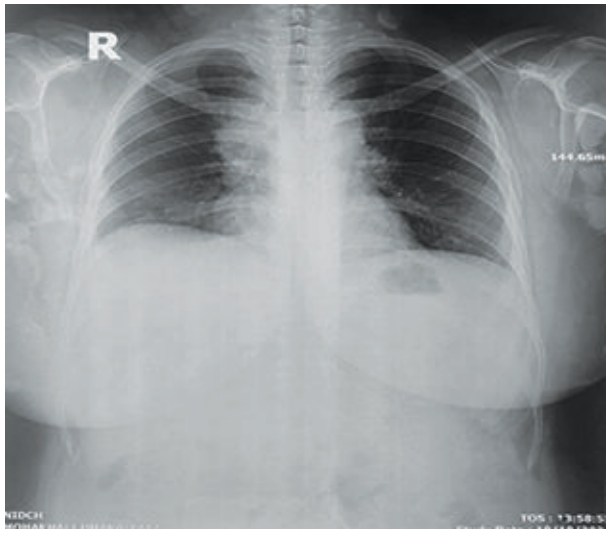


Figure 1: *CXR P/A view showing (mediastinal widening)*

A chest CT scan revealed a soft tissue density filling defect (4.1 × 2.9 × 2.8 cm) within the SVC lumen. This thrombus extended superiorly into the right internal jugular vein via the right brachiocephalic vein and into the terminal left brachiocephalic vein. A soft tissue lesion in the right infraclavicular region suggested lymphadenopathy, but no significant mediastinal lymphadenopathy was found

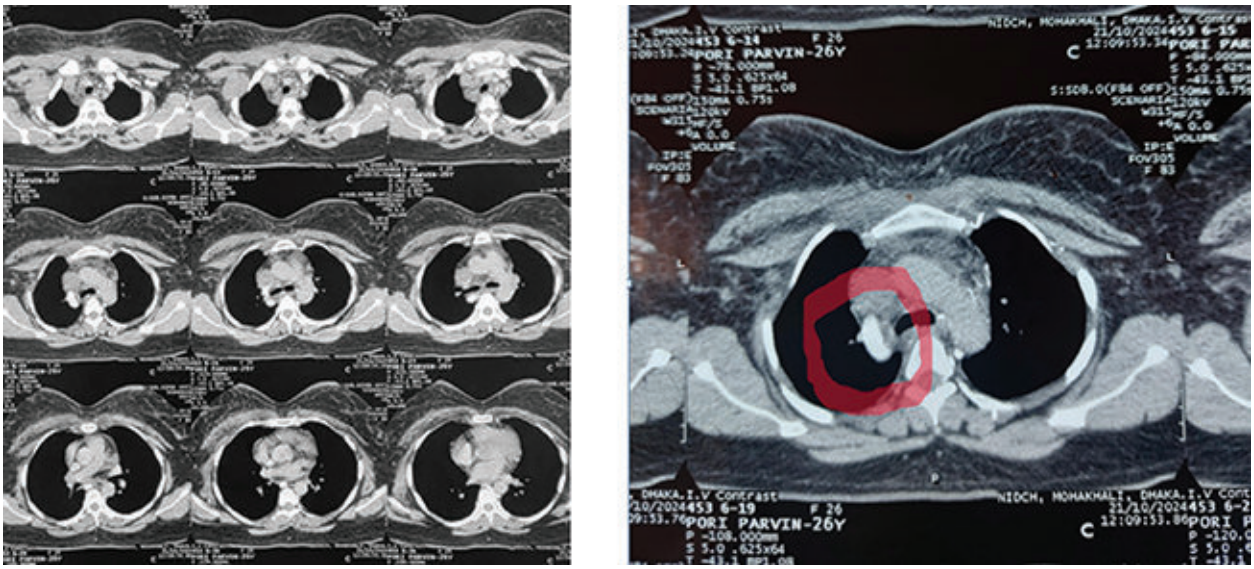


Figure 2 (A&B): *CT scan of Chest showing soft tissue density filling defect within the SVC lumen. This thrombus extended superiorly into the right internal jugular vein via the right brachiocephalic vein and into the terminal left brachiocephalic vein. A soft tissue lesion in the right infraclavicular region suggested lymphadenopathy, but no significant mediastinal lymphadenopathy was found.*

[Figure 3]. CT Pulmonary Angiogram showed an SVC thrombus (4.8 × 3.5 × 3.0 cm) extending into the right brachiocephalic vein and the terminal left brachiocephalic vein [Figure 4].

A core biopsy from the right cervical lymph node showed histopathological features consistent with intermediate-grade non-Hodgkin's lymphoma [Figure 5]. Immunohistochemistry confirmed high-grade B-cell lymphoma, favoring DLBCL, non-GCB type [Figure 6].

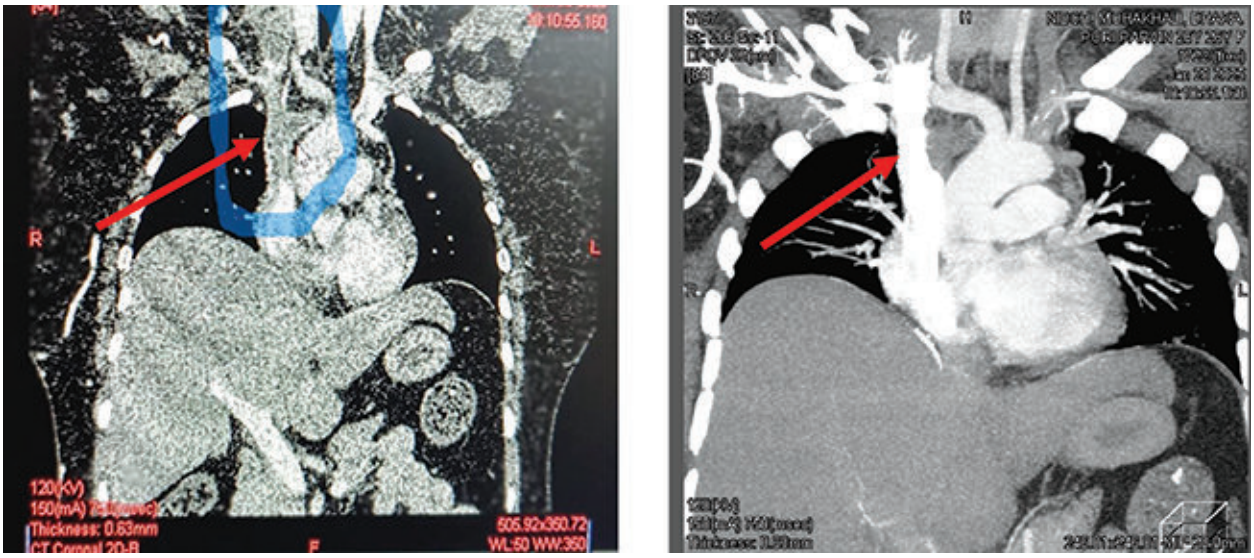
Figure 3 (A&B): CT scan of Chest showing soft tissue density filling defect within the SVC lumen. This thrombus extended superiorly into the right internal jugular vein via the right brachiocephalic vein and into the terminal left brachiocephalic vein. A soft tissue lesion in the right infraclavicular region suggested lymphadenopathy, but no significant mediastinal lymphadenopathy was found.

Figure 4: CT Pulmonary Angiogram showing SVC thrombus (4.8 × 3.5 × 3.0 cm) extending into the right brachiocephalic vein and the terminal left brachiocephalic vein.

She was started with subcutaneous enoxaparin 60 mg every 12 hours for 7 days, transitioning to oral rivaroxaban. Significant clinical improvement,

Figure 3: *CT Pulmonary Angiogram showing SVC thrombus (4.8 × 3.5 × 3.0 cm) extending into the right brachiocephalic vein and the terminal left brachiocephalic vein.*

including reduced shortness of breath, facial and upper chest edema, and neck pain, was observed. Following LMWH. Once stable, the patient was referred to a hemato-oncologist for further evaluation and management.



A B

Figure 4: *(A) CTPA (Before Treatment), (B) CTPA Showing SVC thrombus is reduced in size from 4.8x3.5x3cm to 2.7x1.6 cm.*

Discussion:

Superior vena cava (SVC) syndrome, characterized by obstructed blood flow, can arise from external compression, intraluminal thrombosis, or tumor infiltration. First documented in 1757 due to a syphilitic aneurysm, SVC syndrome was historically over 90% linked to malignancies [11,12]. However, recent data indicate about 35% of cases now have benign origins, often thrombotic, stemming from increased use of intravascular devices like central venous catheters and pacemakers[13]. SVC syndrome caused by an acute, spontaneous thrombus without underlying tumor compression or intravascular devices is extremely rare[14]. Paraneoplastic thrombosis in the SVC has been reported in various cancers, including lung, renal cell, and ovarian carcinoma [14-16]. While Doppler ultrasound aids thrombus detection, contrast venography or CT angiography remains the gold standard for definitive SVC obstruction diagnosis[17].

We present a case of a young, immunocompetent female with no significant medical history who developed SVC thrombosis as a rare initial manifestation of non-Hodgkin's lymphoma (NHL), without indwelling devices or mediastinal lymphadenopathy. Imaging revealed a large thrombus extending from the SVC into both brachiocephalic veins and the right internal jugular vein, notably without the typical bulky mediastinal mass seen in lymphoma-related SVC syndrome[6].

Histopathological analysis confirmed intermediate-grade NHL, with immunohistochemistry identifying it as high-grade B-cell lymphoma, most consistent with diffuse large B-cell lymphoma (DLBCL), non-germinal center B-cell (non-GCB) type. While DLBCL often presents with rapidly enlarging lymphadenopathy, B symptoms, and extranodal involvement, SVC thrombosis as an isolated presenting feature is rarely reported[18,19].

Malignancy-associated thrombosis is often attributed to a hypercoagulable state induced by tumor factors that activate the coagulation cascade. This paraneoplastic prothrombotic state, combined with vessel wall invasion and stasis, fulfills Virchow's triad, predisposing to spontaneous thrombus formation[20]. While thromboembolic events are not uncommon in lymphoma patients, central vein involvement, particularly the SVC, without external compression, remains unusual.

Historically, SVC syndrome was managed with open surgical repair using bypass grafts [21]. Currently, management depends on etiology and symptom severity. For malignancy-related cases, initial treatment targets the primary tumor with chemotherapy or radiation therapy [7]. Acute or life-threatening presentations may warrant endovascular interventions like stenting or

thrombolysis. Anticoagulation is recommended for thrombosis, especially with central venous devices or after stenting [22]. Our patient received systemic chemotherapy based on histological diagnosis, with supportive anticoagulation for thrombus management.

For SVC syndrome caused by indwelling intravascular device-related thrombus, primary treatment involves device removal, anticoagulation, and catheter-directed thrombolysis[23]. In rare cases of SVC thrombosis without a tumor or device-related cause, anticoagulation is preferred, with many clinicians recommending thrombolytic therapy initially. For rapid symptom relief in acute thrombosis-related SVC obstruction, balloon angioplasty with stent placement is a widely accepted and effective first-line treatment[17].

Conclusion and recommendations

This case highlights a rare presentation of superior vena cava (SVC) syndrome due to intraluminal thrombosis, occurring without common risk factors like mediastinal masses or intravascular devices. It underscores the importance of considering thrombotic etiologies in patients with suspected or known malignancy, even when typical features are absent.The case emphasizes maintaining a high index of suspicion for underlying malignancy in SVC syndrome presentations and the necessity of comprehensive diagnostic workup, including imaging and histopathology, to guide treatment. Given its rarity, further studies and long-term follow-up are crucial to understand recurrence, identify complications, and optimize management strategies for thrombosis-related SVC syndrome in malignancy.

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Conflict of interest: None declared

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CASE REPORT

Congenital Lobar Emphysema: A Case Report of Rare Cause of Respiratory Distress in Neonate

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Abstract:

Congenital lobar emphysema is one of the many causes of the respiratory distress syndrome in infants, and its early recognition is important because proper surgical therapy can be lifesaving. Congenital lobar emphysema (CLE) is a rare condition characterized by over inflation of one or more lobes of the lung, resulting in compression of adjacent lung tissue and impaired respiratory function. We report the case of a one-month-old female infant, Faiza, who presented with progressive respiratory distress and feeding difficulties since the tenth day of life. Despite multiple hospital visits and empirical antibiotic therapy, her symptoms persisted. Upon admission to National Institute of Diseases of the Chest and Hospital (NIDCH), clinical evaluation revealed dyspnea, subcostal retractions, and decreased breath sounds over the left hemithorax. Radiological imaging studies confirmed the diagnosis of congenital lobar emphysema and underwent left upper lobectomy with successful outcomes. This case highlights the importance of prompt recognition and considering CLE in the differential diagnosis of persistent respiratory distress in early infancy with appropriate management of this condition to prevent complications and ensure favorable outcomes.

Keywords: *Congenital lobar Emphysema, Neonate, surgical treatment, good prognosis and outcome.*

[Chest Heart J. 2024; 48(1) : 60-66]

Introduction

Congenital lobar emphysema (CLE) is a rare congenital pulmonary anomaly characterized by overexpansion of one or more lobes of the histologically normal lung, without alveolar wall destruction. This condition results in compression of the adjacent lung parenchyma and impaired ventilation, often manifesting as recurrent respiratory distress. There is air trapping in the lung during the expiratory phase of respiration due to deficient bronchial cartilage, which causes repeated episodes of respiratory distress. The affected lobe is essentially non-functional because of over distention and air trapping. It is frequently

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recognized in newborns; however, a few cases do not get evident until adulthood. This disease is potentially reversible if diagnosed and treated on time.[15] CLE poses a significant diagnostic and therapeutic challenge due to its variable presentation and potential overlap with other pulmonary conditions such as pneumonia or pneumothorax. If diagnosed early, CLE is potentially reversible, with surgical resection of the affected lobe often resulting in excellent outcomes.

Congenital lobar emphysema (CLE) is a congenital anomaly of the lung, with a prevalence of 1 in 20,000 to 1 in 30,000[1]. Most of the cases present in the neonatal period, with a male to female ratio of 3:1[2,3]. CLE has also been reported with other associated anomalies with double superior vena cava and horse shoe kidney[4]. One case is reported with polysplenia, a syndrome characterized by bilateral bilobed lungs and bilateral pulmonary atria along with liver, which is symmetrically placed in the midline and multiple nodules of spleen[5].

Case report:

Faiza, a 1-month-old female infant, second issue of non-consanguineous parents, presented with complaints of respiratory distress and feeding difficulty since 10 days of age. She was delivered at term by lower uterine cesarean section (LUCS) without any perinatal complications. The mother reported noticing progressive respiratory difficulty, particularly during feeding episodes. Despite receiving empirical antibiotic treatment at multiple local healthcare facilities, her symptoms failed to resolve, prompting referral to our tertiary care center. On admission to the National Institute of Diseases of the Chest and Hospital (NIDCH), Faiza appeared ill, lethargic, and dyspneic, with marked subcostal retractions and oxygen saturation was 88-89% at room air. Physical examination revealed reduced chest wall movement on the left side, tracheal deviation to the right, hyper resonance on percussion and markedly diminished breath sounds over the left hemithorax. A frontal radiograph of the chest shows marked over distention of the left upper lobe with mediastinal shift to the right. A subsequent computed tomography (CT) scan of chest confirmed hyper-aeration of the left upper lobe with associated mediastinal displacement. Routine hematological and biochemical investigations were within normal limits. Further evaluation led to the diagnosis of left-sided congenital or infantile lobar emphysema.

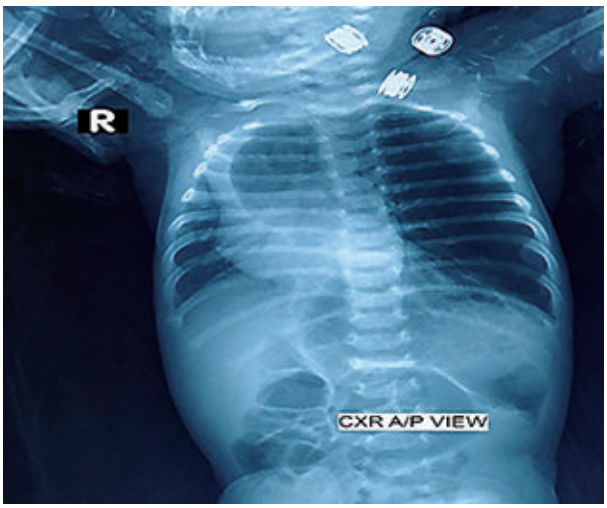

Figure 1: *CXR*

Management and Outcome:

The patient underwent a left upper lobectomy under general anesthesia with one-lung ventilation. Intraoperative findings revealed an emphysematous and markedly over expanded left upper lobe, while the adjacent left lower lobe

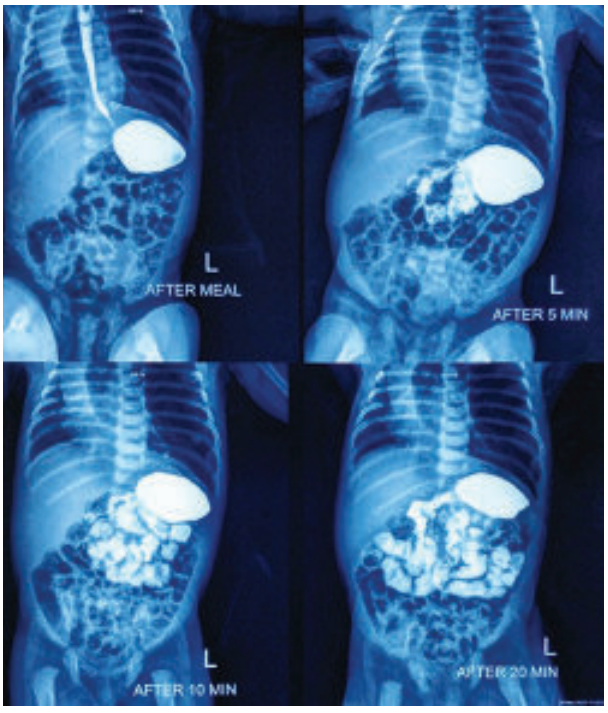

Figure 2: *Contrast follow through*

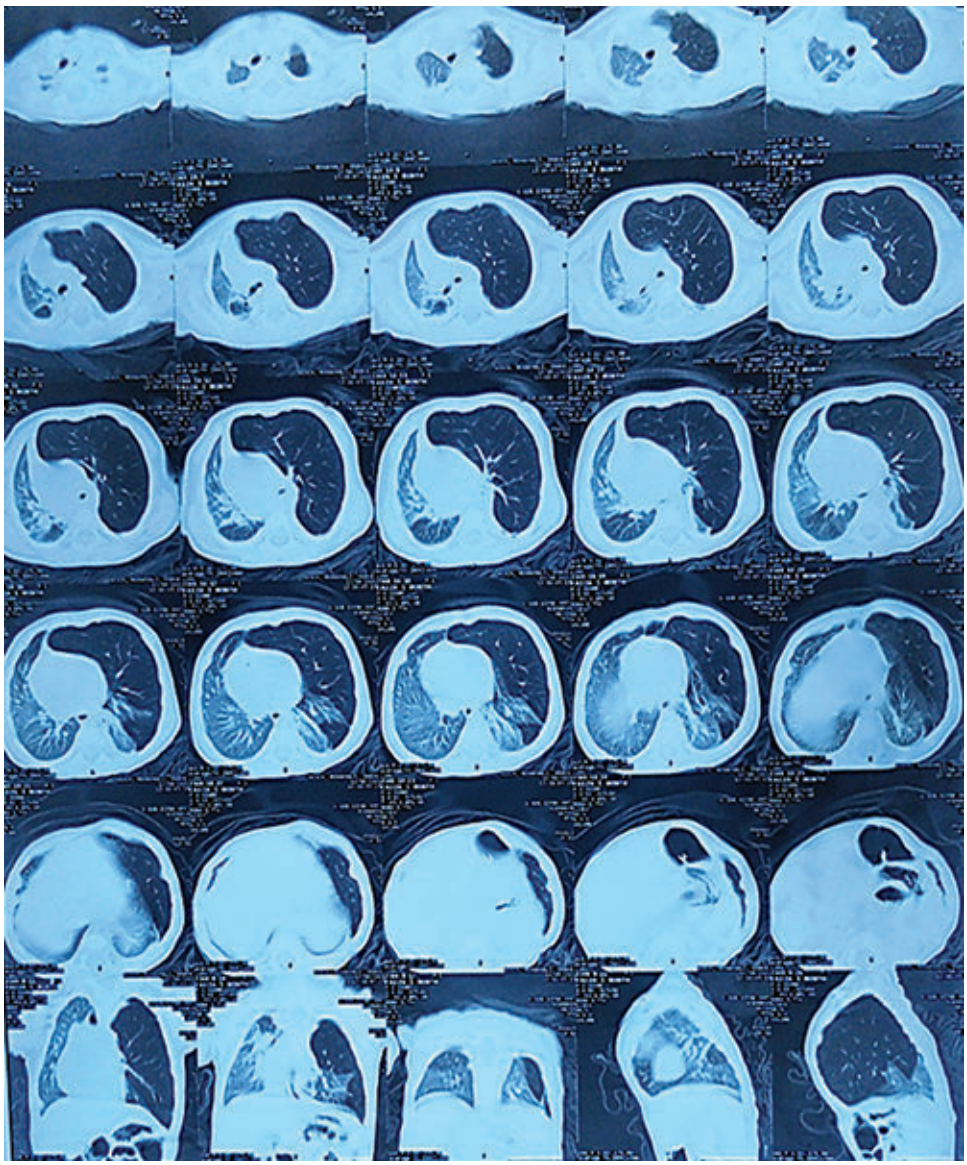

Figure 3: *CT scan of chest*

appeared partially collapsed due to compressive effects. The resection proceeded without complications.

Postoperatively, the patient experienced an uneventful recovery. Clinical and radiological assessments confirmed satisfactory re-expansion of the remaining lung parenchyma. The intercostal chest drain was removed on the third postoperative day. Faiza demonstrated significant clinical improvement, including resolution of respiratory distress and feeding difficulties, and was discharged in stable condition with scheduled follow-up.

Per operative pictorial

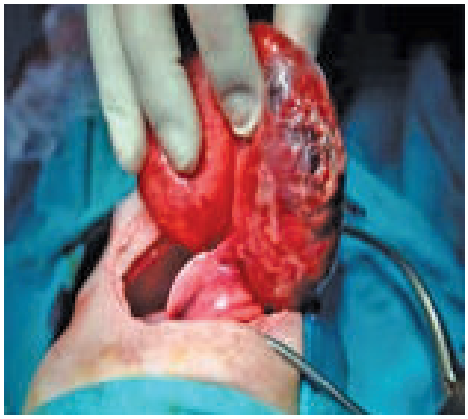

Figure 4: *Emphysematous left upper lobe*

Figure 5: *After resection of Left upper lobe*

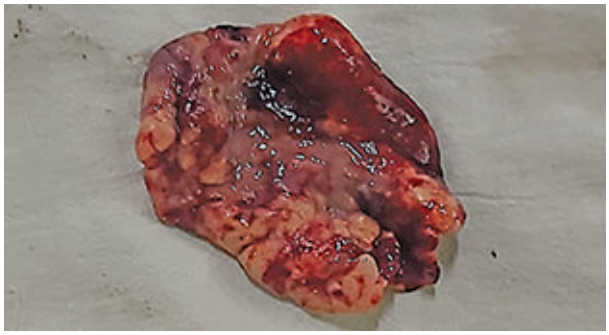

Figure 6: *specimen after resection*

Figure 7: *post-operative Chest X-ray*

Figure 8: *Post-operative status during discharge*

Discussion:

Congenital lobar emphysema (CLE) is an uncommon congenital malformation, characterized by alveolar distension and pulmonary hyperinflation, with contralateral pulmonary atelectasis[3]. The clinical diagnosis of CLE can be challenging and chest radiography is often diagnostic, which typically shows hyperlucency of the affected lobe, widened intercostal spaces, diaphragmatic flattening, and mediastinal shift away from the affected side. In some cases, the mediastinum may herniate into the contralateral hemithorax.

Although most cases present in the neonatal period, approximately 5% are diagnosed by six months of age, and some are detected even later in childhood. Prenatal ultrasonography may identify CLE in utero, and familial cases have also been reported[6,7,8]. The incidence of left upper lobe involvement is 43% of all cases, our infant belonging to this group; the middle right lobe is affected in 35% of cases, the upper right lobe in 21% of cases, while bilateral involvement occurs in 20% of cases[9]. Pneumonia & pneumothorax is a common misdiagnosis for CLE.[21] It has some synonyms: infantile lobar emphysema, Congenital lobar overinlfation, Congenital lobar or segmental bronchomalacia, Emphysema of infancy or childhood. Two histopathological forms of CLE exist: the hypoalveolar type (fewer than expected alveoli) and the polyalveolar type (greater than expected alveoli).

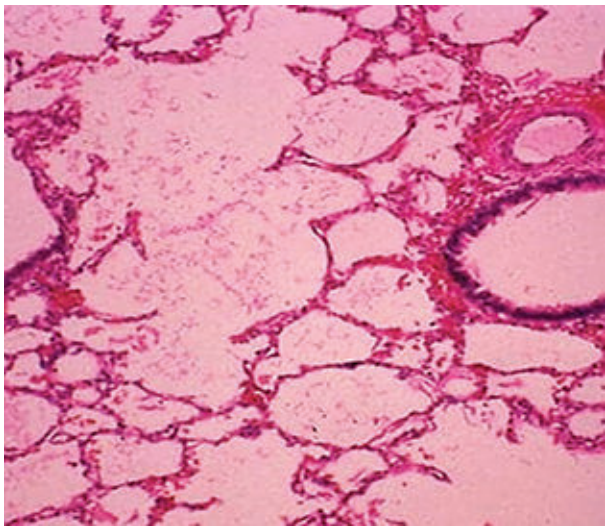

Figure 9: *Histopathology of congenital lobar emphysema with marked over distention of all alveoli.*

Pathophysiology

The fundamental mechanism involves defective bronchial cartilage, resulting in airway collapse during expiration and subsequent air trapping. This leads to progressive over inflation of the affected lobe, compression of adjacent lung tissue, and impaired pulmonary function.

Etiology

The etiology of CLE remains idiopathic in approximately 50% of cases. Identifiable causes include bronchial cartilage defects (25%), extrinsic vascular compression, bronchial stenosis, mucous plugging, abnormal bronchial secretions and mediastinal displacement[10]. In 10% of cases, congenital lobar emphysema can be associated with congenital cardiac malformations, which are excluded by echocardiography[11].

Clinical presentation

Typically, infants with CLE appear normal at birth. 50% of cases, Symptoms typically manifest within the first few days of life which includes- dyspnea, cyanosis, chest retractions, wheezing, and feeding difficulties. Physical examination may reveal asymmetric chest expansion, hyper-resonance, diminished breath sounds, and tracheal deviation. Progressive hypercapnia and respiratory failure may ensue if untreated.

Differential Diagnosis

1. Congenital cystic adenomatoid malformation.
2. Post pneumonic pneumatocele
3. Tension Pneumothorax
4. Congenital diaphragmatic hernia

Investigations / Diagnostic workup

1. Chest radiography- Chest X-ray is often the first diagnostic modality, revealing hyperinflation of the affected lobe, contralateral mediastinal shift, and adjacent lung atelectasis. Lateral and decubitus views help delineate non-collapsing emphysematous lobes.[19]
2. CT scan of chest- CT scan provides detailed anatomical and vascular information. It typically demonstrates a hyperlucent, hyper expanded lobe with preserved yet attenuated vascular markings, along with mediastinal displacement and compression of uninvolved lobes.[20]
3. MRI of chest- Used selectively to evaluate vascular supply. CT/MRI, allows diagnosis and initiation of early treatment for a favorable prognosis [11-14].
4. Prenatal USG- Can detect CLE as hyperechoic lung segments with normal vascular flow.
5. Bronchoscopy- Assesses bronchial anatomy and to remove the mucous plug or aspirated foreign body which should be performed at the same anaesthetic period for thoracotomy.
6. Ventilation-Perfusion Scanning: - Nuclear imaging shows delayed alveolar emptying and diminished perfusion of the affected lobe due to vascular compression.

Concomitant malformations

CLE is frequently associated with congenital cardiac anomalies (14–20%). Common abnormalities include Patent ductus arteriosus (PDA), Atrial septal defect (ASD), Ventricular septal defect (VSD), Total pulmonary venous return anomaly (TAPVR), and Tetralogy of Fallot (TOF). Embryologic overlap in the development of the heart and lungs during weeks 4–6 of gestation may account for this association. Therefore, disruptions during this critical window may result in simultaneous cardiopulmonary anomalies. A

thorough cardiovascular evaluation is warranted before surgical intervention.

Concomitant malformations accompanying congenital lobar emphysema*

Cardiac malformations 14-20%	Patent ductus arteriosus Atrial septal defect Ventricular septal defect Tetralogy of Fallot Pulmonary stenosis Pulmonary valve atresia Aortic coarctation Pulmonary hypertension Left aortic arch Right descending aorta Left ligamentum arteriosum Double superior Vana cava
Renal anomalies	Aplastic kidney Horseshoe kidney
Musculoskeletal anomalies	Pectus excavatum Hiatal hernia Diaphragmatic hernia
Gastrointestinal tract	Omphalocele Pyloric stenosis
Others	Cleft palate Chondroectodermal dysplasia Chondrodystrophy

Figure 10: *Concomitant malformations*

Treatment

Surgical lobectomy is the treatment of choice in symptomatic infants and usually results in complete recovery. Special attention must be given during anaesthetic induction to avoid rapid over-inflation of the affected lobe. Segmental resection, as an alternative to lobectomy, has been employed in select cases with localized disease. [14] Conservative management may be considered in asymptomatic or mildly symptomatic cases, particularly in older children with stable clinical status and normal bronchoscopic findings

Learning Points

a. Early-Onset Respiratory Distress: CLE should be considered in the differential diagnosis of neonates and infants with unexplained or persistent respiratory distress, particularly when unresponsive to antibiotics or conventional therapy.

b. Radiological Clues Are Key: Chest X-ray and CT scan are essential for diagnosis. Findings such as lobar hyperinflation, mediastinal shift, and compression of adjacent lung structures are characteristic of CLE.

c. Mimics Other Conditions: CLE is frequently misdiagnosed as pneumonia, pneumothorax, or congenital cystic lung lesions, underscoring the importance of a high index of suspicion.

d. Cardiac Evaluation is Crucial: Up to 20% of CLE cases are associated with congenital heart defects; echocardiographic assessment should be performed routinely before surgical planning.

e. Definitive Management is Surgical: Lobectomy of the affected lobe is curative in symptomatic patients and typically results in excellent long-term respiratory outcomes.

f. Conservative Approach Possible: Asymptomatic or mildly symptomatic patients may be managed conservatively with close monitoring, especially in older children.

Take-Home Message

Congenital lobar emphysema (CLE), though rare, should be considered in the differential diagnosis of neonates presenting with persistent respiratory distress, especially in cases unresponsive to conservative management. Congenital lobar emphysema is a potentially life-threatening condition characterized by over inflation of one or more lobes of the lung. Early recognition, accurate diagnosis, and prompt surgical intervention are pivotal in preventing complications and ensuring favorable clinical outcomes.

Funding Statement

The study didn't receive any funding.

Ethical Approval

The study is exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient or the publication of this case report and the accompanying images.

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The Cardiac Society of Australia and New Zealand. Clinical exercise stress training. Safety and performance guideline. Med J Aust 1996; 164 : 282-4.

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