



ISSN 1562 - 5044

<http://chabjournal.org>

Indexed: BMDC

Indexed & Member: Cross Ref.

Indexed: BanglaJOL

Chest & Heart Journal

Volume 48

Number 02

July 2024

A Journal
and
Official Organ
of the Chest &
Heart Association
of Bangladesh

Chest & Heart Journal

Volume 48, Number 02, Page 67-123

July 2024

CONTENTS

EDITORIAL

- Precision Medicine in Pulmonology - A New Horizon 67
Mir Iftekhar Mostafiz

ORIGINAL ARTICLES

- Sensitivity and Specificity of Gene Xpert of Bronchoalveolar Lavage Fluid in the Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis 69
Ahmed Imran Kabir, AKM Mosharraf Hossain, Mohammed Mirazur Rahman, Muhammad Shakhawath Hossain, Mir Iftekhar Mostafiz, Rezaul Haque, Aminul Islam, Shish Mohammad Sarkar, Md. Sharif Ahsan
- A Comparative Study between Vibratory PEP Device (Acapella) With 'Usual Airway Clearance' to See the Outcome during Acute Exacerbation of Bronchiectasis 74
Miraz Mahmud, Golam Sarwar Liaquat Hossain Bhuiyan, Md. Zahirul Islam, Md. Ziaul Karim, Md. Khairul Anam, Zerin Zindia Hossain, Rezaul Haque, Muhammad Shakhawath Hossain, Ashraful Alam Khan, Goutam Sen, Sharmin Sultana, Tanveer Ahmed Chowdhury
- COVID-19 Infection, Immunization and Lung Function Parameters in a Community of Bangladesh: A Cross- Sectional Study 83
Mohammed Atiqur Rahman, Shamim Ahmed, Rajashish Chakraborty, Samprity Islam, Golam Sarwar Liaquat Hossain Bhuiyan, Manal Mizanur Rahman, Susanta Kumar Paul, Kazi Rahila Ferdousi
- Study of 2 Minute Walk Test in the Assessment of Functional Capacity in Patients with Stable Chronic Obstructive Pulmonary Disease 90
Sumya Zabin Sonia, Md. Zahirul Islam, Golam Sarwar Liaquat Hossain Bhuiyan, Md Tawhidul Alam SK Shahinur Hossain, Mir Iftekhar Mostafiz, Rezaul Haque, Tasnuba Tahsin Tofa Aminul Islam, Md Rousan Arif
- Evaluation of Serum Immunoglobulin E (IgE) Level in Newly Diagnosed Bronchial Asthma Patients in Rajshahi Medical College Hospital 100
Md. Rezaul Islam, Md Masudur Rahman, Ahmad Zainuddin Sani, Md. Mozammel Hoque Md Jakaria Mahmud, Md Hosna Sadat Patwary, Muhammad Shakhawath Hossain, Sharmin Sultana, Mohammed Mirazur Rahman

REVIEW ARTICLE

- The Expanding Role of Biologics in Severe Asthma: Current Evidence and Next-Generation Approaches 108
Md. Hamza, Sheikh Nazmul Islam, Nowroj Ahmed, Md. Shafiqul Islam

CASE REPORTS

- Mycotic Pseudoaneurysm Mimicking Community-Acquired Pneumonia: A Rare Diagnostic Vigilance 115
Rezaul Hoque, Mst Shamima Akter, Md. Zahirul Islam, Golam Forhad Jilani, Naveed Rahman, Tasnuba Tahsin Tofa, Sumya Zabin Sonia, Md. Shahjahan Ali
- Multifocal Giant Cell Tumor of the Ribs Presenting with Chest Pain and Fever: A Rare Case 120
Towhida Akter Chowdhury, Mohammad Abdullah Al Hasan, Md. Zahiduzzaman, Abrar Fayaz Labib, Mirza Md Saief, Muhammad Shakhawath Hossain, Mahmud Rahim, Mohammed Mirazur Rahman

Chest & Heart Journal

chabjournal.org

Publication of The Chest & Heart Association of Bangladesh

Dedicated to Scientific & Professional Development of Pulmonologist & Cardiologist

ISSN: 1562-5044

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PUBLISHED BY:

Editor in Chief
on behalf of the Chest and Heart
Association of Bangladesh

INDEX

Indexed in: BMDC
Member: Cross Ref.
Indexed in: Cross Ref.
Indexed in: BanglaJOL

PRINTED BY:

Asian Colour Printing
130 DIT Extension Road
Fakirpool, Dhaka-1000, Bangladesh
Phone: 49357726, 58313186
E-mail: asianclr@gmail.com

Final revision on 25th August, 2025
Publication on 20th September, 2025

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EDITORIAL

Precision Medicine in Pulmonology- A New Horizon

Mir Iftekhar Mostafiz

[*Chest Heart J.* 2024; 48(2) : 67-68]

With an exponential rise in the growth of medical technologies and advances in clinical research, global healthcare is showing strong growth in development across various sectors, including pulmonology. Precision medicine is a modern approach to medicine that emphasizes patient-tailored and catered treatment based on genetics, environment, lifestyle and other patient-specific factors in the field of pulmonology. The prioritization and importance of precision medicine is growing day by day which aim to cater to individualized indexes, subtypes, complications and other factors of any disease. By successful integration of multi-omics technology and enhancing treatment paradigms, there is great potential for enhanced clinical outcomes, revolutionary personalization of patient treatment, and improved outcome of respiratory care overall.

COPD Phenotyping:

COPD patients exhibit vastly differing factors and unique indicators in clinical presentation, radiological patterns, and treatment responses. Multidimensional indexes like BODE and treatable traits models create foundations to stratify patients and optimize treatment and care. Advances such as triple-inhaler therapy and biologics underscore the importance of precision in therapy selection for COPD management. Quantitative CT and MRI, provide deeper insights into phenotypes like airway-dominant disease versus emphysema-dominant disease. These imaging tools could guide phenotype-specific therapies. Artificial intelligence algorithms are being tested to analyze multidimensional data (e.g., lung function, exacerbation history, biomarkers) for dynamic endotype identification. This approach moves

beyond static phenotypes and adapts treatment plans in real-time. Eosinophilic COPD is gaining recognition as a specific endotype. Biologic therapies like mepolizumab (anti-IL-5) showing mixed but promising results for patients with high eosinophilic inflammation¹.

Bronchiectasis and Endotypes:

Study on bronchiectasis highlights the utility of endotyping that means classifying disease based on biological mechanisms. Bronchiectasis involves diverse etiologies, including immunodeficiency, chronic infections, and systemic autoimmune conditions. Advances in multi-omics, particularly proteomics and metabolomics, enable the identification of specific endotypes related to distinct inflammatory pathways and microbiome profiles. Tailored treatments such as immunoglobulin replacement for immunodeficiency-related endotypes and targeted anti-inflammatory therapies can be given. Recent findings suggest that the lung microbiome in bronchiectasis is a potential marker for monitoring disease progression. Formation of NETs (NETosis) is a unique inflammatory mechanism in bronchiectasis. Targeting NET-associated proteins might emerge as a new therapeutic approach for patients with neutrophilic endotypes. Neutrophil elastase, is now considered critical in endotyping bronchiectasis. Anti-protease therapies, currently under development, show promise for managing patients with high protease activity².

Precision Medicine in Chronic Respiratory Diseases (CRDs)-Challenges and opportunities:

Biomarkers like blood eosinophils and genetic markers to classify disease subtypes and predict

therapeutic responses are emphasized. Precision medicine enables tailored therapies, such as biologics for severe asthma, which align with individual endotype characteristics. Precision medicine is instrumental in early detection, prevention, and minimizing exacerbations in CRDs. Implementing Polygenic Risk Scores (PRS) to predict susceptibility to diseases like asthma and COPD. PRS combines multiple genetic markers to assess individual risk and optimize preventive strategies. Proteomics, transcriptomics are enabling early detection of CRDs, particularly in at-risk populations such as smokers or individuals with a family history of respiratory diseases. This could lead to preemptive therapeutic interventions. The “treatable traits” model is expanding beyond traditional phenotypes. This personalized trait-based approach complements the endotype framework in precision medicine³.

There are some weaknesses in the studies like limited real-world data, overgeneralization risks and insufficient exploration of multinational and inter-racial contexts. To ensure clinical utility, further studies should validate Bronchiectasis, Asthma and COPD endotypes over time. Explore machine learning for better stratification and prediction of treatment responses in precision medicine.

Conclusion:

Precision medicine represents a paradigm shift in respiratory care, promising personalized

treatment based on robust and critical biological insights. Future research should focus on global applications, integrating artificial intelligence, and addressing implementation challenges to bring precision medicine into routine clinical practice.

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References:

1. Lopez-Campos JL, Centanni S. Current approaches for phenotyping as a target for precision medicine in COPD management. *COPD*. 2018; 15:108–17. 10.1080/15412555.2018.1443064 [DOI] [PubMed] [Google Scholar]
2. Martins, M., Keir, H. R., & Chalmers, J. D. (2023). Endotypes in bronchiectasis: moving towards precision medicine. A narrative review. *Pulmonology*, 29(6), 505–517. <https://doi.org/10.1016/j.pulmoe.2023.03.004>
3. Wesnawa MADP, Asmara OD, Supadmanaba IGP. Emerging Role of Precision Medicine in Diagnosis and Treatment of Chronic Respiratory Disease. *J Respirasi* 2024; 10: 85–92. [Journal]

ORIGINAL ARTICLE

Sensitivity and Specificity of Gene Xpert of Bronchoalveolar Lavage Fluid in the Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis

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Abstract

Background: A substantive number of active pulmonary tuberculosis patients may exhibit negative sputum smear for acid fast bacilli (AFB). Early diagnosis of Pulmonary Tuberculosis (PTB) in this group of patients can reduce tubercular transmission. For the diagnosis of PTB different modalities of investigations like sputum smear and gene X-pert, mycobacterial culture, radiology based investigations like Chest X-ray and CT scan of chest or CT guided fine needle aspiration cytology (FNAC) are there. Study of Gene X-pert on bronchoalveolar lavage (BAL) offer a good option for the early diagnostic challenge of sputum smear negative pulmonary tuberculosis.

Objective: To find out diagnostic yields of Gene X-pert on bronchoalveolar lavage in diagnosing Sputum smear negative pulmonary tuberculosis patient.

Material and Methods: This intervention based observational, cross-sectional study will be conducted among all the symptomatic and/or radiologically relevant patients who are smear negative but suspected to have pulmonary tuberculosis attending in the department of Respiratory Medicine, Bangladesh Medical University (BMU) within one year after the clearance of IRB.

Results: Xpert MTB/ RIF was detected 37.5% cases on BAL fluid. In all cases rifampicin was sensitive. AFB culture on BAL fluid was used as the gold standard. AFB culture was positive 28.57% patients. Considering AFB culture as reference standard sensitivity, specificity, positive predictive Value (PPV), negative predictive value (NPV) of Xpert MTB/RIF on BAL fluid in patients with sputum smear and Xpert negative PTB were 80% (64.6-90.7%), 72.7% (74.8-86.7%), 61.0% (53.8-75.6%), 91.43% (82.3-95.3%) respectively.

Conclusion: Gene X-pert MTB/ RIF on broncho-alveolar lavage (BAL) is an useful tool for the diagnosis of smear negative PTB patients.

Keywords: Bronchoalveolar lavage, Pulmonary Tuberculosis, Fiberoptic Bronchoscopy.

[Chest Heart J. 2024; 48(2) : 69-73]

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Submission on: 4 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

Introduction:

Tuberculosis is an airborne bacterial infection caused by *Mycobacterium Tuberculosis*. Tuberculosis can be acquired by breathing contaminated air droplets coughed or sneezed a person who has active tuberculosis. It is a major health problem worldwide with variable clinical presentation. It is the tenth leading cause of death worldwide and 7th leading cause of death in Bangladesh. Initial approach is detection of AFB in sputum with staining and Gene Xpert. Mycobacterial cultures considered as the gold standard though takes 6-8 weeks for diagnosis. Microscopic examination is rapid, inexpensive, economical, but it is less sensitive requiring more than 10000 bacilli per millimeter to detect AFB. A substantive number of pulmonary tuberculosis patients remain undiagnosed by conventional sputum microscopy. More than one third of the patients with pulmonary tuberculosis cannot produce sufficient sputum or sputum smear negative¹. Clinical and radiological based diagnosis can lead to over or under diagnosis of tuberculosis. Fiberoptic bronchoscopy can help early confirmative diagnosis in such patients.

A number of studies confirm the utility of FOB over sputum examination in the diagnosis of PTB both from higher microscopy and higher culture positivity results. FOB and various bronchoscopy guided procedures can provide a rapid and definitive diagnosis of PTB in sputum smear negative patients with minimal complications. It can provide sample from the specific site of the lung and direct visualization of bronchial tree under local anesthesia. It is a safe procedure and well tolerated by most of the patients. Bronchoalveolar lavage is the best diagnostic material for the diagnosis of pulmonary tuberculosis. Diagnosis rate is 86.6 % with minimal complications with expert hands.

Bronchoscopic diagnosis of pulmonary tuberculosis traditionally relies on acid-fast bacilli smear microscopy, Gene Xpert and mycobacterial culture². The sensitivity of ZN staining on BAL remains 41% while mycobacterial culture is 86%³. The advantage of MTB-PCR of BAL fluid is that it is less time consuming, low complexity, high sensitivity and specificity, low cost and less manpower involved. Bronchoalveolar lavage Gene Xpert

has a superior diagnostic yield to detect *Mycobacterium tuberculosis* and rifampicin resistance⁴.

Our aim of this study is to see whether mycobacterium culture and Gene Xpert on bronchoalveolar lavage fluid provide additional diagnostic yield in patients who are negative for AFB smear and Gene Xpert.

Methodology

This intervention based observational, cross-sectional study will be conducted among all the symptomatic and/or radiologically relevant patients who are smear negative but suspected to have pulmonary tuberculosis attending in the department of Respiratory Medicine, Bangladesh Medical University (BMU), Dhaka from July, 2019 to June, 2020.

Inclusion Criteria:

- Patients clinically and/or radiologically compatible with pulmonary tuberculosis
- Sputum examination is negative for AFB smear and gene X-pert and
- Has given informed written consent.

Exclusion criteria:

- Patients who have contraindications to FOB (IHD, arrhythmia, respiratory failure)
- Patients with extrapulmonary tuberculosis (pleural effusion, accessible lymph nodes)
- Patients not willing to give informed written consent
- Patients with previous history of lung malignancy

Total 56 patients were enrolled as study population. Informed written consent was obtained from all participants. All patients were subjected to full medical history including age, sex, occupation, family history, smoking status and meticulous physical examinations. All subjects did routine laboratory investigations which include chest x-ray, complete blood count (CBC), Erythrocyte sedimentation rate (ESR), serum creatinine, urine R/E, ECG, sputum for AFB and gene Xpert. Specific investigations included CT scan of chest, bronchoscopy with mycobacterial culture and gene X-pert on bronchoalveolar lavage. All the data

obtained were documented in a preformed data questionnaire and analyzed by using the Statistical Packages for Social Science (SPSS-23).

Results

In this study, 64 patients were included initially; 6 patients were unfit for FOB, 2 patients didn't give consent and there was no drop out from the study. So, final enrolled patients were 56 cases. The baseline demographic, clinical features are shown in table 4. Among the 56 cases, Xpert MTB/RIF was detected 37.5% cases; AFB culture was positive 28.57% cases.

Table I

Demographic and clinical characteristics of patients with sputum smear negative PTB (n=56)

Characteristics	n (%)
Age (Years) Mean $\pm$ SD	42.8 $\pm$ 16.4
Sex:	
Male	32(57.14%)
Female	24(42.9%)
Symptoms:	
Cough	56(100%)
Sputum expectoration	20(35.0%)
Haemoptysis	8(14.0%)
Chest pain	5(8.9%)
Weight loss	30(53.58%)
Anorexia	22(39.28%)
Co-morbidities:	
DM	6(10.7%)
CKD	1(1.79%)
COPD	12(21.43%)
HTN	3(5.36%)

Table I shows mean age of the patients was 42.8 $\pm$ 16.4 years. According to gender, males (57.14%)

were predominant than females (42.9%). Common clinical findings were cough (100.0%), anorexia (39.28%), weight loss (53.58%) and sputum expectoration (35%). Among the co-morbidities, DM (10.7%), COPD (21.43%), CKD (1.79%) patients. Table II shows among the study subjects 39.28% were smoker and 60.71% were non smoker.

Table II

Distribution of the study patients by smoking status (n=56)

Smoking status	Frequency	Percentage (%)
Smoker	22	39.28
Non smoker	34	60.71
Total	56	100.0

Table III

Distribution of the study patients by chest X-ray findings (n=56)

Chest examination	Frequency	Percentage (%)
Bilateral patchy opacity	18	32.14
Apical opacity	15	26.79
Cavitary lesion	12	21.42
Mediastinal lymphadenopathy	5	8.92
Thick wall cavity	3	5.35
Nodule	2	3.57
Other opacities	1	12.5

Table III shows bilateral patchy opacity was present in 32.14% patients, apical opacity in 26.79 patients, cavitary lesion in 21.42% patients, mediastinal lymphadenopathy in 8.92% patients, thick walled cavity in 5.35% patients, nodule in 3.57% patients and other opacities in 12.5% patients on CXR. Table IV shows in smear negative patients total AFB culture positive in BAL fluid was 62.5%.

Table V shows, using the AFB culture as the gold standard, Xpert MTB/RIF in BAL fluid in patients

Table IV

Characteristics of Xpert MTB/RIF and AFB culture in BAL fluid

Gene Xpert	AFB Culture		Total	p value
	Disease positive	Disease negative		
Positive	13(23.21%)	8 (14.28%)	21 (37.5%)	<0.001
Negative	3 (10.71%)	32 (57.14%)	35 (62.5%)	
Total	16 (28.57%)	40 (71.42%)	56 (100%)	

Table-V

Performance values of gene Xpert MTB/RIF on BAL fluid comparing with AFB culture in patients with sputum smear negative PTB.

	Value (%)	(95% CI)
Sensitivity	81.25	(64.6-90.7)
Specificity	80.0	(74.8-86.7)
Positive predictive Value (PPV)	61.0	(53.8-75.6)
Negative predictive value (NPV)	91.43	(82.3-95.3)

with sputum smear and Xpert negative PTB had sensitivity 81.25% (64.6-90.7%), specificity of 80.0%(74.8-86.7%) , positive predictive Value (PPV) 61.0% (53.8-75.6%), negative predictive value (NPV) 91.42% (82.3-95.3%).

Discussion:

Tuberculosis is considered one of the deadliest diseases worldwide. For breaking the chain of the transmission early diagnosis is so important. Fiberoptic bronchoscopy with BAL fluid study plays a significant role in the diagnosis of patients who are suspected to have PTB clinically and radiologically but sputum smear and gene Xpert is negative. FOB and gene Xpert is increasingly being employed for diagnosis of tuberculosis. In this study design 95 smear negative clinically and radiologically suspected tuberculosis patients were calculated and expected to be included but due to worldwide pandemic of COVID-19 bronchoscopy was not possible to continue as it is an aerosol generating procedure and 56 smear negative patients were included.

Our study shows that pulmonary tuberculosis is equally prevalent both in rural and urban areas educated and poorly educated people. Cough is the most frequent symptom followed by weight loss, anorexia, sputum expectoration and haemoptysis were also observed.

Here, we performed fiber optic bronchoscopy successfully over study subjects after meticulous screening. None of them had any major complications during and after the procedure like cardiac arrhythmia, myocardial infarction and major oxygen desaturation. Minor complications includes transient and moderate episodes of desaturation, transient laryngospasm and mild epistaxis for which no active management were required other than supplemental oxygen therapy.

In our study, using mycobacterial culture as the reference standard, gene Xpert MTB/RIF on BAL fluid showed a good sensitivity comparing to the previous studies. Due to the ability to detect nucleic acid of bacilli, gene Xpert was more sensitive than culture for a diagnosis of PTB and diagnosed additional cases compared to culture alone.

Here, in this study we got some cases we got few cases who were gene negative on Xpert MTB/RIF assay but revealed growth on mycobacterial culture. A possible explanation for this discrepancy could be the presence of PCR inhibitors or absence of sufficient nucleic acid materials in those specimens. Another reason could be that BAL fluid samples in this study were contaminated with little blood, which could have affected the result using Xpert MTB/RIF assay. In support of this speculation, the sensitivity of Xpert MTB/RIF on blood stained sputum was lower because blood is a known inhibitor of DNA amplification⁴.

Eight cases were identified to be Xpert MTB/RIF positive but mycobacterial culture negative, similar situation was also observed in many studies^{1,6}. One explanation for this result between Xpert MTB/RIF and mycobacterial culture may be the nature of the PCR test. The Xpert/MTB assay amplifies any DNA whether it originates from live or dead bacilli. So it cannot be assumed that a positive result equates active disease. Furthermore, in our clinical settings few of this group of patients received non TB antibiotics when symptom duration was less than two weeks. Beta-lactams are reported to have early antitubercular activity comparable to other conventional ATT drugs other than isoniazide⁷.

In this study while correlating radiological lesion and positive bacteriology it was observed that patients with bilateral lesion had more positive bacteriology as compared to unilateral lesion,

whereas more positive bacteriology cases were observed among minimal and moderately advanced, non-cavitary lesion carrying patients rather than the ones carrying far advanced and cavitary lesions. This observation can be explained by the fact that the patients with far advanced, cavitary lesions are more probable of having taken anti-tubercular therapy..

In our study we did not evaluate the patients for other alternative diagnosis. The BAL was not examined for non tuberculous mycobacteria (NTM) or malignant cells. HIV is not prevalent in Bangladesh. So it was not possible to compare the diagnostic yield in HIV positive against the negative patients. The cost effectiveness of gene xpert on BAL fluid on culture was not evaluated too. Our study had few limitations. Fiberoptic bronchoscopy is a safe interventional procedure. But still is not free of social stigmata and lack of awareness as it is not widely available in Bangladesh and patients are not familiar with this procedure for screening purpose. We could not manage few patients to give informed written consent and a bulk of patients refused to undergo bronchoscopy for being an interventional procedure.

Conclusion

Xpert MTB/RIF on bronchoalveolar lavage (BAL) is a useful tool for bacteriological diagnosis of pulmonary tuberculosis in sputum smear and gene Xpert negative patients. It has good sensitivity and specificity for diagnosis of sputum smear and gene xpert negative pulmonary tuberculosis patients. We can use Xpert MTB/RIF of bronchoalveolar lavage (BAL) fluid to confirm SSNPTB for early diagnosis and management.

References

1. Theron G, Peter J, Meldau R, Khalfey H, Gina P, Matinyena B, Lenders L, Calligaro G, Allwood B, Symons G, Govender U. Accuracy and impact of Xpert MTB/RIF for the diagnosis of smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid. *Thorax*. 2013 Nov 1;68(11):1043-51.
2. Bashir YU, Nahvi N, Khan S, Jahan T. Diagnostic utility of bronchoalveolar lavage Xpert MTB/RIF assay in suspected cases of pulmonary tuberculosis. *Int J Contemp Med Res*. 2019;6(6):F8-11.
3. Saglam L, Akgun M, Aktas E. Usefulness of induced sputum and fiberoptic bronchoscopy specimens in the diagnosis of pulmonary tuberculosis. *Journal of international medical research*. 2005 Mar;33(2):260-5.
4. Lee HY, Seong MW, Park SS, Hwang SS, Lee J, Park YS, Lee CH, Lee SM, Yoo CG, Kim YW, Han SK. Diagnostic accuracy of Xpert® MTB/RIF on bronchoscopy specimens in patients with suspected pulmonary tuberculosis. *The International journal of tuberculosis and lung disease*. 2013 Jul 1;17(7):917-21.
5. Meyer AJ, Atuheire C, Worodria W, Kizito S, Katamba A, Sanyu I, Andama A, Ayakaka I, Cattamanchi A, Bwanga F, Huang L. Sputum quality and diagnostic performance of GeneXpert MTB/RIF among smear-negative adults with presumed tuberculosis in Uganda. *PloS one*. 2017 Jul 7;12(7):e0180572.
6. Walters E, Goussard P, Bosch C, Hesselning AC, Gie RP. GeneXpert MTB/RIF on bronchoalveolar lavage samples in children with suspected complicated intrathoracic tuberculosis: a pilot study. *Pediatric pulmonology*. 2014 Nov;49(11):1133-7.
7. Pagliotto AD, Caleffi-Ferracioli KR, Lopes MA, Baldin VP, Leite CQ, Pavan FR, de Lima Scodro RB, Siqueira VL, Cardoso RF. Anti-Mycobacterium tuberculosis activity of antituberculosis drugs and amoxicillin/clavulanate combination. *Journal of microbiology, immunology and infection*. 2016 Dec 1;49(6):980-3.

ORIGINAL ARTICLE

A Comparative Study between Vibratory PEP Device (Acapella) with ‘Usual Airway Clearance’ to see the Outcome during Acute Exacerbation of Bronchiectasis

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Abstract

Background: People with bronchiectasis suffer from chronic cough and sputum production. Repeated acute exacerbation may result in increased incidence of hospitalization and decline in health related quality of life. Physiotherapy involvement in the management of bronchiectasis is supported by international guidelines which states that individuals with a chronic productive cough or difficult clearing sputum should be taught on airway clearance technique (ACT). So, during an acute exacerbation of bronchiectasis, intensive ACTs and follow up are required to facilitate expectoration of sputum from lungs. But which ACTs such as “vibratory pep device (Acapella)” or ACBT is more effective in acute exacerbation of bronchiectasis need to be determined.

Objective: To compare the efficacy of vibratory pep device (Acapella) in acute exacerbation of bronchiectasis to ‘usual airway clearance’ technique.

Materials and Methods: This cross-sectional study was carried out at the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka from January 2022 to December 2022. Total 60 patients of bronchiectasis were selected and they were allocated to one of the two groups according to the inclusion and exclusion criteria. Detailed physical examination and relevant investigations were done.

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Submission on: 12 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

Group 1 (n=30) was required to perform airway clearance twice daily with vibratory PEP device (Acapella). Group 2(n=30) performed ACBT. All patients were provided with a patient's diary and 28 sputum containers; two for each day. Amount of sputum production was measured in all patients during and after the acapella and usual airway clearance technique (ACBT). Time consumption of the procedure, perception of breathlessness, cough, chest pain, exercise tolerance, hemoptysis, comfort of the procedure, pts well-being was recorded during 14 days of study period. All the information were recorded in a tabulated data sheet and all data were analyzed statistically.

Results: The mean duration of time consumption was found 27.1 ± 2.2 minutes in Acapella group and 19.9 ± 2.3 minutes in ACBT group. The difference was statistically significant between two groups ($p < 0.05$). At 2 weeks the mean sputum production was found 5.9 ± 4.9 in Acapella group and 9.9 ± 3.6 in ACBT group. Average mean sputum production was more in Acapella group that was 23.5 ± 3.7 and 18.3 ± 2.1 in acapella group and ACBT group respectively which was found statistically significant ($p < 0.05$). Comparing time consumption was observed more among the acapella user rather than ACBT (27.1 ± 2.2 to 19.9 ± 2.3 accordingly) and it was statistically significant ($p < 0.05$). Exercise tolerance was improved to acapella users (291.1 ± 28.7) compared to ACBT users (250.0 ± 25.9), and it was found significant ($p < 0.05$). Perception of breathlessness, cough, exercise tolerance, fatigue, appetite comfort of the device was improved equally among both the study group.

Conclusion: Sputum production was more in the group using Vibratory Pep Device (Acapella), most of the patient found the device user friendly, they spent more time with the device for airway clearance and found adhered with the therapy more comfortably. So, Vibratory Pep Device (Acapella) offers an user friendly alternative to "usual airway clearance (ACBT)".

Keywords: ACT (airway clearance technique), ACBT (active cycle of breathing technique), ABG (arterial blood gas), PEP (positive expiratory pressure), AE COPD, (acute exacerbation of COPD), Bpm, COPD (chronic obstructive pulmonary disease), CT (computed tomography),

[Chest Heart J. 2024; 48(2) : 74-82]

Introduction

Bronchiectasis is a chronic lung diseases results in repeated respiratory infections, productive cough, shortness of breath and decreased exercise tolerance^{1,2}. Management includes medication and physiotherapy³⁻⁵. Aetiology includes infectious and acquired causes, including measles,⁶ pneumonia, tuberculosis, immune system problems, cystic fibrosis.⁷⁻⁹ The secretions in bronchiectasis enhances the amount of bacteria in the lungs, resulting in airway blockage and further breakdown of the airways.⁹ It is classified as an obstructive lung disease.¹⁰ Cultures of the mucus produced may be useful to determine treatment in those who have acute worsening and at least once a year.¹¹

Acute exacerbation of bronchiectasis usually occurs due to infection. In these cases, antibiotics are recommended¹². Bronchodilators and inhaled steroids may be used but there are no studies to determine effectiveness.¹⁴

Bronchiectasis affects between 1 per 1000 and 1 per 250,000 adults.²⁰ Women and elder pts are commonly affected.⁹ Individuals with a chronic productive cough or difficulty in clearing sputum is benefited by airway clearance technique (ACT)^{4,6,19,20} and during an acute exacerbation intensive ACTs are required⁴. Acapella (vibratory PEP device) facilitates independent airway clearance.

The guidelines recommends that patients with bronchiectasis should be taught and should practise, individualised airway clearance techniques and that this is best delivered by a respiratory physiotherapist. The grade of relevant recommendations ranges from weak (ERS, BTS) to strong (SEPAR, TSANZ)²²⁻²⁴. Overall, airway clearance techniques show a short-term improvement in quality of life, cough related measures and sputum volume expectoration¹³. The BTS guideline recommends the active cycle of breathing techniques (ACBT) or oscillating positive expiratory pressure²⁶. Active cycle of breathing technique is composed of breathing

control, thoracic expansion exercise and forced expiratory technique²⁷. The active cycles of breathing technique include breathing control, thoracic expansion exercises and forced expiration in a set cycle^{3,24}.

The Acapella® is a device used in bronchiectasis to help people clearing sputum (phlegm) from their lungs. Smiths Medical Portex It combines the benefits of PEP therapy and airway vibrates to mobilize pulmonary secretions. When breathing out through the Acapella®, air flows through a counterweighted plug which will help keeping airways wide open to get air behind sputum to help move it upwards. This cycle should continue for 10-20 minutes or until clearing all of sputum. Materials and Methods

Materials and Methods: This cross-sectional study was carried out at the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka from January 2022 to December 2022. Total 60 patients of bronchiectasis were selected and they were allocated to one of the two groups according to the inclusion and exclusion criteria.

Inclusion criteria:

- Patients of all age group.
- Patients who are diagnosed as acute exacerbation of bronchiectasis.

Exclusion criteria:

- Patients with severe comorbid diseases, eg acute heart failure, acute coronary syndrome, respiratory failure.
- Pts not given written consent.
- Critically ill patients.
- Patients who were smear and Xpert MTB/RIF positive.

Operational definition

Bronchiectasis: is a disease in which there is permanent enlargement of parts of the airways of the lung. It usually presents with chronic cough, sputum production, shortness of breath, coughing up blood, and chest pain.

PEP device(Acapella): device that provides Positive Expiratory Pressure (PEP) Therapy and oscillation for patients who have bronchiactasis.

Airway clearance technique: Different strategies used to eliminate excess secretions from bronhial tree.

Active cycle of breathing technique (ACBT): It combines breathing control followed by expiratory technique with an open glottis combined with periods of breathing control.

Study Procedure

This cross-sectional study was carried out on patients admitted in different medicine wards of Respiratory Medicine, National Institute of Diseases of the chest and Hospital (NIDCH), Mohakhali, Dhaka. A total 60 cases of acute exacerbation of bronchiectasis were recruited in this study who presented with at least 10 ml daily amount of sputum. All the subjects will be further grouped into two (I-II). The groups includes: bronchiectatic pts using acapella (Group-I) n=30, bronchiectatic pts using usual airway clearance technique (Group-II) n=30. Patients were selected by systematic randomised sampling method with single blinded technique. Slip of papers were kept folded with marking of either acapella or ACBT, pts were then offered to pick up folded slip of paper within which either acapella or ACBT written but the pt were unaware of this. Pts were then performed acapella or ACBT according to their selections. Patients selections were done with the help of another clinician to make sampling single blinded. All study population of acute exacerbation of bronchiectasis were given same antibiotics (inj. amikacin) to make the uniformity of initial treatment among both groups. All subjects undergoing the study was given necessary information and informed consent was taken on a predesigned proforma/Data collection sheet. Detailed history was taken from each case and a thorough clinical examination was done, routine laboratory investigations: including complete Blood count (CBC), sputum for culture and sensitivity, sputum for AFB, ECG, Random blood sugar (RBS), liver and renal function tests, and chest X-ray / HRCT scan of chest, spirometry, ABG analysis.

Amount of sputum production was recorded and measured in all pts in both study groups. Time consumption of the device, exercise tolerance, pts feelings of breathlessness and feeling of well-being were recorded in both groups, during and after the Acapella and usual airway clearance technique (ACBT).

Observations and Results

Table-I
Distribution of the study patients by demographic characteristics (n=60)

	Acapella (n=30)		ACBT (n=30)		P value
	n	%	n	%	
Age (years)					
d"30	9	30.0	2	6.7	
31-50	6	20.0	11	36.7	
>50	15	50.0	17	56.7	
Mean±SD	46.2	±14.7	51.4	±14.8	a0.177ns
Range (min-max)	25.0	-65.0	22.0	-66.0	
Sex					
Male	21	70.0	22	73.3	b0.500ns
Female	9	30.0	8	26.7	
Educational status					
Illiterate	18	60.0	14	46.7	
School	8	26.7	12	40.0	b0.522ns
College	4	13.3	4	13.3	
Occupational status					
Employee	7	23.3	7	23.3	
Housewife	9	30.0	8	26.7	
Labourer	14	46.7	12	40.0	b0.360ns
Professional	0	0.0	3	10.0	
Marital status					
Married	30	100.0	30	100.0	-
Unmarried	0	0.0	0	0.0	

ns= not significant

aP value reached from unpaired t-test

bP value reached from chi square test

Table-II
Distribution of the patients according to risk factors (n=60)

Risk factors	Acapella(n=30)		ACBT(n=30)		P value
	n	%	n	%	
Living in overcrowded area	2	6.7	2	6.7	0.694ns
Nutritional status	5	16.7	10	33.3	0.136ns
H/O past pneumonia / Pul. TB	30	100.0	18	60.0	0.001s

s= significant, ns= not significant

P value reached from chi square test

Table-III
Lung function at admission (n=60)

	Acapella(n=30)	ACBT(n=30)	P value
	Mean±SD	Mean±SD	
FVC (%)	40.4±11.6	43.1±10.9	0.369ns
FEV1 (%)	31.5±15.2	33.4±12.6	0.600ns
FEV1/FVC	75.4±16.3	76.4±19.8	0.837ns

ns= not significant

P value reached from unpaired t-test

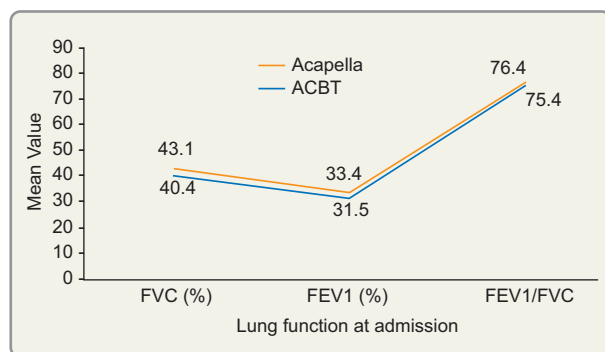


Figure 1: Line diagram showing lung function at admission between two groups

Table-IV

Lung function at 2 weeks (n=60)

	Acapella (n=30) Mean±SD	ACBT (n=30) Mean±SD	P value
FVC (%)	41.2±11.4	43.7±11.1	0.392ns
FEV1 (%)	32.4±14.9	34.1±12.6	0.637ns
FEV1/FVC	75.2±16.3	76.5±19.8	0.782ns

ns= not significant

P value reached from unpaired t-test

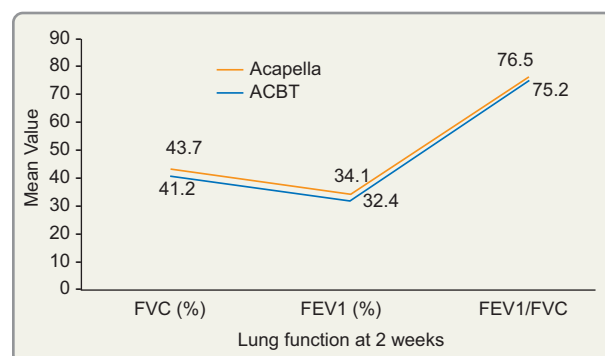


Figure 2: Line diagram showing lung function at 2 weeks between two groups.

Table-V

Amount of sputum production in different follow up (n=60)

	Acapella (n=30) Mean±SD	ACBT (n=30) Mean±SD	P value
At admission	19.8±3.4	18.6±2.2	0.099ns
At 1 week	34.8±4.9	21.3±2.3	0.001s
At 2 weeks	5.9±4.9	9.9±3.6	0.001s
Average	23.5±3.7	18.3±2.1	0.001s

s= significant, ns= not significant

P value reached from unpaired t-test

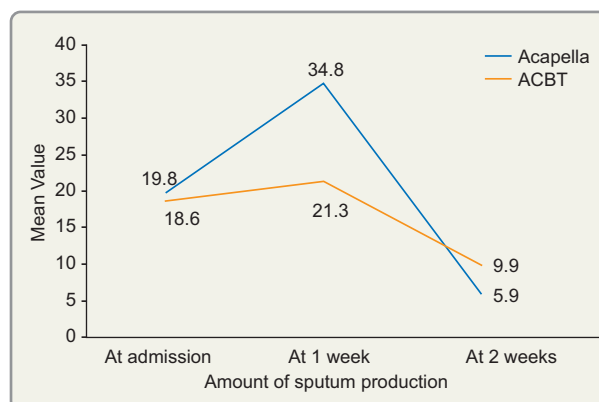


Figure 3: Line diagram showing amount of sputum production in different follow up

Table-VI

Distribution of the study patients according to improvement of sputum production (n=60)

	Acapella (n=30) n	%	ACBT (n=30) n	%	P value
1. Complete improvement (>50% reduction of sputum production at the end of treatment)	24	80.0	17	56.7	
2. Partial improvement (25%- 49%reduction of sputum production at the end oftreatment)	3	10.0	5	16.7	0.138 ns
3. Not improvement (<25%reduction of sputum production at the end of treatment)	3	10.0	8	26.7	

ns= not significant

P value reached from chi square test

Table-VII

Duration of time consumption of the study patients (n=60)

	Acapella (n=30) Mean±SD	ACBT (n=30) Mean±SD	Mean difference (95% CI)	P value
Duration of time consumption (minutes)	27.1±2.2 (0.57 to 6.00)	19.9±2.3		0.001st
Range (min-max)	23.0-32.0	16.0-25.0		

s= significant

P value reached from unpaired t-test

Table-VIII
Distribution of the patients according to comfort (n=60)

Comfort	Acapella(n=30)		ACBT(n=30)		P value
	n	%	n	%	
Perception of breathlessness					
Improved	24	80.0	23	76.7	0.500ns
Unchanged	6	20.0	7	23.3	
Cough					
Improved	24	80.0	25	83.3	0.739ns
Unchanged	6	20.0	5	16.7	
Exercise tolerance					
Improved	18	60.0	16	53.3	0.602ns
Unchanged	12	40.0	14	46.7	
Fatigue					
Improved	27	90.0	28	93.3	0.500ns
Unchanged	3	10.0	2	6.7	
Appetite					
Improved	24	80.0	26	86.7	0.365ns
Unchanged	6	20.0	4	13.3	
Comfort with device					
Comfort	27	90.0	25	83.3	0.353ns
Dislike	3	10.0	5	16.7	
Chest pain					
no	27	90.0	23	76.7	0.149ns
yes	3	10.0	7	23.3	
Hemoptysis					
no	27	90.0	28	93.3	0.500ns
yes	3	10.0	2	6.7	
Pts well-being					
Improved	24	80.0	23	76.7	0.348ns
No comment	6	20.0	5	16.7	
Dislike	0	0.0	2	6.7	

ns= not significant

P value reached from chi square test

Discussion

The aim of management of bronchiectasis involves medication and physiotherapy to improve airway clearance and exercise tolerance and improve health related quality of life. Involved airways (bronchi) become enlarged and thus less able to clear secretions. These secretions increase the amount of bacteria in the lungs, resulting in airway blockage and further breakdown of the airways.

Devices such as Vibratory Pep Device (Acapella) may facilitate independent airway clearance.

Bronchiectasis guidelines recommend airway clearance techniques. Overall, airway clearance

techniques show a short-term improvement in quality of life, cough-related measures and sputum volume expectoration

In this study the mean age was found 46.2±14.7 years in acapella group and 51.4±14.8 years in ACBT group. Male patients were predominant in both groups (70.0% vs 73.3%) between both groups. Illiterate was found 18(60.0%) in acapella group and 14(46.7%) in ACBT group. Most of the patients were labourer in both groups (46.7% vs 40.0%). All patients were married in both groups. No significant difference was regarding age, sex, educational status, occupational status and marital

status between two groups. In a study found mean age of Acapella use belonged to adults (65% cases and in ACBT (49% cases) which are similar to this study.

All patients had cough, sputum production, dyspnoea and fever between two groups. Weight loss was found 14(46.7%) in acapella group and 15(50.0%) in ACBT group. Chest pain was 15(50.0%) and 16(53.3%) in acapella group and ACBT group respectively. The difference was not statistically significant between two groups ($p>0.05$).

In a study found selected all pts with bronchiectasis with acute exacerbation presented with increased cough, changes in sputum (volume, colour and viscosity), breathlessness, hemoptysis and/or constitutional upset (malaise, tiredness). So, patient's selection criteria are similar in this study.

Regarding risk factors, H/O past pneumonia / pulmonary TB was significantly higher in acapella group than ACBT group (100.0% vs 60.0%). However, living in overcrowded area and nutritional status were not statistically significant between two groups ($p>0.05$). A study found most common causes of bronchiectasis are measles, pneumonia, tuberculosis, immune system problem, as well as genetic problems like, cystic fibrosis²⁹. between two groups. A study found chronic lung infections (29.3%), pulmonary TB (17.74%), consolidation (14%), pulmonary sequestration (4%) as a risk factor and aetiology for development of bronchiectasis.³⁰ So, regarding etiology and risk factor our study population carries similar causes of bronchiectasis.

Regarding chest X-ray at admission, it was observed that majority patients had bilateral bronchiectasis in both groups, that was 15(50.0%) in acapella group and 17(56.7%) in ACBT group. Fibrosis with bronchiectasis was found 9(30.0%) in acapella group and 7(23.3%) in ACBT group. The difference was not statistically significant ($p>0.05$) between two groups.

Regarding growth of organism we found growth in 27(90.0%) in acapella group and 26(86.7%) in ACBT group, that was not statistically significant between two groups ($p>0.05$). In acapella group, acinetobacter species (20.0%), candida species (20.0%) and klebsiella (20.0%) were common, however in ACBT group, pseudomonas (20.0%) and

streptococcus (20.0%) were common organism. The difference was not statistically significant ($p>0.05$) between two groups. A study on bacteriological profile found streptococcus (1%), pseudomonas (10%), klebsiella (3%), Moraxella (1%), acinetobacter (1%), and TB (3%)²⁹, which are similar to our study. However, local organism and antibiotic sensitivity pattern may vary in different geographical area. Antibiotic selection was based on local organism, antibiotic sensitivity and resistance pattern, cost effectivity, availability. Meropenem, amikacin, piperacillin-tazobactam, moxifloxacin and co- amoxiclav were mostly used antibiotics.

There was no significant group difference found in between pre and post treatment lung function. FVC, FEV1, FEV1/FVC did not show significant changes between groups at day one and final day at study period. Regarding lung function at admission, the mean FVC was $40.4\pm 11.6\%$ in acapella group and $43.1\pm 10.9\%$ in ACBT group. The mean FEV1 was $31.5\pm 15.2\%$ and $33.4\pm 12.6\%$ in acapella group and ACBT group respectively. The mean FEV1/FVC was 75.4 ± 16.3 in acapella group and 76.4 ± 19.8 in ACBT group. The difference was not statistically significant between two groups ($p>0.05$).

Regarding lung function at 2 weeks, the mean FVC was $41.2\pm 11.4\%$ in acapella group and $43.7\pm 11.1\%$ in ACBT group. The mean FEV1 was $32.4\pm 14.9\%$ and $34.1\pm 12.6\%$ in acapella group and ACBT group respectively. The mean FEV1/FVC was 75.2 ± 16.3 in acapella group and 76.5 ± 19.8 in ACBT group. The difference was not statistically significant between two groups ($p>0.05$).

At 1 week the mean sputum was found 34.8 ± 4.9 in acapella group and 21.3 ± 2.3 in ACBT group. At 2 weeks the mean sputum was found 5.9 ± 4.9 in acapella group and 9.9 ± 3.6 in ACBT group. Average mean sputum was 23.5 ± 3.7 and 18.3 ± 2.1 in acapella group and ACBT group respectively. Which were statistically significant ($p<0.05$) between two groups. The mean daily volume of sputum expectorated was fluctuated over the period of antibiotic therapy, although a greater amount of sputum was expectorated during Acapella use.

Regarding duration of time consumption Acapella use was more observed. Mean difference (95% CI)

of time was 2 min (-1.74 to 5.74). JE Patterson et al in his study 'Acapella[®] versus usual airway clearance during acute exacerbation in bronchiectasis: a randomized crossover trial' found mean duration of Acapella[®] session was greater than usual airway clearance session and approached significance [mean difference 4.02 minutes 95% CI -0.22 to 8.26] p value 0.06³¹ complete improvement was found 24(80.0%) in acapella group and 17(56.8%) in ACBT group. The difference was not statistically significant between two groups (p>0.05).

The mean duration of time consumption was found 27.1±2.2 minutes in acapella group and 19.9±2.3 minutes in ACBT group. The difference was statistically significant between two groups (p<0.05).

At 2 weeks mean exercise capacity was found 291.1±28.7 steps/min in acapella group and 250.0±25.9 steps/min in ACBT group. Which was statistically significant between two groups (p<0.05).

Perception of breathlessness, cough, exercise tolerance, fatigue, appetite comfort of the device was improved equally among both the study group. Which was not statistically significant between two groups.

Conclusion

Sputum production was more in the group using vibratory pep device(Acapella) compared to 'usual airway clearance' technique (ACBT). This device is user friendly, pts spend more time with the devicea for airway clearance and found adhered with the therapy more comfortably. So, vibratory pep device (Acapella) offers user friendly, better alternative to 'usual airway clearance' (ACBT).

References

1. Barker AF. Bronchiectasis. *N Engl J Med* 2002; 346(18): 1383–93.
2. O'Neill K, O'Donnell AE, Bradley JM. Airway clearance, mucoactive therapies and pulmonary rehabilitation in bronchiectasis. *Respirology* 2019; 24(3): 227–37.
3. Chalmers JD, Aliberti S, Blasi F. Management of bronchiectasis in adults. *Eur Respir J* 2015; 45(5): 1446–62.
4. José, R. J.; Brown, J. S. (2014). "Bronchiectasis". *British Journal of Hospital Medicine*. 75 (Suppl 10:C146–51): C146–C151
5. Chang AB, Bell SC, Torzillo PJ, Byrnes CA, Maguire GP, Holland AE, et al. Thoracic Society of Australia and New Zealand guidelines: chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand. *Med J Australia* 2015; 202(1): 21–4.
6. Sydney Morning Herald. 22 April 2010. Archived from the original on 9 August 2022. Retrieved 9 August 2022.
7. José RJ, Brown JS. Bronchiectasis. *British Journal of Hospital Medicine* 2014; 75 (Suppl 10): C146–51.
8. Colledge NR, Walker BR, Ralston SH, editors. *Davidson's principles and practice of medicine*. 21st ed. Edinburgh: Churchill Livingstone/Elsevier. 2010.
9. McShane PJ, Naureckas ET, Tino G, Strek ME. Non-cystic fibrosis bronchiectasis. *American Journal of Respiratory and Critical Care Medicine* 2013; 188(6): 647–56.
10. Brant WE, Helms CA, editors. *Fundamentals of diagnostic radiology*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins. 2006; 518.
11. Michael F Lisa ML, Shaffer BL. *Blueprints pathophysiology II: pulmonary, gastrointestinal, and rheumatology: notes & cases*. 1st ed. Malden, Mass: Blackwell Pub. 2003;
12. British Thoracic Society, *Quality Standards for Clinically Significant Bronchiectasis in Adults*. 2012.
13. Lee AL, Burge AT, Holland AE. Airway clearance techniques for bronchiectasis. *The Cochrane Database of Systematic Reviews* 2015; 11: CD008351.
14. Kapur N, Petsky HL, Bell S, Kolbe J, Chang AB. Inhaled corticosteroids for bronchiectasis. *The Cochrane Database of Systematic Reviews* 2018; 5(5): CD000996.
15. Corless JA, Warburton CJ. Surgery vs non-surgical treatment for bronchiectasis. *The Cochrane Database of Systematic Reviews* 2000; (4): CD002180.
16. Corris PA. Lung transplantation for cystic fibrosis and bronchiectasis. *Seminars in*

- Respiratory and Critical Care Medicine 2013; 34(3): 297–304.
17. Cottin V, Cordier JF, Richeldi L. Orphan Lung Diseases: A Clinical Guide to Rare Lung Disease. Springer 2015; 30.
 18. Robert D, Andrew B, Anna S. Oxford Handbook of Tropical Medicine. 4th ed. Oxford University Press. 2014; 223.
 19. Polverino E, Goeminne PC, McDonnell MJ, Aliberti S, Marshall SE, Loebinger MR, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. *Eur Respir J* 2017; 50.
 20. Pereira MC, Athanazio RA, Dalcin PTR, Figueiredo MRF, Gomes M, Freitas CG, et al. Brazilian consensus on non-cystic fibrosis bronchiectasis. *J Bras Pneumol* 2019; 45(4).
 21. Martinez GMA, Maiz L, Oliveira C, et al. Spanish Guidelines on treatment of bronchiectasis in adults. *Arch Bronconeumol* 2018.
 22. Al-Jahdali H, Alshimemeri A, Mobeireek A, et al. The Saudi Thoracic Society guidelines for diagnosis and management of noncystic fibrosis bronchiectasis. *Ann Thorac Med* 2017.
 23. Webber BA, Pryor JA, editors. *Physiotherapy for respiratory and cardiac problems*. Churchill, Livingstone. 1993.
 24. Nafeez S, Arun G, Maiya KT, Siva KT. Active cycle of breathing technique versus conventional chest physical therapy on airway cleanse in bronchiectasis. *Advances in Physiotherapy* 2009.
 25. Spinou A, Fragkos KC, Lee KK, et al. The validity of health-related quality of life questionnaires in bronchiectasis: a systematic review and meta-analysis. *Thorax* 2016.
 26. Guan WJ, Huang Y, Chen CL, et al. Macrolides, mucoactive drugs and adherence for the management of bronchiectasis. *Eur Respir J* 2018.
 27. Chalmers JD, Aliberti S, Polverino E, et al. The EMBARC European
 28. Visser SK, Bye PTP, Fox GJ, et al. Australian adults with bronchiectasis: The first report from the Australian Bronchiectasis Registry. *Respir Med* 2019.
 29. Haworth CS, Bilton D, Chalmers JD, et al. Inhaled liposomal ciprofloxacin in patients with non-cystic fibrosis bronchiectasis and chronic lung infection with *Pseudomonas aeruginosa* (ORBIT-3 and ORBIT-4): two phase 3, randomized controlled trials. *Lancet Respir Med* 2019; 7: 213–226.30.
 - Régis G, Bopaka Wiam E, Hind J, Hasna J, and Hicham A Bronchiectasis: a bacteriological profile *Pan Afr Med J*. 2015; 22: 378.
 31. Umoh VA, Alasia DD, Akpan EE, Jumbo HE, Ekwere ME, Umoh IO, et al. Psychological distress and health-related quality of life among stable patients with bronchiectasis. *Niger J Clin Pract* 2022; 25(2): 144-152.
 32. Patterson JE, Bradley JM, Hewitt O, Bradbury I, Elborn JS. Airway clearance in bronchiectasis: a randomized crossover trial of active cycle of breathing techniques (ACBT) versus Acapella®. *Respiration* 2005; 72: 239–242.
 33. Nicolini A, Cardini F, Landucci N, Lanata S, Ferrari Bravo M, Barlascini C. Effectiveness of treatment with high frequency chest wall oscillation in patients with bronchiectasis. *BMC Pulmonary Medicine* 2013;13(21):18.

ORIGINAL ARTICLE

COVID-19 Infection, Immunization and Lung Function Parameters in a Community of Bangladesh: A Cross-Sectional Study

Mohammed Atiqur Rahman¹, Shamim Ahmed², Rajashish Chakraborty³, Samprity Islam⁴, Golam Sarwar Liaquat Hossain Bhuiyan⁵, Manal Mizanur Rahman⁶, Susanta Kumar Paul⁷, Kazi Rahila Ferdousi⁸

Abstract

Introduction: COVID-19, caused by SARS-CoV-2, has affected millions worldwide, leading to significant acute and long-term health challenges. Post-COVID syndrome often includes persistent respiratory symptoms and reduced lung function, with limited data from Bangladesh on these sequelae.

Aim: This study aimed to assess socio-demographic, clinical, vaccination status, and lung function parameters in patients following COVID-19 infection and assess the effects of these parameters on post-COVID symptoms.

Methods: A cross-sectional study was conducted from August 2022 to July 2023 on 1,000 RT-PCR-confirmed COVID-19 recovered patients aged ≥ 18 years in Gazipur, Bangladesh. Data on demographics, comorbidities, vaccination status, and clinical symptoms were collected through structured interviews. Lung function was assessed using spirometry (FEV1, FVC, FEV1/FVC), and the six-minute walk test (6MWD). Data analysis was performed using SPSS with descriptive and inferential statistics.

Results: The cohort was predominantly male (56.1%) and married (77.1%), with most patients aged >50 years. Underweight prevalence was high (38.1%), and 30.6% were current smokers. Hypertension (17.7%) and diabetes (10.2%) were the most common comorbidities. Common symptoms included fever (92.7%), cough (88.3%), breathlessness (53.6%), and fatigue (49.7%). Only 22.9% were fully vaccinated. Spirometry showed reduced lung volumes (mean FEV1: 1.78 L, FVC: 2.49 L) with a mean FEV1/FVC ratio of 77.26%. The 6MWD averaged 325.46 m, indicating impaired exercise capacity.

Conclusion: Fever, cough, breathlessness, and fatigue were the most common symptoms of COVID-19 infection. Mean spirometric parameters and six-minute walk distance were reduced in patients with COVID-19 infection even 4 weeks after recovery. The majority of respondents (72.8%) had received at least one dose of vaccination against COVID-19.

Keywords: COVID-19 infection, vaccination, lung function parameters

[Chest Heart J. 2024; 48(2) : 83-89]

Introduction

Coronavirus disease (COVID-19), first reported in December 2019 in Wuhan, China, is caused by

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) declared COVID-19 a global pandemic on

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Submission on: 20 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

March 11, 2020, and as of September 12, 2022, over 586 million laboratory-confirmed cases and 6.42 million deaths had been reported worldwide.¹

The pandemic has overwhelmed healthcare systems globally and caused substantial socioeconomic disruption due to prolonged lockdowns. Despite advances in clinical research that have improved understanding and management of SARS-CoV-2 infection, ongoing transmission remains a major challenge, due to the emergence of new variants driving successive waves of infection. In Bangladesh, over 2.01 million cases and approximately 29,307 deaths have been recorded.²

The most common initial symptoms of COVID-19 include fever, dry cough, tachypnea, and dyspnea.³ Non-respiratory symptoms reported include confusion, chest pain, vomiting, nausea, anosmia, dyspepsia, skin rash, discoloration of fingers or toes, and viral conjunctivitis.^{4,5}

COVID-19 vaccines have been shown to reduce SARS-CoV-2 infection, transmission, hospitalization, and mortality. In Bangladesh, vaccination began on 27 January 2021, with mass rollout starting on 7 February 2021. The Directorate General of Drug Administration (DGDA) approved seven vaccines (Pfizer–BioNTech, Moderna, Oxford–AstraZeneca, Sinopharm, Janssen, Sputnik V, and Sinovac). To date, approximately 140.5 million doses have been administered, with 85,287,956 individuals receiving at least one dose and 56,191,252 fully vaccinated.⁶

Aims and Objective

This study aims to assess symptoms of COVID-19 infection, lung function parameters, and COVID-19 vaccination status in the community. Materials and Method

Study Design

This cross-sectional study was conducted in Kaliakair, Gazipur, Dhaka, Bangladesh, over a period of one year from August 2022 to July 2023, following approval from the Institutional Review Board (IRB).

Inclusion Criteria

The study recruited participants aged above 18 years, with a confirmed RT-PCR positive diagnosis

for COVID-19, who had recovered and passed at least four weeks after the infection.

Exclusion Criteria

Patients with history of dementia and active lung infections were excluded. Participants who had not fully recovered, were less than four weeks post-COVID infection or were unable to perform spirometry or six-minute walk testing were also not included.

Procedure and data collection

Participants who met the selection criteria were enrolled in the study after written informed consent. Sociodemographic information such as age, gender, marital status, and educational background was recorded. Data on COVID-19 diagnosis, infection severity, and type of care received (home care, hospitalization, or ICU admission) were collected. Information on pre-existing comorbidities, including diabetes, hypertension, asthma, chronic obstructive pulmonary disease (COPD), coronary artery disease, and smoking history, was also obtained. Participants' vaccination status (none, one dose, or two doses) was documented. Lung function parameters (FEV1, FVC, FEV1/FVC ratio) were determined using a handheld spirometer following standard protocols. Six-minute walk distance was also measured to assess exercise capacity and functional status. Participant confidentiality was maintained, and personal information was securely stored. No financial incentives were offered to participants.

Results

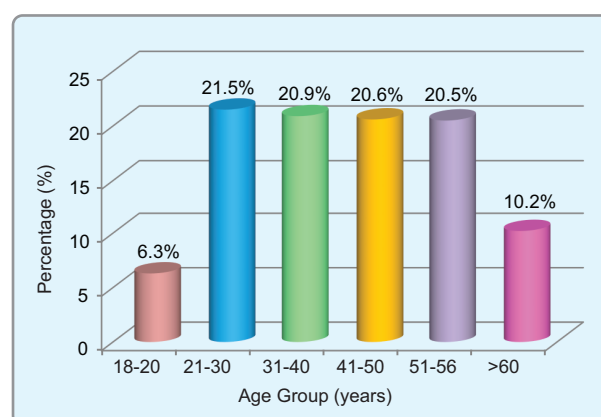


Figure 1: Age Distribution of Participants (n=1000)

Table-I
Socio-demographic characteristics of the Participants(n=1000)

Characteristics	
Age, years (mean +SD)	41.06(+ 13.97)
Sex, n (%)	
Male	561(56.1%)
Female	439 (43.9%)
Marital status	
Married	771(77.10%)
Unmarried	229(22.90%)
Educational status, n (%)	
No formal education	247(24.70%)
Primary school	185(18.50%)
Below Secondary school	146(14.60%)
Secondary school completed	209(20.90%)
Higher Secondary school completed	114(11.40%)
Graduate or Above	99(9.9%)

Table 2 presents the socio-demographic characteristics of the study participants. The mean age was 41.06 ± 13.97 years, with a male predominance (56.1%) compared to females (43.9%). The majority of participants (77.1%) were married.

Regarding educational attainment, nearly one-fourth (24.7%) had no formal education, while 18.5% had completed only primary education. A smaller proportion (14.6%) had education below the Secondary School Certificate (SSC) level. Notably, 20.9% had completed SSC, indicating that a substantial portion had at least basic secondary education. The proportion decreased further among higher educational levels, with 11.4% completing Higher Secondary Certificate (HSC) and only 9.9% attaining graduation or higher degrees

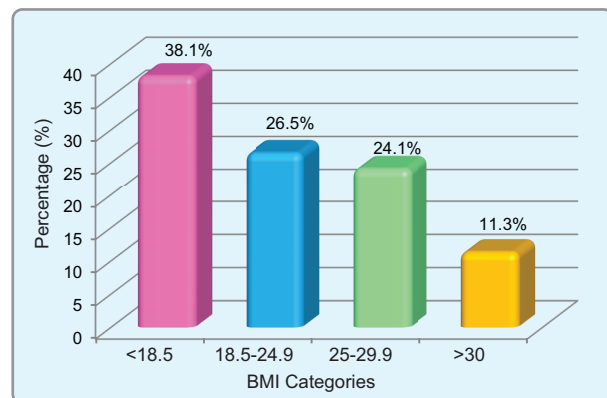


Figure 2: Body Mass Index (BMI) of the Patients (n=1000)

Figure 2 illustrates the Body Mass Index (BMI) distribution among 1,000 patients. The mean Body Mass Index (BMI) of the participants was 24.03 ± 5.58 kg/m². Overall, 64.6% of participants had a BMI below 25, comprising 38.1% underweight and 26.5% normal weight individuals. In contrast, 35.4% were classified as overweight (24.1%) or obese (11.3%).

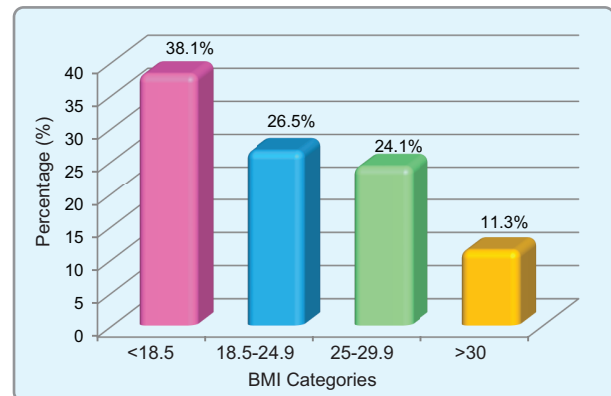


Figure 3: Smoking Habit of the Study Subjects (n=1000)

Figure 3 shows that one-third of participants (30.6%) were current smokers. Of the remaining 694 participants (69.4%), 23 (2.3%) were ex-smokers and 671 (67.1%) were never-smokers.

Table-II
Co-Morbidities of the Patients (n=1000)

Co-Morbidities	No.	Percentage
Hypertension	177	17.70
DM	102	10.20
Asthma	62	6.20
COPD	107	10.70
CVD	11	1.10
Coronary artery disease	23	2.30
CKD	21	2.10
Cancer	6	0.60

Table 2 presents data on the prevalence of co-morbidities among 1000 patients. Hypertension (17.70%) is the most common co-morbidity, followed by Diabetes Mellitus (DM) (10.20%). Asthma (6.20%) and Chronic Obstructive Pulmonary Disease (COPD) (10.70%) are present in a notable proportion of patients. Cerebrovascular Disease (CVD) (1.10%), coronary artery disease (2.30%), and chronic kidney disease (CKD) (2.10%) are less frequent. Only 6 patients (0.60%) have been diagnosed with cancer.

Table-III
Symptoms during COVID-19 infection

Respiratory symptoms	Nos.	Percentage
Fever	927	92.70
Cough	883	88.30
Breathlessness	536	53.60
Fatigue	497	49.7
Anosmia	344	34.40
Chest pain	251	25.1
Phlegm	193	19.30
Wheezing	134	13.40

Table 3 provides the distribution of COVID-19 symptoms among 1000 participants, including the number of participants and the percentage experiencing each symptom. Fever (92.70%) and cough (88.30%) are the most common symptoms. Breathlessness (53.60%) and fatigue (49.70%) were prevalent in almost half of the patients. Anosmia (loss of smell) is reported by 34.40% of participants, which is a well-documented symptom of COVID-19. Less common symptoms like wheezing (13.40%) and chest pain (25.10%) may indicate complications or comorbidities in some patients.

Table-IV
Site of Covid-19 care participants (n=1000)

COVID Care Site	No.	Percentage
Home	609	60.90
Inpatient	379	37.90
Intensive care unit	12	1.20
Total	1000	100

Table 4 presents data on where COVID-19 patients (N=1000) received care during their illness. The distribution of care sites provides insights into the severity of cases and healthcare system utilization. 379 patients (37.90%) were admitted as inpatients, meaning more than one-third of the cases required hospital care. 609 patients (60.90%) were treated at home, suggesting they had mild symptoms or stable conditions that did not require hospitalization. 12 patients (1.20%) required ICU admission, indicating they had severe or life-threatening complications. The ICU percentage is relatively low, which is expected since only the most severe cases (e.g., respiratory failure, multi-organ complications) require intensive care.

Table-V
COVID-19 vaccination dose (N1000)

No. of Doses	No.	Percentage
Single	499	49.90
Double	229	22.90
None	272	27.20
Total	1000	100

Table 5 provides the distribution of COVID-19 vaccination doses among 1000 participants. The high proportion of single-dose recipients (49.90%) suggests that many participants are in the process of completing their vaccination schedule. The unvaccinated group (27.20%) represents a significant portion of the population, which could reflect vaccine hesitancy, lack of access, or other barriers to vaccination. The fully vaccinated group (22.90%) is relatively small, indicating that a majority of participants may not yet have completed their vaccination schedule.

Table-VI
Pulmonary function & Exercise capacity among the study respondents (N=1000)

Spirometry parameters	Mean±SD
FVC (L)	2.49 (±0.76)
FEV1 (L)	1.78 (±0.69)
FEV1/FVC (%)	77.26 (±19.36)
Exercise Capacity Test	Mean±SD
6MWD, m	325.46(±84.20)

Table 6 provides spirometry and 6-minute walk test (6MWT) results for 1000 study respondents. The FEV1/FVC ratio is a key measure of airflow obstruction. A normal value is typically >70%. In our study, the mean value of FEV1/FVC ratio is 77.26% suggested that, on average, the study participants have normal airflow or restrictive airflow. However, the large standard deviation (±19.36) indicates significant variability. The 6MWD measures the distance a person can walk in 6 minutes, reflecting functional exercise capacity. The mean distance was 325.46 meters.

Discussion

The demographic data collected in this study provides critical context for understanding the overall trends in post-COVID-19 recovery. Our sample was composed predominantly of individuals between the

ages of 21 and 50. This age distribution may reflect the fact that this group experiences both moderate initial illness and a higher rate of comorbidities, which predispose them to prolonged symptoms after the acute phase.⁷ In comparison, Chen et al. and Brooks et al. reported a higher prevalence of post-COVID symptoms in older populations, particularly those aged 60 and above, who are known to experience greater vulnerability to the virus.^{4,8} However, our study found that the >60 age group accounted for only 10.20% of the sample, which could be due to higher mortality rates and greater challenges in accessing healthcare among the elderly in Bangladesh. This observation is consistent with global studies⁹, which reported that the elderly are less likely to recover from severe COVID-19 and, therefore, are underrepresented in long-term follow-up studies. This study also found a slight male predominance in the patient population (56.10%), which is similar to other studies conducted in South Asia. Research by Guan et al. has shown that males tend to have higher rates of severe COVID-19 outcomes due to behavioral risk factors, such as higher smoking rates and more prevalent comorbidities like hypertension and diabetes.³ This male predominance in long COVID cases could also be explained by differences in immune responses between genders, with females typically having a more robust immune response to viral infections but also a higher risk of developing autoimmune conditions.¹⁰

Smoking and Lung Function

This study was the high proportion of current smokers (30.60%) among participants, which significantly influences lung function. Smoking is a known risk factor for chronic respiratory diseases, and this is especially relevant in the context of COVID-19 recovery. Studies have shown that individuals with a history of smoking are more likely to experience severe complications from COVID-19, including acute respiratory distress syndrome (ARDS) and long-term pulmonary dysfunction.¹¹ The spirometry data collected in our study revealed that the mean FEV1 was 1.78 L, and FVC was 2.49 L, both of which are lower than the normal expected values for healthy adults. This suggests that the patients, particularly smokers, are at a higher risk for persistent pulmonary dysfunction. The finding is in line with Longue et

al.¹², which documented significant reductions in FEV1 and FVC among smokers recovering from COVID-19. The FEV1/FVC ratio (77.26%) in our study also falls within the range of obstructive lung disease, a finding that echoes the results from Mo et al.¹³, where smokers recovering from COVID-19 exhibited similar spirometry results. These findings underscore the need for targeted rehabilitation strategies for smokers recovering from COVID-19. These should include not only physical rehabilitation but also smoking cessation programs, as smoking exacerbates the risk of both short-term and long-term pulmonary complications. Additionally, healthcare providers should closely monitor lung function in smokers recovering from COVID-19 to prevent further deterioration of lung capacity.

Co-Morbidities and Their Impact on Lung Function

This study also revealed that a significant proportion of patients had pre-existing comorbidities, with hypertension (17.70%) and diabetes (10.20%) being the most common. This is consistent with previous studies¹⁴, who found that individuals with underlying conditions, particularly cardiovascular diseases and diabetes, are at a heightened risk for severe COVID-19 outcomes and long-term respiratory symptoms. Hypertension and diabetes have long been recognized as risk factors for poor prognosis in viral respiratory infections, and this study supports the hypothesis that these conditions contribute to persistent lung dysfunction post-COVID.¹⁵ Study by Talman S et al.¹⁶ on post-COVID pulmonary outcomes found that patients with pre-existing lung diseases, such as asthma and COPD, are more likely to experience sustained pulmonary abnormalities. In our study, 10.70% of participants had COPD, which is a known risk factor for reduced lung function and respiratory complications. These findings highlight the importance of a multidisciplinary approach to post-COVID care, where patients with comorbidities should receive specialized attention to manage their underlying conditions and prevent further lung damage.

Vaccination and Post-COVID Lung Function

Vaccination status was another critical variable in our study. We found that 27.20% of participants

were unvaccinated, 49.90% had received one dose, and 22.90% were fully vaccinated. This distribution reflects the challenges in vaccine accessibility and hesitancy observed in many countries, particularly in low- and middle-income regions such as Bangladesh. These findings are consistent with the study by Nalbandian et al.^{14,17} which also observed that vaccination, while beneficial in preventing severe disease and death, does not fully prevent long-term respiratory consequences in some patients. However, the reduction in severe disease severity and hospitalization observed in vaccinated individuals suggests that vaccination plays a crucial role in reducing the overall burden of post-COVID respiratory issues. This aligns with the findings of Zerin et al.^{5,6}, which emphasized the importance of post-COVID rehabilitation programs, even for vaccinated individuals, to help restore lung function and improve quality of life.

Comparison with Other Studies

These findings are consistent with several studies conducted globally on post-COVID pulmonary outcomes. For instance, Ziauddeen et al.¹⁸ found that even mild cases of COVID-19 can lead to significant long-term pulmonary sequelae, including reductions in FEV1 and FVC. Similarly, Tenforde et al.¹⁹ reported that patients with pre-existing respiratory conditions, such as COPD and asthma, had worse outcomes following COVID-19 infection. Additionally, the study by Wisnivesky et al.²⁰ on post-COVID rehabilitation emphasized the importance of comprehensive care for individuals recovering from COVID-19, especially those with significant comorbidities. Our findings reinforce this by highlighting the need for targeted pulmonary rehabilitation programs for post-COVID patients, particularly those with chronic diseases like hypertension, diabetes, and COPD.

Conclusion:

Fever followed by respiratory symptoms was the most common symptom of COVID-19 infection. Lung function parameters were impaired even four weeks after infection. The majority of respondents (72.8%) had received at least one dose of COVID-19 vaccination.

Recommendations

1. Regular monitoring of symptoms and lung function of patients after COVID-19 infection.

2. Implement targeted pulmonary rehabilitation programs for individuals recovering from COVID-19, especially those with pre-existing conditions.
3. Enhance vaccination coverage and awareness to reduce the severity of COVID-19 and its long-term effects.

Acknowledgement

We would like to express our sincere gratitude to the participants for their time and willingness to participate in this study. We extend our thanks to the medical staff and health officers in Kaliakair, Gazipur, for their support during data collection. Special thanks to the institutional review board for their approval and guidance, and to all who contributed their knowledge and expertise, helping us to successfully complete this research.

Funding: Bangabandhu Sheikh Mujib Medical University

Conflict of interest: None declared

References

1. Biancolella M, Colona VL, Mehrian-Shai R, Watt JL, Luzzatto L, Novelli G, Reichardt JK. COVID-19 2022 update: transition of the pandemic to the endemic phase. *Human genomics*. 2022 Jun 1;16(1):19.
2. Lytton SD, Ghosh AK. SARS-CoV-2 variants and COVID-19 in Bangladesh—Lessons learned. *Viruses*. 2024 Jul 4;16(7):1077.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*. 2020 Apr 30;382(18):1708-20.
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia JA. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The lancet*. 2020 Feb 15;395(10223):507-13.
5. Yang X, Yu Y, Xu J, Shu H, Xia JA, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective,

- observational study. *The lancet respiratory medicine*. 2020 May 1;8(5):475-81.
6. Zerín T, Haque S, Jahan S, Farjana NE, Begum MA, Islam S, Akter S. Strategic Plan and Limitations in Tackling Delta Variant Outbreak in Bangladesh.
 7. Ayoubkhani D, Bermingham C, Pouwels KB, Glickman M, Nafilyan V, Zaccardi F, Khunti K, Alwan NA, Walker AS. Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study. *bmj*. 2022 May 18;377.
 8. Brooks D, Solway S. ATS statement on six-minute walk test. *American journal of respiratory and critical care medicine*. 2003 May 1;167(9):1287-.
 9. Culver BH, Graham BL, Coates AL, Wanger J, Berry CE, Clarke PK, Hallstrand TS, Hankinson JL, Kaminsky DA, MacIntyre NR, McCormack MC. Recommendations for a standardized pulmonary function report. An official American Thoracic Society technical statement. *American journal of respiratory and critical care medicine*. 2017 Dec 1;196(11):1463-72.
 10. Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L, Zhou X, Liu X, Huang X, Yuan S, Chen C. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. *Respiratory research*. 2020 Jun 29;21(1):163.
 11. Hui DS, Ei Azhar E, Madani TA, Ntoumi F, Kock RA, Dar O, Ippolito G, Mchugh TD, Memish ZA, Drosten C, Zumla A. The continuing epidemic threat of novel coronaviruses to global health-the latest novel coronavirus outbreak in Wuhan, China. *International Journal of Infectious Diseases*.;91.
 12. Logue JK, Franko NM, McCulloch DJ, McDonald D, Magedson A, Wolf CR, Chu HY. Sequelae in adults at 6 months after COVID-19 infection. *JAMA network open*. 2021 Feb 1;4(2):e210830-.
 13. Mo X, Jian W, Su Z, Chen MU, Peng H, Peng P, Lei C, Chen R, Zhong N, Li S. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *European Respiratory Journal*. 2020 Jun 18;55(6).
 14. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, Cook JR, Nordvig AS, Shalev D, Sehrawat TS, Ahluwalia N. Post-acute COVID-19 syndrome. *Nature medicine*. 2021 Apr;27(4):601-15.
 15. World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation.
 16. Talman S, Boonman-de Winter LJ, De Mol M, Hoefman E, Van Etten RW, De Backer IC. Pulmonary function and health-related quality of life after COVID-19 pneumonia. *Respiratory medicine*. 2021 Jan 1;176:106272.
 17. Sohn S, Savova GK. Mayo clinic smoking status classification system: extensions and improvements. In *AMIA Annual Symposium Proceedings 2009 Nov 14 (Vol. 2009, p. 619)*.
 18. Ziauddeen N, Gurdasani D, O'Hara ME, Hastie C, Roderick P, Yao G, Alwan NA. Characteristics and impact of Long Covid: Findings from an online survey. *PloS one*. 2022 Mar 8;17(3):e0264331.
 19. Tenforde MW. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States, March–June 2020. *MMWR. Morbidity and mortality weekly report*. 2020;69.
 20. Wisnivesky JP, Govindarajulu U, Bagiella E, Goswami R, Kale M, Campbell KN, Meliambro K, Chen Z, Aberg JA, Lin JJ. Association of vaccination with the persistence of post-COVID symptoms. *Journal of General Internal Medicine*. 2022 May;37(7):1748-53.

ORIGINAL ARTICLE

Study of 2 Minute Walk Test in the Assessment of Functional Capacity in Patients with Stable Chronic Obstructive Pulmonary Disease

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Abstract

Background: COPD is now one of the top three causes of death worldwide and 90% of these deaths occur in low and middle income country. Assessment of functional capacity is vital for appropriate therapy, standard rehabilitation program and also a strong predictor of survival in patients of chronic obstructive pulmonary disease. Field walking tests are simpler and cheaper, require less technical expertise and equipment. Incremental shuttle walking test and the widely practiced 6MWT is a good predictor of functional status for patients with COPD. 2MWT is more feasible in some settings as frail elderly patients were unable to complete a single trial of 6MWT but better able to tolerate 2MWT. So to find a cut off value of walking distance 2MWT and validity of the test this study is necessary. We search relation between 2MWT and airflow limitation of COPD patients. We also search relation of the test with 6MWT.

Objective: To assess the usefulness of 2MWT as an assessment tool of functional capacity of stable COPD patients.

Materials and Methods: This cross sectional study was conducted in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH) from February, 2022 to March, 2023. Eight five (85) stable COPD patients with mild to very severe airflow obstruction were enrolled in this study. Baseline data (FEV1, FEV1/FVC, resting pulse rate, respiratory rate and SpO2) were collected and then all the patients were subjected to perform 2 min walk Test (2MWT) and 6MWT under normal ambient conditions. Then pertinent post-exercise data (walking distance, pulse rate, respiratory rate, SpO2) were collected. The Statistical Package for Social Science (SPSS) v.23 was used for statistical analysis. **Results:** Out of 85 patients, Majority 30(35.3%) patients had severe COPD, 27(31.8%) had very severe, 18(21.2%) had moderate and 10(11.8%) had mild COPD. Mean pulse, SpO2, respiratory rate - at the end of 2 minute walk test and 6 minute walk test were

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Submission on: 6 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

statistically significant ($p < 0.05$) compare with baseline. Mean distance walked was found 96.6 ± 36.2 meter in the end of 2 minute and 250.3 ± 91.8 meter in the end of 6 minute. Significant relationship was found between severity of COPD and 2MWT ($p < 0.001$). Based on the receiver-operator characteristic (ROC) curves 2 minute walk test had area under curve 0.886. Receiver-operator characteristic (ROC) was constructed by using 2 min walk test, which gave a cut off value > 95.7 meter, with 82.5% sensitivity and 85.7% specificity for prediction of severe FEV1. Based on the receiver-operator characteristic (ROC) curves 6 min walk test had area under curve 0.839. Receiver-operator characteristic (ROC) was constructed by using 6 min walk test, which gave a cut off value > 286.5 meter, with 89.4% sensitivity and 71.4% specificity for prediction of severe FEV1. The validity of 2 minute walk test vs 6 minute walk test evaluation for severity of airflow limitation of COPD was correlated by calculating sensitivity (84.7%), specificity (96.2%), accuracy (88.2%), positive predictive value (98.0%) and negative predictive value (73.5%).

Conclusion: This study concluded that the 2MWT is a reliable, valid, and sensitive test for the assessment of functional status in patients with stable COPD. It is practical, simple, quick, easy to administer, and well-tolerated by patients with stable COPD.

Keyword: 6 minute walk test, 2 minute walk test, Airflow limitation

[Chest Heart J. 2024; 48(2) : 90-99]

Introduction:

Chronic obstructive pulmonary disease is a widespread cause of mortality, morbidity and economic burden worldwide that is both substantial and increasing¹. COPD is now one of the top three causes of death worldwide and 90% of these deaths occur in low and middle income country. The prevalence and burden of COPD are projected to increase over the coming decades due to continued exposure to COPD risk factors and aging of world's population. Often prevalence of COPD is directly related to the prevalence of tobacco smoking, although in many countries outdoor, occupational and indoor air pollution (burning of wood and other biomass fuels) are major risk factors². COPD is a significantly widespread and neglected public health issue in Bangladesh mainly due to heavy burden of smoking and biomass fuel usage and often under diagnosed among patients³ (Alam et al., 2015). The Prevalence in population of 40 years and above was found to be 21.5pp8% with a total of 60,42,400 people⁴ (Hassan, 2020).

Chronic Obstructive Pulmonary Disease primarily consists of chronic bronchitis, small airway disease and parenchymal destruction (emphysema). It is considered in a person usually aged more than 40 years who presents with progressive persistent shortness of breath, chronic and recurrent cough, sputum production and or history of recurrent exposure to risk factors. Clinically spirometry is needed to confirm, the presence of post-bronchodilator FEV1/FVC less than 0.70 confirms the diagnosis.

Functional status assessment is necessary to determine the root cause of changes in functional status, to document physical disability, to determine need for long term care, to certify for assistance with healthcare and homecare need to perform a preoperative evaluation and to evaluate for lung transplantation referral⁵ (Downs, 2011). The method used to perform a functional assessment include activities of daily living (ADL) and instrumental ADL tools, pulmonary function test (PFT), exercise test, anthropomorphic and self-report measurements. The American Thoracic Society⁶ (ATS) guidelines suggests the use of functional assessment tools, such as exercise testing, be performed when less physically rigorous tools (PFT, history and physical) do not adequately explain the functional changes. Exercise performance captures the integrated and multisystem effects of COPD and predicts adverse outcome such as mortality⁷ (Spruit et al., 2012). There are several laboratory based and field tests are validated in COPD. Exercise tolerance can be assessed by cycle ergometry or treadmill exercise and step ergometry which are expensive.

Field walking tests are simpler and cheaper, require less technical expertise and equipment. Incremental shuttle walking test and the widely practiced 6MWT is a good predictor of functional status for patients with COPD. Standardized self-paced, timed walking tests like 6MWT, 2MWT are useful in clinical practice as they require minimal facilities and relevant to routine functioning. A

2MWT was first proposed by Butland et al. (1982)⁸ and was reported to be a valid test. A more recent study by Eiser et al. (2003)⁹ reported that 2MWT was a reliable test and was sensitive to bronchodilator therapy. A good correlation has been found with PFTs. Several studies have also found it effective for assessing arterial hypoxemia and recommended its use as a marker of disease severity and the need for oxygen supplementation¹⁰ (Rusanov et al., 2008). Oxygen saturation, total walking distance, heart rate, breathing frequency and leg fatigue were been measured. Frail elderly patient undergoing pulmonary rehabilitation were better able to tolerate 2MWT.

Materials and Methods:

The Cross-sectional observational study was carried out at respiratory lab and spirometry room in the Department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka, Bangladesh from February, 2022 to March, 2023.

Inclusion criteria:

1. Stable COPD Patient attending of outpatient department in NIDCH
2. Patients age ≥ 40 years.
3. Patients who are fit for spirometry.

Exclusion criteria:

- Other chronic lung diseases like Asthma, Bronchiectasis, DPLD
- Chronic respiratory failure with long term oxygen therapy
- Dementia
- Concomitant heart failure
- Disease with mobility impairment (Orthopedic or Neurological disease).
- Unstable angina, Acute ECG change suggestive of myocardial infraction.
- Pregnancy, lactation
- Any malignancy

Purposive sampling was done in this study. Before commence of the study, prior ethical approval was taken from the ERC of NIDCH. Among COPD patients who were attending the Outpatient Department 85 stable patients were selected (according to inclusion and exclusion criteria). All the recruited patients were evaluated

in detail, including present and past clinical history, physical examination. Written informed consent was taken from all the patients after proper explanation about the study protocol. 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), FEV₁ and FEV₁/FVC ratio. A repeat spirometry was performed 20 min after inhaling 200 µg of salbutamol to obtain post bronchodilator FVC, FEV₁ and FEV₁/FVC ratio. All patients with FEV₁/FVC ratio $< 70\%$ and fixed airway obstruction on spirometry (Post bronchodilator improvement in FEV₁ of < 200 ml and $< 12\%$) were included in the study.

Then all the patients were categorized according to GOLD stage of severity into mild, moderate, severe and very severe on the basis of FEV₁. After that Recording of baseline SpO₂, heart rate, respiratory rate at rest were done. Then all the patients were subjected to 2MWT and 6MWT. Walking distance (primary outcome) and other parameter including pulse rate, Respiratory rate, SPO₂ were recorded at the end of 2 minute walk test and 6 minute walk test,

Almost two third (64.7%) patients belonged to age group 56-70 years. The mean age was 60.2 ± 8.2 years with range from 40 to 80 years. Male patients were predominant 74 (87.1%) with male female ratio was 6.7:1. Most of the (70.6%) patients came from rural area. Majority (97.6%) patients came from lower middle class family. The mean socioeconomic status was 15429.4 ± 4978.0 taka with

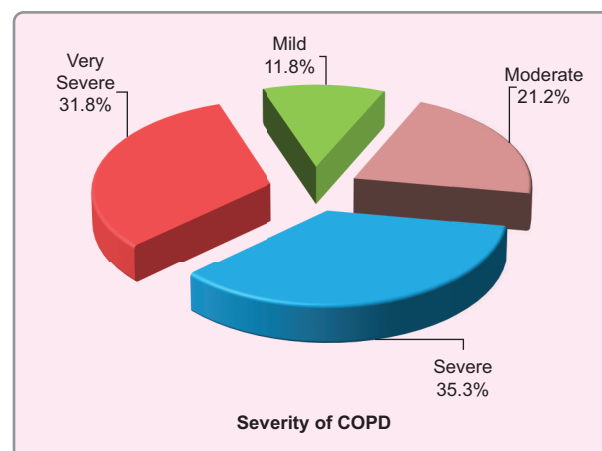


Figure 1: Pie chart showing severity of airflow obstruction in COPD patients according to post bronchodilator FEV₁ (n=85)

range from 9000 to 30000 taka. Majority (40.0%) patients were underweight followed by normal weight 28(32.9%), overweight 12(14.1%) and obese 11(12.9%). Mean BMI was $20.6 \pm 3.8 \text{ kg/m}^2$. 42(49.4%) patients were smoker, 33(38.8%) were ex-smoker and 10(11.8%) were non smoker. Only (12.9%) patients had biomass fuel exposure.

Regarding severity of COPD, majority 30(35.3%) patients had severe COPD, 27(31.8%) had very severe, 18(21.2%) had moderate and 10(11.8%) had mild COPD.

Table I

Pulse rate in different stages of 2 minute and 6 minute walk test (n=85)

Pulse (beats/min)	Mean $\pm$ SD
Baseline	85.3 $\pm$ 6.5
At the end of 2 minute	91.5 $\pm$ 4.9
P value (Baseline vs At the end of 2 minute)	0.001 ^s
At the end of 6 minute	93.7 $\pm$ 5.5
P value (Baseline vs At the end of 6 minute)	0.001 ^s

s= significant

P value reached from paired t-test

Table I shows that mean pulse rate was found 85.3 $\pm$ 6.5 beats/min in baseline, 91.5 $\pm$ 4.9 beats/min in the end of 2 minute and 93.7 $\pm$ 5.5 beats/min in the end of 6 minute. Mean pulse rate - at the end of 2 minute and 6 minute were statistically significant ($p < 0.05$) compare with baseline

Table-II

SpO₂ in different stages of 2 minute and 6 minute walk test (n=85)

SpO ₂ (%)	Mean $\pm$ SD
Baseline	92.8 $\pm$ 2.5
At the end of 2 minute	91.2 $\pm$ 2.9
P value (Baseline vs At the end of 2 minute)	0.001 ^s
At the end of 6 minute	90.7 $\pm$ 2.8
P value (Baseline vs At the end of 6 minute)	0.001 ^s

s= significant

P value reached from paired t-test

Table II shows that mean SpO₂ was found 92.8 $\pm$ 2.5 percent in baseline, 91.2 $\pm$ 2.9 percent in the end of 2 minute and 90.7 $\pm$ 2.8 percent in the end of 6

minute. Mean SpO₂ - at the end of 2 minute and 6 minute were statistically significant ($p < 0.05$) compare with baseline.

Table-III

Respiratory rate in different stages of 2 minute and 6 minute walk test (n=85)

Respiratory rate (breaths/min)	Mean $\pm$ SD
Baseline	14.3 $\pm$ 1.6
At the end of 2 minute	15.8 $\pm$ 1.9
P value (Baseline vs At the end of 2 minute)	0.001 ^s
At the end of 6 minute	16.2 $\pm$ 2.2
P value (Baseline vs At the end of 6 minute)	0.001 ^s

s= significant

P value reached from paired t-test

Table III shows that mean respiratory rate was found 14.3 $\pm$ 1.6 breaths/min in baseline, 15.8 $\pm$ 1.9 breaths/min in the end of 2 minute and 16.2 $\pm$ 2.2 breaths/min in the end of 6 minute. Mean respiratory rate - at the end of 2 minute and 6 minute were statistically significant ($p < 0.05$) compare with baseline

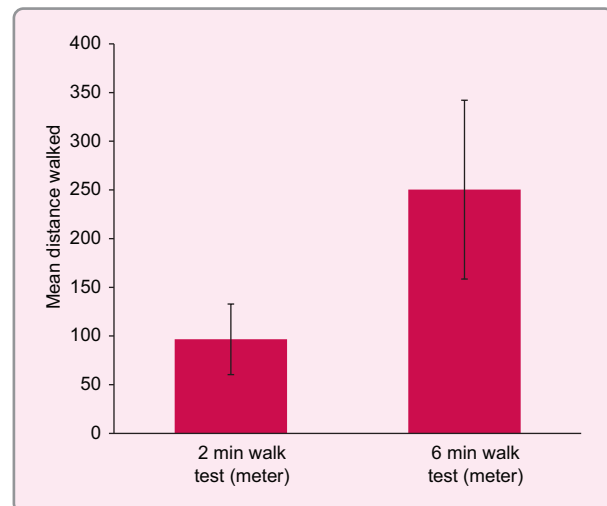


Figure 2: Bar diagram showing distance walked at the end of 2 minute and 6 minute walk test (n=85)

Bar diagram shows mean distance walked was found 96.6 $\pm$ 36.2 meter in the end of 2 minute and 250.3 $\pm$ 91.8 meter in the end of 6 minute

Table-IV

Association between severity of airflow limitation of COPD and distance walked in 2 minute and 6 minute walk test(n=85)

	Severity of COPD				F value	df	P value
	Mild	Moderate	Severe	Very severe			
	(n=10) Mean±SD	(n=18) Mean±SD	(n=30) Mean±SD	(n=27) Mean±SD			
2 min walk test (meter)	164.2±27.2	109.4±27.5	83.3±25.7	77.8±17.4	36.88	3	0.001 ^s
Range (min-max)	115.0-195.0	35.0-160.0	31.0-141.0	40.0-125.0			
6 min walk test (meter)	403.6±65.3	282.6±84.7	228.0±67.2	196.8±52.4	25.75	3	0.001 ^s
Range (min-max)	284.0-508.0	100.0-396.0	94.0-376.0	95.0-310.0			

s= significan

P value reached from ANOVA test.

Table IV shows that mean 2 minute walk test was found 164.2±27.2 meter in mild, 109.4±27.5 meter in moderate, 83.3±25.7 meter in severe and 77.8±17.4 meter in very severe. The mean 6 minute walk test was found 403.6±65.3 meter in mild, 282.6±84.7 meter in moderate, 228.0±67.2 meter in severe and 196.8±52.4 meter in very severe. The difference were statistically significant ($p<0.05$) among four groups.

The area under the receiver-operator characteristic (ROC) curves for prediction of severe FEV_1 is depicted in table XI. Based on the receiver-operator characteristic (ROC) curves 2 min walk test had area under curve 0.886. Receiver-operator characteristic (ROC) was constructed by using 2 min walk test, which gave a cut off value d"95.7 meter, with 82.5% sensitivity and 85.7% specificity for prediction of severe FEV_1 .

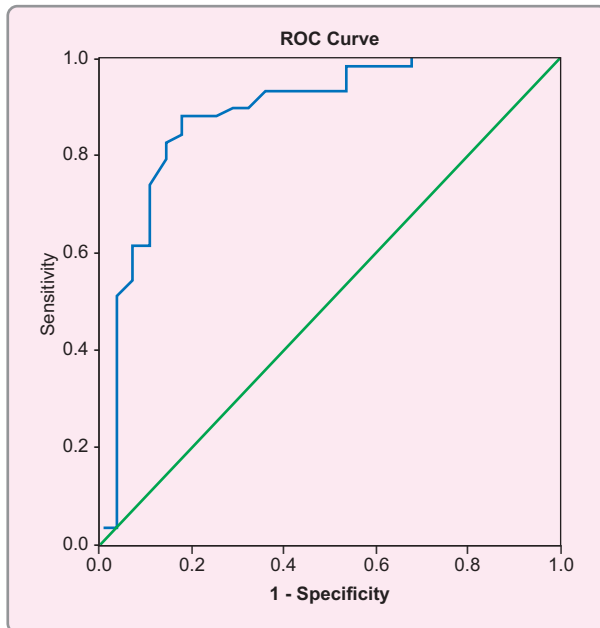


Figure 3: Receiver-operator characteristic curves of 2 minute walk test

Receiver-operator characteristic (ROC) curve of 2 min walk test for prediction of airflow limitation severity of stable COPD

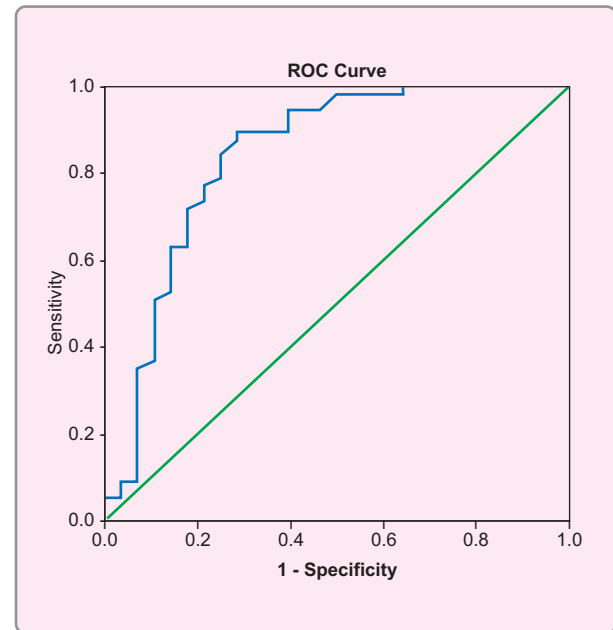


Figure 4: Receiver-operator characteristic curves of 6 min walk test

Receiver-operator characteristic (ROC) curve of 6 min walk test for prediction of severity of airflow limitation of stable COPD

Table-V

Receiver-operator characteristic (ROC) curve of 2 min walk test for prediction severity of airflow limitation of stable COPD

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
2 min walk test	d"95.7	82.5	85.7	0.886	0.802	0.969

Table-VI

Receiver-operator characteristic (ROC) curve of 6 minute walk test for prediction of severity of airflow limitation of stable COPD

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
6 minute walk test	≤286.5	89.4	71.4	0.839	0.735	0.943

Table-VII

Comparison between 2 minute walk test and 6 minute walk test for evaluation of stable COPD (n=85)

2 minute walk test	6 minute walk test	
	Positive(n=59)	Negative(n=26)
Positive (n=51)	50 (True positive)	1 (False positive)
Negative (n=34)	9 (False negative)	25 (True negative)

2 minute walk test evaluation for stable COPD, true positive 50 cases, false positive 1 case, false negative 9 cases and true negative 25 cases in identification by 6 minute walk test.

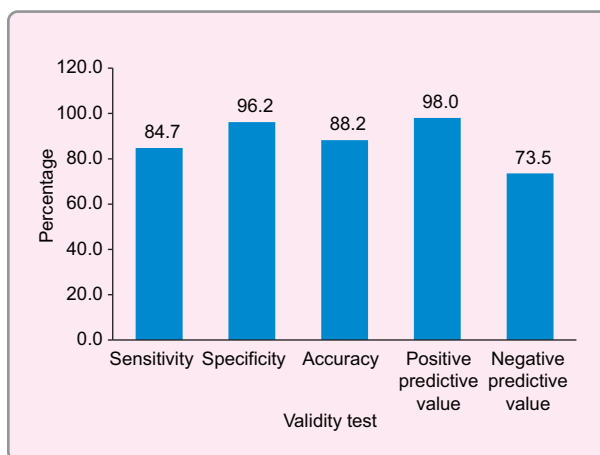


Figure 5: Bar diagram showing sensitivity, specificity, accuracy, positive and negative predictive values of the 2 minute walk test for prediction of severity of airflow limitation of stable COPD

The area under the receiver-operator characteristic (ROC) curves for prediction of severity of airflow limitation is depicted in table XII. Based on the

receiver-operator characteristic (ROC) curves 6 minute walk test had area under curve 0.839. Receiver-operator characteristic (ROC) was constructed by using 6 minute walk test, which gave a cut off value d"286.5 meter, with 89.4% sensitivity and 71.4% specificity for prediction of severity of airflow limitation

The validity of 2 minute walk test vs 6 minute walk test for prediction of severity of airflow limitation of stable COPD was correlated by calculating sensitivity (84.7%), specificity (96.2%), accuracy (88.2%), positive predictive value (98.0%) and negative predictive value (73.5%).

Discussion:

This cross sectional study was carried out with an aim to assess the usefulness of 2MWT as an assessment tool of functional capacity of COPD patient who were attending in outpatient department of NIDCH.

85 patients with stable COPD (mild to severe disease) who fulfilled the inclusion and exclusion criteria during the period from February, 2022 to March, 2023 were included in this study. The present study findings were discussed and compared with previously published relevant studies.

In this study it was observed that almost two third (64.7%) patients belonged to age group 56-70 years. The mean age was 60.2 ± 8.2 years. In another study where they showed mean age was 61.2 ± 10.2 years¹¹. Other study reported that mean age was 62.3 ± 7.9 years¹⁶. These findings are also consisted with our study.

In our study we observed that male patients were predominant 74(87.1%). Male female ratio was 6.7:1. Similarly, Different study demonstrated that majority of COPD patients were male. Their study findings almost similar with our study¹¹⁻¹³.

According to BMI, Majority 34(40.0%) patients were underweight followed by normal weight 28(32.9%), overweight 12(14.1%) and obese 11(12.9%) in our study. Mean BMI was 20.6 ± 3.8 kg/m². A study described that mean BMI was 26 ± 6 kg/m²¹⁴. In a study mean BMI was 27.1 ± 6.6 kg/m²¹⁶. Another study reported that mean BMI was 24.2 ± 5.1 kg/m²¹¹. The above authors showed that BMI was higher their study than my study. Due to variation of ethnicity, height, weight BMI is inconsistent with our study.

Regarding smoking status in this study we observed that 42(49.4%) patients were smoker, 33(38.8%) were ex-smoker and 10(11.8%) were nonsmoker. In a study we found that 29.9% patients were still current smokers¹². Another study obtained that 71% were ex-smoker, 20% were current smoker and 9% were never smoker¹⁵. Their findings were consisted with our study.

In our study it was observed that 32(37.6%) patients were hypertensive followed by 17(20.0%) patients were Diabetics, 6(7.1%) patients were suffering from CKD, 2(2.4% patients) were diagnosed as IHD and 1(1.2%) was a case of Parkinson disease.

We investigated our patients with spirometry. We observed that mean post bronchodilator FVC was $52.4 \pm 13.6\%$, mean post bronchodilator FEV₁ was $43.8 \pm 20.9\%$ and mean post bronchodilator FEV₁/FVC ratio was 55.8 ± 9.4 . Johnston et al. (2017)

revealed that mean FEV1 was found 47.8 ± 20.2 percent and FEV1/FVC was 45.0 ± 15.0 . Another study also found mean FEV1 was $46.3 \pm 19.9\%$ of predicted value¹³. A study described that mean FVC was found $66.6 \pm 18.7\%$, mean FEV₁ was $50.2 \pm 16.5\%$ and mean FEV₁/FVC ratio was 57.8 ± 8.2 ¹².

Regarding mMRC grading of COPD patients in this study, it was observed that most of the patients 33(38.8%) had symptoms under mMRC grade 2 followed by 26(30.6%) patients were under mMRC grade 3, 20(23.5%) were under mMRC grade 1 and 6(7.1%) were under grade 0. A study demonstrated that majority (37%) patients had mMRC grade 2¹⁵. The above mentioned studies finding were almost similar in this study.

Mean pulse rate was 85.3 ± 6.5 beats/min in baseline, 91.5 ± 4.9 beats/min in the end of 2 MWT and 93.7 ± 5.5 beats/min in the end of 6MWT. Mean pulse rate was at the end of 2 MWT and 6MWT were statistically significant ($p < 0.05$) compare with baseline. A study had observed that the mean increase of heart rate during the walking tests was 28.5 bpm at the 2MWT and 29.0 bpm at the 6MWT (treatment effect: 0.5 bpm [95%CI -3.5 to 4.4], $p = 0.827$)¹¹. Another study showed mean heart rate was significantly different at the end of the 6MWT and 3MStepT (106.2 ± 16.3 vs. 112.9 ± 13.4 bpm, $p = 0.002$)¹⁶. These finding were almost similar with our study.

In this present study mean SpO₂ was found 92.8 ± 2.5 percent in baseline, 91.2 ± 2.9 percent at the end of 2MWT and 90.7 ± 2.8 percent at the end of 6MWT. Mean SpO₂ - at the end of 2MWT and 6MWT were statistically significant ($p < 0.05$) compare with baseline. A study done found baseline oxygen saturation was higher than 91% in the study patients with range from 91% to 98%¹³. Another study reported that mean SpO₂ was found 94.4 ± 0.6 percent¹². Gloeckl et al. (2016) demonstrated that median oxygen saturation after walking test was found 93.8 percent in 2MWT and 93.3 percent in 6MWT. Findings of their studies were consisted with our study¹¹.

Baseline mean respiratory rate was found 14.3 ± 1.6 breaths/min in baseline, 15.8 ± 1.9 breaths/min at the end of 2MWT and 16.2 ± 2.2 breaths/min at the end of 6MWT. Mean respiratory rate - at the end of 2MWT and 6MWT were statistically significant ($p < 0.05$) compare with baseline.

In this current study we observed that mean walking distance was found 96.6 ± 36.2 meter at the end of 2MWT and 250.3 ± 91.8 meter at the end of 6MWT. In a study Johnston et al. (2017) revealed that mean distance walked was found 132.5 ± 27.3 meter at the end of 2 minute walk test, and 330.5 ± 96.0 meter at the end of 6 minute walk test. A study found that at 6MWD was found 432.6 ± 96.3 meter¹⁶. Sanchez-Martínez et al. (2020) obtained that mean 6-min walking distance was 349.1 ± 84.7 meters¹². Another study reported that patients walked a shorter distance during the 2MWT (150 m [95% CI: 134–165]) than during 6MWT (397 m [95% CI: 347–447]). Mean walking speed during the 2MWT (4.5 km/h [95% CI: 4.0–5.0]) was significantly ($p = 0.002$) higher than during 6MWT (4.0 km/h [95% CI: 3.5–4.5]). Mean walking distance of 2MWT and 6MWT was lower in our study as because majority of patients had severe airflow limitation according to GOLD stages.

In present study we observed that mean distance at the end of 2 minute walk test was found 164.2 ± 27.2 meter in mild, 109.4 ± 27.5 meter in moderate, 83.3 ± 25.7 meter in severe and 77.8 ± 17.4 meter in very severe. The mean distance at the end of 6 minute walk test was found 403.6 ± 65.3 meter in mild, 282.6 ± 84.7 meter in moderate, 228.0 ± 67.2 meter in severe and 196.8 ± 52.4 meter in very severe. The difference were statistically significant ($p < 0.05$) among four groups. Which was similar to the findings of a study found that mean distance at the end of 2 minute walk test was 163.0 ± 20.79 meter in mild, 119.80 ± 17.72 meter in moderate and 98.45 ± 17.36 meter in severe¹⁷. The mean distance at 6 minute walk test was found 426.0 ± 69.31 meter in mild, 308.0 ± 85.11 meter in moderate and 196.15 ± 37.73 meter in severe COPD. The difference were statistically significant ($p < 0.05$) among three groups. These results are in agreement with those of Spruit et al. (2010)¹⁴. Who found that severe airflow limitation by GOLD stage is a significant clinical determinant of poor 6MWD performance. These results suggest that the degree of airflow limitation explains the variance in 6MWD in patients with moderate to very severe COPD, a finding previously suggested by other authors^{18,19}.

Based on the receiver-operator characteristic (ROC) curves 2 minute walk test had area under curve 0.886. Receiver-operator characteristic

(ROC) was constructed by using 2 minute walk test, which gave a cut off value ≥ 95.7 meter, with 82.5% sensitivity and 85.7% specificity for prediction of airflow limitation severity of COPD. A study revealed that a change in 2MWD of 5.5 m (the anchor-based MID) had the best combination of sensitivity (0.76) and specificity (0.74) for identifying participants who achieved the minimum clinically important change in 6MWD of at least 25 m, with AUC of 0.81 (95% CI 0.66–0.95, $P = 0.001$), that correlated with my study¹⁵.

Based on the receiver-operator characteristic (ROC) curves 6 min walk test had area under curve 0.839. Receiver-operator characteristic (ROC) was constructed by using 6 min walk test, which gave a cut off value ≥ 286.5 meter, with 89.4% sensitivity and 71.4% specificity for prediction of severity of airflow limitation. In a study done by Sanchez-Martínez, et al. (2020) reported that the two were adjusted by baseline status (poor or non-poor 6MWT performance)¹². The AUCs of the two models were similar (0.811 vs. 0.806), implying that non-pulmonary factors have non-inferior discriminative ability compared to pulmonary factors. Another study showed that the area under the receiver operating characteristic (ROC) curve for the current model was 0.851 (0.834–0.869), with a sensitivity of 77.9% and a specificity of 77.5%¹⁴.

In this study we observed that Comparison of 2MWT and 6MWT in evaluation for severe airflow limitation (according to GOLD). In 2MWT true positive cases were 50, false positive was 1 case, false negative were 9 cases and true negative were 25 cases in comparison to 6MWT which had positive case were 59 and negative were 26. The validity of 2 min walk test vs 6 min walk test for evaluation of airflow limitation severity of COPD was correlated by calculating sensitivity (84.7%), specificity (96.2%), accuracy (88.2%), positive predictive value (98.0%) and negative predictive value (73.5%).

Conclusion:

This study has demonstrated that significant relationship was found between airflow limitation severity of COPD and 2MWT. Based on the receiver-operator characteristic was constructed by using 2MWT, which gave a cut off value < 95.7 meter is a better sensitivity, specificity for

prediction of severe airflow limitation. A significant correlation was found between 2MWT and 6MWT. The 2MWT is a reliable, valid, and sensitive test for the assessment of functional status in patients with severe stable COPD. It is practical, simple, quick, easy to administer, and well-tolerated by patients with severe stable COPD symptoms.

References:

1. Global initiative for chronic obstructive lung disease (GOLD) 2022. Global Strategy for The Diagnosis, Management And Prevention Of Chronic Obstructive Pulmonary Disease (2022 Report), Available from: <https://goldcopd.org/2022-gold-reports>
2. Eisner, M.D., Anthonisen, N., Coultas, D., Kuenzli, N., Perez-Padilla, R., Postma, D., Romieu, I., Silverman, E.K. and Balmes, J.R., 2010. An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*, 182(5), pp.693-718.
3. Alam, D.S., Chowdhury, M.A., Siddiquee, A.T., Ahmed, S. and Clemens, J.D., 2015. Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 12(6), pp.658-667.
4. Hassan, M.R., 2020. Bangladesh guidelines for chronic obstructive pulmonary disease. Beximco Pharmaceuticals Ltd., pp. 1-121.
5. Downs, C.A., 2011. Functional assessment of chronic obstructive pulmonary disease. *Journal of the American Academy of Nurse Practitioners*, 23(4), pp.161-167.
6. American Thoracic Society ATS Statement/: Guidelines for the Six-Minute Walk Test., 2002. *American Journal of Respiratory and Critical Care Medicine*, 166, pp.111-117.
7. Spruit, M.A., Polkey, M.I., Celli, B., Edwards, L.D., Watkins, M.L., Pinto Plata, V., Vestbo, J., Calverly, P.M., Tal-Singer, R., Agusti A. and Coxson, H.O., 2012. Predicting outcomes from 6-minute walk distance in chronic obstructive pulmonary disease. *Journal of American Medical Directors Association*, 13(3), pp.291-297.
8. Butland, R.J., Pang, J.A.C.K., Gross, E.R., Woodcock, A.A. and Geddes, D.M., 1982. Two-, six-, and 12-minute walking tests in respiratory disease. *British medical journal (Clinical research ed.)*, 284(6329), p.1607-1608.
9. Eiser, N., Willsher, D. and Dore, C.J., 2003. Reliability, repeatability and sensitivity to change of externally and self-paced walking tests in COPD patients. *Respiratory medicine*, 97(4), pp.4
10. Rusanov, V., Shitrit, D., Fox, B., Amital, A., Peled, N. and Kramer, M.R., 2008. Use of the 15-steps climbing exercise oximetry test in patients with idiopathic pulmonary fibrosis. *Respiratory medicine*, 102(7), pp.1080-1088.
11. Gloeckl, R., Teschler, S., Jarosch, I., Christle, J.W., Hitzl, W. and Kenn, K., 2016. Comparison of two-and six-minute walk tests in detecting oxygen desaturation in patients with severe chronic obstructive pulmonary disease—a randomized crossover trial. *Chronic respiratory disease*, 13(3), pp.256-263.
12. Sánchez-Martínez, M.P., Bernabeu-Mora, R., Martínez-González, M., Gacto-Sánchez, M., Martín San Agustín, R. and Medina-Mirapeix, F., 2020. Stability and predictors of poor 6-min walking test performance over 2 years in patients with COPD. *Journal of Clinical Medicine*, 9(4), p.1155.
13. Starobin, D., Kramer, M.R., Yarmolovsky, A., Bendayan, D., Rozenberg, I., Sulkes, J. and Fink, G., 2006. Assessment of functional capacity in patients with chronic obstructive pulmonary disease: correlation between cardiopulmonary exercise, 6 minute walk and 15 step exercise oximetry test. *IMAJ-RAMAT GAN*, 8(7), p.460.
14. Spruit, M.A., Watkins, M.L., Edwards, L.D., Vestbo, J., Calverley, P.M., Pinto-Plata, V., Celli, B.R., Tal-Singer, R., Wouters, E.F. and Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study investigators, 2010. Determinants of poor 6-min walking distance in patients with

- COPD: the ECLIPSE cohort. *Respiratory medicine*, 104(6), pp.849-857.
15. Johnston, K.N., Potter, A.J. and Phillips, A.C., 2017. Minimal important difference and responsiveness of 2-minute walk test performance in people with COPD undergoing pulmonary rehabilitation. *International Journal of Chronic Obstructive Pulmonary Disease*, pp.2849-2857.
 16. Beaumont, M., Losq, A., Péran, L., Berriet, A.C., Couturaud, F., Le Ber, C. and Reyckler, G., 2019. Comparison of 3-minute Step Test (3MStepT) and 6-minute Walk Test (6MWT) in Patients with COPD. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 16(3-4), pp.266-271.
 17. Negm, M.F., Abdalla, M.E. and Almahdy, M.A., 2012. Study of 2-min walk test and 15-step exercise oximetry test in the assessment of exercise tolerance in Egyptian patients with chronic obstructive pulmonary disease. *Egyptian Journal of Chest Diseases and Tuberculosis*, 61(4), pp.291-296.
 18. Marin, J.M., Carrizo, S.J., Gascon, M., Sanchez, A., Gallego, B. and Celli, B.R., 2001. Inspiratory capacity, dynamic hyperinflation, breathlessness, and exercise performance during the 6-minute-walk test in chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*, 163(6), pp.1395-1399.
 19. Wegner, R.E., Jorres, R.A., Kirsten, D.K. and Magnussen, H., 1994. Factor analysis of exercise capacity, dyspnoea ratings and lung function in patients with severe COPD. *European Respiratory Journal*, 7(4), pp.725-729.
 20. Leung, A.S., Chan, K.K., Sykes, K. and Chan, K.S., 2006. Reliability, validity, and responsiveness of a 2-min walk test to assess exercise capacity of COPD patients. *Chest*, 130(1), pp.119-125.

ORIGINAL ARTICLE

Evaluation of Serum Immunoglobulin E (IgE) Level in Newly Diagnosed Bronchial Asthma Patients in Rajshahi Medical College Hospital

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Abstract

Introduction: Frequent episodes of wheezing, dyspnoea, chest tightness, and coughing, especially at night or in the early morning, are hallmarks of bronchial asthma, a chronic inflammatory disease of the airways.

Aim of the study: The aim of the current study is to evaluate serum immunoglobulin E (IgE) level in newly diagnosed bronchial asthma patients in rajshahi medical college hospital.

Methods: This case-control study was conducted at the Department of Medicine, Rajshahi Medical College Hospital, Bangladesh. The study duration was 6 months which started from September 2021 to February 2022. Therefore, for this study 25 patients were included as cases, another 25 healthy individuals were included as control. That is, total 50 subjects were included in the study following the inclusion and exclusion criteria.

Result: The mean age of the newly diagnosed bronchial asthma cases was 31.16 ± 8.8 (SD) years. Among the case group, the majority of respondents were in the age group of 21-30 and 31-40 years. A majority of the study population were female in case groups (64%, n=16). It was well noted that the mean FEV1 values and the majority of the cases were having moderate (52%), severe (32%), and mild levels of bronchial asthma (16%) and dyspnoea (72%) was the most common symptom among cases. The mean serum immunoglobulin E (IgE) level of the cases was 735.8 ± 231.3 (SD) kU/L, and among the control group was 169.7 ± 23.2 (SD) kU/L. IgE level was significantly higher in severe bronchial asthma patients compared to moderate and mild bronchial asthma patients.

Conclusion: Serum IgE was significantly higher in patients with bronchial asthma (BA) in comparison to healthy control group. Moreover, a significant serum IgE was also significantly higher in patients with severe BA than the patients with moderate and mild BA.

Keywords: Immunoglobulin E (IgE), Bronchial Asthma, Immunocompromised

[Chest Heart J. 2024; 48(2) : 100-107]

Introduction

A chronic inflammatory disorder named Bronchial asthma is a disorder of the airways

characterized by recurrent episodes of breathlessness, wheezing, chest tightness, and cough, especially at night or in the early

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Submission on: 14 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

morning.¹ It causes considerable morbidity and mortality globally. It is one of the most common chronic, non-communicable diseases and affects around 334 million people around the world. The global prevalence of self-reported, doctor-diagnosed asthma in adults is 4.3%, with wide variation between countries.² The prevalence is lowest in poor nations like China (0.2%) and highest in wealthy nations like Australia (21%).³ By 2025, there might be an extra 100 million asthmatics, according to estimates.⁴ In the past, asthma has been linked to a substantial financial burden. In 2016, over 50% of children with asthma reported having one or more asthma attacks. If left untreated, asthma attacks can result in significant medical expenses and resource usage.⁵ On average, 11.6% of Bangladeshi secondary school students had bronchial asthma. Males were more likely than females to have bronchial asthma (15.6% vs. 7.4%).⁶ Most cases of asthma typically begin in childhood due to sensitization to common inhaled allergens, including pollens, cockroaches, mites from household dust, fungus, and animal dander. These inhaled allergens promote the growth of T helper type 2 (Th2) cells, which in turn stimulates the production and release of Th2 cytokines, interleukin (IL)-4, IL-5, and IL-13.⁷ It is a condition marked by frequent episodes of dyspnoea and wheezing, which differ in intensity and frequency among individuals. Hereditary allergic disorders, early exposure to protein antigens like cow's milk or egg white, recurrent respiratory tract infections, and indoor and outdoor environmental factors are some of the risk factors that contribute to the development of asthma. These risk factors can be further classified as allergic sensitization or exacerbation.⁸ Immunoglobulin (Ig) E-mediated allergies, also known as atopic allergies, account for most human allergies.⁹ The last of the five classes of human antibodies to be identified, immunoglobulin E (IgE) was designated in 1968 and is now frequently linked to the different symptoms of allergic illness.¹⁰ Its function in mammalian evolution seems to be to provide a defense mechanism against animal venoms and parasites, which necessitates the acquisition of a

potent effect or function.¹¹ An increase in serum Immunoglobulin E (IgE) levels is a characteristic of allergic disorders, including asthma. In allergic asthma, immunologic mechanisms mediated by IgE antibodies trigger a hypersensitivity reaction. IgE is essential for the start and spread of the inflammatory cascade and, consequently, the allergic reaction.^{12,13} Atopic disorders (asthma, allergic rhinitis, atopic dermatitis, urticaria), parasite diseases, cutaneous diseases, neoplastic diseases, and immunological deficits are additional ailments that raise blood IgE levels.¹⁴ Research revealed that persons with asthma had a noticeably higher serum total IgE level than those in good health.¹⁵ However, there is a lack of research in our nation on the IgE level in newly diagnosed asthma cases. Serum IgE levels in newly diagnosed instances of bronchial asthma will be assessed as part of the current study, and the relationship between IgE levels and the degree of airflow limitation will also be discussed. The aim of the current study is to evaluate serum immunoglobulin E (IgE) level in newly diagnosed bronchial asthma patients in Rajshahi medical college hospital.

Methods

This case-control study was conducted at the Department of Medicine, Rajshahi Medical College Hospital, Bangladesh. The study duration was 6 months which started from September 2021 to February 2022. Therefore, for this study 25 patients were included as cases, and another 25 healthy individuals were included as control. That is, total 50 subjects were included in the study. Age: >18 years, either gender, newly diagnosed bronchial asthma according to GINA guideline and willing to participate were included among inclusion Criteria for the cases. Previous criteria along with healthy individual were included among inclusion Criteria for the controls. However, patients with Other atopic sign and symptom, documented helminthic or parasitic infection, smoker, person with obesity, pregnant women, immunocompromised patients, chronic respiratory diseases other than asthma were excluded from the study.

Results

In Table 1 the mean age of the newly diagnosed bronchial asthma cases was 31.16 ± 8.8 (SD) years. Among the case group, the majority of respondents were in the age group of 21-30 and 31-40 years of which 36% respondents in each group, followed by in decreasing order 18-20 years and 41-50 years (12% respondents of each), and above 50 years of age group was 4% of respondents. The mean age and age distribution of the subjects were matched between two groups ($p=0.98$ and 0.61 respectively). This table represents the descriptive characteristics of the study population ($n=50$). Regarding educational status, the majority of respondents in the case group (36%) received primary education, only 12% had no formal education, the rest were

studied up to secondary school (28%), higher secondary school (8%), and graduated/above (16%). Both groups presented with a similar level of education ($p = 0.2$). In the terms of occupation, 36% of respondents in the case group were housewives while the others were day laborers, garment workers, housemaids, etc (32%), service holders (20%), Business (8%), and retired (4%). The distribution of the studied subjects by occupational level was also matched between the two groups ($p=0.98$). The majority of respondents in both groups hailed from rural areas (64% and 56% respectively) while 36% and 44% of respondents from both groups hailed from urban areas. No differences were found between the case and control groups concerning the latitude of residence ($p=0.6$).

Table-I
Socio-demographic profile of the study population (n=50)

Variables	Cases n(%) (n=25)	Controls n(%) (n=25)	p value*
Distribution of patients by Age group (Years) (n=50)			
18-20	3 (12)	2 (8)	0.98*
21-30	9 (36)	10 (40)	
31-40	9 (36)	8 (32)	
41-50	3 (12)	4 (16)	
>50	1 (4)	1 (4)	
Total	25 (100)	25 (100)	0.61**
Mean $\pm$ SD	31.16 $\pm$ 8.8	32.44 $\pm$ 8.9	
Distribution of patients by educational status (n=50)			
No formal education	3 (12)	2 (8)	0.2
Primary	9 (36)	4 (16)	
Secondary	7 (28)	10 (40)	
Higher Secondary	2 (8)	7 (28)	
Graduate/Above	4 (16)	2 (8)	
Distribution of patients by occupation (n=50)			
Housewife	9 (36)	8 (32)	0.98
Service	5 (20)	6 (24)	
Business	2 (8)	3 (12)	
Others	8 (32)	7 (28)	
Retired	1 (4)	1 (4)	
Distribution of patients by residence (n=50)			
Rural	16 (64)	14 (56)	0.6
Urban	9 (36)	11 (44)	

Chi-square test* and independent student t-test** was performed to compare between two groups

Cases: 25 newly diagnosed Bronchial Asthma patients.

Controls: 25 healthy individuals.

Chi-square test* was performed to compare between two groups. Cases: 25 newly diagnosed Bronchial Asthma patients. Controls: 25 healthy individuals.

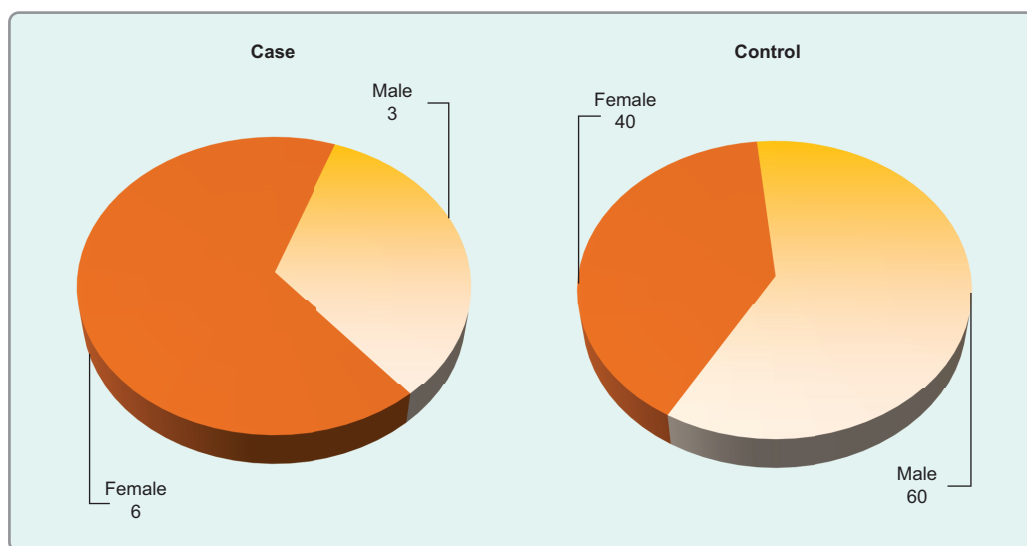


Figure 1: Pie chart showing sex distribution of patients (n=50)

Chi-square test* was performed to compare between two groups; Cases: 25 newly diagnosed Bronchial Asthma patients; Controls: 25 healthy individuals; p value* 0.1

Figure I shows a majority of the study population were female in case groups (64%, n=16) and a majority of the study population were male in the control group (60%, n=15). Both groups were statistically similar regarding gender distribution (p=0.1).

Table-II

Distribution of severity of bronchial asthma according to spirometry/PEF findings among the cases (n=25)

Severity of Bronchial Asthma	FEV1 or PEF	Cases (n)	Percentage
Mild	≥80%	4	16
Moderate	60-80%	13	52
Severe	≤60%	8	32

The distribution of severity of bronchial asthma is given in Table II. It was well noted that the mean FEV1 values and the majority of the cases were

having moderate (52%), severe (32%), and mild levels of bronchial asthma (16%).

Table-III

Distribution of clinical features among the cases (n=25)

Clinical Features*	Cases (n)	Percentage
Chest tightness	11	44
Dyspnoea	18	72
Cough	15	60
Wheeze	14	56
Runny nose	10	40

*Multiple response was considered

From Table III, it was noted that dyspnoea (72%) was the most common symptom among cases followed by cough (60%), wheeze (56%), chest tightness (44%), and runny nose (40%).

Table-IV

Comparison regarding Serum Immunoglobulin E (IgE) between two groups (n=50)

Variables	Cases (n=25) Mean ± SD	Controls (n=25) Mean ± SD	p value*
Serum IgE (kU/L)	735.8 ± 231.3	169.7 ± 23.2	<0.001

Independent student t-test* was performed to compare between two groups

Cases: 25 newly diagnosed Bronchial Asthma patients.

Controls: 25 healthy individuals.

Table-V
Association between serum immunoglobulin E (IgE) level with the severity of bronchial asthma (n=25)

Variable	Mild (≥80%)	Moderate (60-80%)	Severe (≤60%)	p value*
Serum IgE (kU/L)	404 ± 29.4	636.5 ± 55.9	1045 ± 14.4	<0.001

*p value was determined by one way ANOVA test. Post Hoc analysis by Bonferroni method was done.

In Table IV, the mean serum immunoglobulin E (IgE) level of the cases was 735.8 ± 231.3 (SD) kU/L, and among the control group was 169.7 ± 23.2 (SD) kU/L. Serum immunoglobulin E (IgE) level was statistically significantly higher in the case group than in the control group ($p < 0.001$).

Table V showing that the mean serum immunoglobulin E (IgE) level was statistically significantly associated with the severity of bronchial asthma ($p < 0.001$). IgE level was significantly higher in severe bronchial asthma patients compared to moderate and mild bronchial asthma patients. Besides, there was a significantly higher level of serum IgE present in the moderate group of bronchial asthma patients compared to a mild level of asthma patients. It was observed that the more the severity level of asthma, the higher the concentration level of serum IgE.

Discussion

In Table 1 the mean age of the newly diagnosed bronchial asthma cases was 31.16 ± 8.8 (SD) years. Among the case group, the majority of respondents were in the age group of 21-30 and 31-40 years of which 36% respondents in each group, followed by in decreasing order 18-20 years and 41-50 years (12% respondents of each), and above 50 years of age group was 4% of respondents. The mean age and age distribution of the subjects were matched between two groups ($p = 0.98$ and 0.61 respectively). Table 1 also represents the descriptive characteristics of the study population ($n = 50$). Regarding educational status, the majority of respondents in the case group (36%) received primary education, only 12% had no formal education, the rest were studied up to secondary school (28%), higher secondary school (8%), and graduated/above (16%). Both groups presented with a similar level of education ($p = 0.2$). In the terms of occupation, 36% of respondents in the

case group were housewives while the others were day laborers, garment workers, housemaids, etc (32%), service holders (20%), Business (8%), and retired (4%). The distribution of the studied subjects by occupational level was also matched between the two groups ($p = 0.98$). The majority of respondents in both groups hailed from rural areas (64% and 56% respectively) while 36% and 44% of respondents from both groups hailed from urban areas. No differences were found between the case and control groups concerning the latitude of residence ($p = 0.6$). In the present study, the incidence of bronchial asthma was higher in females (64%) than males (36%), being similar to previous reports.¹⁶ The higher prevalence of bronchial asthma in female patients corroborates with the earlier findings and this may be due to increased thoracic size in adult females after puberty when compared to males.^{17,18} Manohar S. et al. also observed that estimation of IgE level among females was 52%, which was higher than compared to males (48%).¹⁹ This was by our study results too. The distribution of severity of bronchial asthma is given in Table III. It was well noted that the mean FEV1 values and the majority of the cases were having moderate (52%), severe (32%), and mild levels of bronchial asthma (16%). In the present study, the most common clinical feature was dyspnoea as seen in 72% of patients followed by cough among 60% and wheeze in 56% of patients. This might be due to severe airway obstruction in many of our study subjects. In a study conducted on the prevalence of asthma in urban and rural children in Tamil Nadu, usual symptoms such as breathlessness (17.9%), wheezing (17.7%) and nocturnal dry cough (20.7%) were reported but without dyspnea.²⁰ In the current study, the mean serum IgE value of bronchial asthma patients was 735.8 ± 231.3 (SD) kU/L which was higher than the healthy control

group (169.7 ± 23.2 kU/L). One of the studies had reported that serum total IgE level was significantly higher ($P < 0.001$) in asthmatic adults compared to that of healthy subjects.¹⁵ An earlier study conducted in India, had recorded that the mean IgE levels ranged from 151.95 IU/ml in normal subjects to 1045.32 IU/ml in severe asthmatics.²¹ The mean total IgE level of the population was found to be 106.6 IU/ml whereas a higher mean total IgE level was observed patients with severe asthma have a higher mean IgE level (280.2 IU/ml).²² Our study was also in agreement with the study by Thirunavukkarasu et al., who investigated serum IgE level in 60 asthmatic patients between 18 and 60 years of age, classified according to the GINA classification (31 male and 29 female), and 13 healthy controls between 18 and 60 years of age. They found that the mean IgE level in the control group was 151 IU/ml and that in the asthmatic group ranged from 404 to 1045 IU/ml.²¹ Thus, the earlier studies cited above showed that serum IgE is higher in bronchial asthma patients that are similar to our study. When comparing the severity of asthma with serum IgE levels in bronchial asthma, the present data indicated that the more severity of asthma, the greater was the elevation in serum IgE. IgE level was significantly higher in severe bronchial asthma patients [1045 ± 14.4 (SD) kU/L] compared to moderate [636.5 ± 55.9 (SD) kU/L] and mild [440 ± 29.4 (SD) kU/L] bronchial asthma patients. This study was in agreement with the study by Davila et al., who investigated 383 patients with allergic asthma (129 mild, 82 moderate, and 172 severe; mean age: 38 ± 15 , 46 ± 16 , and 45 ± 15 years, respectively). They found that serum total IgE levels in adult patients with persistent allergic asthma were high (two-thirds with levels > 150 IU/ml) and extremely variable.²³ They did not find a significant association between serum total IgE levels and asthma severity or airflow limitation, except for a higher percentage of patients with IgE greater than 400 IU/ml in the severe subgroup. It was found that that serum IgE value increased with the increased severity of airway obstruction and it was to be statistically significant ($p < 0.05$) as observed in a study conducted within the age group of 18-60 years.²¹ This suggests that treatment of bronchial asthma patients warrants a necessary correlation between IgE levels and severity of obstruction.

Patients with severe asthma have a higher mean IgE level (280.2 IU/ml) than patients with moderate (145.8 IU/ml) or mild (137.8 IU/ml) asthma hence IgE levels increased as asthma severity increased.^{17,22} The same trend was reflected in both older and younger bronchial asthma patients.²⁴ The present study was in agreement with the study by Sandeep et al., who investigated serum IgE level in 60 asthma patients between 18 and 60 years of age (31 male and 29 female asthmatic patients), classified according to the GINA classification and 13 healthy controls between 18 and 60 years of age.²¹ They found that the mean IgE level in the control group was 151 IU/ml, and that in the asthmatic group was as follows: a mean of 404 IU/ml for patients with mild asthma ($n=19$), a mean of 404 IU/ml for patients with moderate asthma ($n=18$), and a mean of 1045.32 IU/ml for patients with severe asthma ($n=23$). IgE levels were highly significantly higher in severe exacerbated asthma, compared with moderate and mild exacerbated asthma ($P > 0.001$). In summary, the present data suggest that serum IgE levels increased significantly in bronchial asthma and reflect the severity of asthma.

Limitations of The Study

The study was conducted in a single centered hospital with a non- representative sample size. So, the results may not represent the whole community.

Conclusion

The present study findings indicate that serum IgE was significantly higher in patients with bronchial asthma (BA) in comparison to healthy control group. Moreover, a significant serum IgE was also significantly higher in patients with severe BA than the patients with moderate and mild BA. So, serum IgE could be a widely available, easy and convenient tool to screen the presence of BA and to predict the severity of disease. However, before drawing a final conclusion, further extensive studies should be conducted.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

Recommendation

Further larger cohort study is required to get the exact scenario. Government fund is required for a large scale study.

References

- Hossain MI, Parvez M, Zohora FT, Islam MS, Bari L. Prevalence of asthmatic respiratory complications among the rural community of Tangail area in Bangladesh. *Int J Community Med Public Heal*. 2018;5(4):1291.
- Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. *Lancet*. 2018;391(1):783–00.
- To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: Findings from the cross-sectional world health survey. *BMC Public Health [Internet]*. 2012;12(1):204.
- Barua UK, Saha SK, Ghosh DK, Ruble MMK. Epidemiological Study on Bronchial Asthma at Shaheed Suhrawardy Medical College Hospital, Dhaka. *J Shaheed Suhrawardy Med Coll*. 2013;5(2):77–80.
- Perry R, Braileanu G, Palmer T, Stevens P. The Economic Burden of Pediatric Asthma in the United States: Literature Review of Current Evidence. *Pharmacoeconomics [Internet]*. 2019;37(2):155–67.
- Sarkar S, Mumu S, Mia M, Flora M, Hafez M. Prevalence of Bronchial Asthma Among Secondary School Students in Dhaka City. *Bangladesh Med J*. 2014;41(1):28–31.
- Kudo M, Ishigatsubo Y, Aoki I. Pathology of asthma. *Front Microbiol*. 2013;4(1):1–16.
- Mamun M, Saim A, Salauddin A, Hossain F, Afrin M. Prevalence of asthma and its associated factors among the undergraduate students of Bangladesh Agricultural University. *Int J Nat Soc Sci*. 2016;3(1):32–6.
- Hellman LT, Akula S, Thorpe M, Fu Z. Tracing the origins of IgE, mast cells, and allergies by studies of wild animals. *Front Immunol*. 2017;8(1):1–22.
- Platts-Mills TAE, Heymann PW, Commins SP, Woodfolk JA. The discovery of IgE 50 years later. *Ann Allergy, Asthma Immunol [Internet]*. 2016;116(3):179–82. Available from: <http://dx.doi.org/10.1016/j.anai.2016.01.003>
- Mukai K, Tsai M, Starkl P, Marichal T, Galli SJ. IgE and mast cells in host defense against parasites and venoms. *Semin Immunopathol [Internet]*. 2016;38(5):581–03.
- Peng Z. Vaccines targeting IgE in the treatment of asthma and allergy. *Hum Vaccin*. 2009;5(5):302–9.
- Sandeep T, Roopakala MS, Silvia CRWD, Chandrashekara S, Rao M. An earlier study conducted in India, had recorded that the mean IgE levels ranged from 151.95 IU/ml in normal subjects to 1045.32 IU/ml in severe asthmatics[25]. The mean total IgE level of the population was found to be 106.6 IU/ml whereas higher mean to. *Lung India*. 2010;27(3):138–40.
- Unal D, Gelincik A, Elitok A, Demir S, Olgac M, Coskun R, et al. Impact of high serum Immunoglobulin E levels on the risk of atherosclerosis in humans. *Asia Pac Allergy*. 2017;7(2):74.
- Parveen T, Begum N, Begum S. Allergen Skin Test Reactivity and Serum Total IgE Level in Adult Bronchial Asthmatic Patients. *J Bangladesh Soc Physiol*. 2009;4(1):1–6.
- McGowan JP, Shah SS, Small CB, Klein RS, Schnipper SM, Chang CJ, et al. Relationship of serum immunoglobulin and IgG subclass levels to race, ethnicity and behavioral characteristics in HIV infection. *Med Sci Monit*. 2005;12(1):CR11–6.
- Anupama N, Sharma MV, Nagaraja HS, Bhat MR. The serum immunoglobulin E level reflects the severity of bronchial asthma. *Thai J Physiol Sci*. 2005;18(3):35–40.
- Farid R, SEDAGHATNIA R, PISH NR, MASOUD A, Farid F. Serum levels of total IgE and IgE binding factor (Soluble CD23) in atopic disorders. 2001;
- S. Manohar, R. Selvakumaran. Estimation of serum immunoglobulin E (IgE) level in allergic asthma and allergic rhinitis patients before and after treatment. *Eur J Exp Biol*. 2012;2(6):2199–205.

20. Sibi Chakravarthy K, Singh RB, Swaminathan S, Venkatesan P. Prevalence of asthma in urban and rural children in Tamil Nadu. *Natl Med J India*. 2002;15(5):260–3.
21. Sandeep T, Roopakala MS, Silvia CRWD, Chandrashekara S, Rao M. Evaluation of serum immunoglobulin E levels in bronchial asthma. *Lung India Off Organ Indian Chest Soc*. 2010;27(3):138.
22. Borish L, Chipps B, Deniz Y, Gujrathi S, Zheng B, Dolan CM, et al. Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. *Ann Allergy, Asthma Immunol*. 2005;95(3):247–53.
23. Davila I, Valero A, Entrenas LM, Valveny N, Herráez L. Relationship between serum total IgE and disease severity in patients with allergic asthma in Spain. *J Investig Allergol Clin Immunol*. 2015;25(2):120–7.
24. Nielsen NH, Menne T. The relationship between IgE mediated and cell mediated hypersensitivities in an unselected Danish population: the Glostrup Allergy Study, Denmark. *Br J Dermatol*. 1996;134(4):669–72.

REVIEW ARTICLE

The Expanding Role of Biologics in Severe Asthma: Current Evidence and Next-Generation Approaches

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Abstract

Severe asthma remains a challenging condition despite advancements in conventional therapies. Biologics have revolutionized treatment by targeting specific inflammatory pathways, offering personalized therapy for patients with uncontrolled disease. This review explores the current landscape of biologic therapies, including their mechanisms of action, dosing regimens, efficacy, and safety profiles. We also discuss emerging biologic targets and future directions in asthma management.

Keywords: Severe asthma, biologics, monoclonal antibodies, IL-5 inhibitors, IgE blockers, personalized medicine

[Chest Heart J. 2024; 48(2) : 108-114]

Introduction

Severe asthma affects 5-10% of asthmatics but accounts for a disproportionate burden of morbidity and healthcare costs¹. Despite high-dose inhaled corticosteroids (ICS) and long-acting β_2 -agonists (LABAs), many patients remain symptomatic. Biologic therapies, which target specific inflammatory mediators, have transformed treatment paradigms, particularly for type 2 (T2)-high asthma. This review examines approved biologics, their mechanisms, dosing, adverse effects, and next-generation approaches.

Biologics are monoclonal antibodies (mAbs) engineered to inhibit specific immune pathways. Unlike small-molecule drugs, biologics offer high specificity, reducing off-target effects². They are indicated for severe eosinophilic or allergic asthma inadequately controlled by standard therapy.

Five biologics are currently approved, targeting distinct pathways³ (Table I).

The therapeutic effects of asthma biologics are mediated through precise targeting of key inflammatory pathways⁴. Omalizumab binds to free IgE, preventing its interaction with Fc ϵ RI receptors on mast cells and basophils, thereby inhibiting allergen-induced degranulation and subsequent bronchoconstriction. For eosinophilic asthma, mepolizumab and reslizumab neutralize IL-5, while benralizumab targets the IL-5 receptor (IL-5R α), both leading to marked depletion of eosinophils in blood and airways⁶. Dupilumab exerts broader anti-inflammatory effects by blocking the shared IL-4 receptor alpha (IL-4R α), thereby inhibiting signaling of both IL-4 and IL-13; this dual blockade reduces mucus hypersecretion, airway remodeling, and IgE

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Submission on: 8 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

Table-I
FDA-Approved Biologics for Severe Asthma

Drugs	Target	Dosing	Key Indication(s)
Omalizumab	IgE	75–375 mg SC q2–4 wk (per IgE & weight)	Moderate–severe allergic asthma with perennial aeroallergen sensitivity
Mepolizumab	IL-5	100 mg SC q4 wk (fixed dose)	Severe eosinophilic asthma (≥ 6 y); also approved for Eosinophilic granulomatosis with polyangiitis, Hypereosinophilic syndrome
Reslizumab	IL-5	3 mg/kg IV q4 wk (weight-based; adults ≥ 18 y)	Severe eosinophilic asthma; monitor for anaphylaxis
Benralizumab	IL-5Ra	30 mg SC q4 wk $\times 3$, then q8 wk	Severe eosinophilic asthma (≥ 12 y)
Dupilumab	IL-4Ra	Loading dose: 400 mg SC, then 200 mg SC q2wk	Severe type 2 asthma (eosinophilic and/or high FeNO); also for Chronic rhinosinusitis with nasal polyps
Tezepelumab	TSLP	210 mg SC q4 wk	Severe asthma across phenotypes (T2-high and T2-low)

production⁷. Most recently, tezepelumab has introduced a novel upstream approach by neutralizing thymic stromal lymphopoietin (TSLP), an epithelial-derived alarmin that initiates multiple inflammatory cascades, including T2 and non-T2 pathways⁸. These distinct mechanisms enable personalized intervention based on a patient's dominant inflammatory phenotype, with growing evidence supporting combination approaches for refractory cases.

The dosing regimens for asthma biologics vary by agent and are tailored to patient-specific factors such as weight, biomarker levels, and clinical response. Omalizumab dosing is based on serum IgE levels and body weight, administered subcutaneously every 2–4 weeks, while Mepolizumab and Tezepelumab are administered as fixed-dose subcutaneous injections every 4 weeks. Benralizumab is given subcutaneously every 4 weeks for the first three doses, followed by every 8 weeks thereafter. Reslizumab, in contrast, is administered as a weight-based intravenous infusion (3 mg/kg) every 4 weeks. Dupilumab is administered subcutaneously every 2 weeks as a fixed dose (not weight-based), with dosing regimens varying by indication.

Practical considerations for administration include guidance on missed doses: if a dose is delayed by less than 7 days, it should be administered as

soon as possible, whereas delays exceeding 7 days may require consultation of the treatment protocol, as some agents necessitate re-initiation of therapy⁹. Proper storage is critical for maintaining drug stability; all currently approved asthma biologics require refrigeration at 2–8°C and should be protected from light¹⁰. Prior to administration, subcutaneous formulations should be allowed to reach room temperature for approximately 15–30 minutes to minimize injection discomfort. Healthcare providers should verify proper injection techniques and rotate injection sites to reduce local reactions.

The Global Initiative for Asthma (GINA) 2024 guidelines¹¹ emphasize a phenotype-driven approach for biologic therapy in severe asthma, recommending biologics for patients aged ≥ 6 years who remain uncontrolled despite adherence to optimized Step 5 treatment (high-dose ICS-LABA plus additional controller if needed). Key considerations include:

1. Confirming Severe Asthma:

- Exclude mimics (e.g., vocal cord dysfunction, GERD, poor inhaler technique).
- Document frequent exacerbations (≥ 2 /year) or daily symptoms despite maximal therapy.

2. Phenotype Identification:

- Allergic asthma (T2-high): Elevated IgE (30–700 IU/mL) + positive allergen sensitization → omalizumab.
- Eosinophilic asthma (T2-high): Blood eosinophils ≥ 150 cells/ μ L → anti-IL-5/IL-5R (mepolizumab, benralizumab).
- Mixed T2 inflammation: High FeNO (≥ 25 ppb) + eosinophils ≥ 150 ± nasal polyps → dupilumab.
- Non-T2 or broad phenotype: Low biomarkers → tezepelumab (preferred for its upstream TSLP inhibition).

3. Biomarker Thresholds:

- Eosinophils: ≥ 300 cells/ μ L predicts better response to anti-IL-5 agents.
- FeNO: ≥ 50 ppb suggests dupilumab responsiveness.

4. Special Populations:

- Pediatrics: Omalizumab (≥ 6 y), dupilumab (≥ 12 y).
- Pregnancy: Omalizumab has the most reassuring safety data in pregnancy among asthma biologics, based on registry studies.

GINA 2024¹¹ stresses re-evaluation at 4–6 months for efficacy (exacerbation reduction, lung function improvement) before continuing therapy. Switching biologics is advised for partial/non-responders, guided by phenotype and biomarker reassessment.

Recent meta-analyses of biologic therapies for severe asthma demonstrate substantial clinical benefits across key outcome measures¹². The most consistent finding is a 40–70% reduction in annualized exacerbation rates compared to placebo, with the magnitude of effect varying by specific biologic and patient phenotype. Lung function

improvements, as measured by change in FEV₁, show a clear hierarchy: dupilumab demonstrates the greatest benefit (+0.32 L), followed by tezepelumab (+0.23 L) and omalizumab (+0.15 L), reflecting their differential mechanisms of action and target populations¹². Perhaps most notably, dupilumab exhibits exceptional steroid-sparing effects, enabling 50–80% reductions in maintenance oral corticosteroid doses while maintaining asthma control in steroid-dependent patients¹³. These efficacy outcomes are particularly robust in patients with elevated T2 biomarkers (eosinophils ≥ 150 cells/ μ L or FeNO ≥ 25 ppb), reinforcing the importance of phenotype-guided treatment selection¹⁴. Real-world evidence generally corroborates trial findings, though with slightly attenuated effect sizes, likely reflecting the heterogeneity of clinical practice populations.

Special Populations

The use of biologics in special populations requires careful consideration of age-specific approvals, safety profiles, and comorbidities. In pediatrics, omalizumab is approved for children ≥ 6 years with moderate-to-severe allergic asthma, while dupilumab is indicated for those ≥ 12 years with T2-high asthma, particularly with comorbid atopic dermatitis or nasal polyps¹⁷. For pregnant patients, omalizumab is the preferred option due to its established safety profile, whereas other biologics (e.g., anti-IL-5 agents, dupilumab) should be used only if the potential benefit justifies the risk, given limited human data¹⁸. In the elderly, biologic selection must account for polypharmacy interactions (e.g., immunosuppressants) and immunosenescence, which may alter drug metabolism and infection risk; dose adjustments are generally unnecessary, but close monitoring for adverse effects (e.g., herpes zoster reactivation with dupilumab) is advised¹⁹. Shared decision-making, weighing individual risks and benefits, is essential across all these populations.

Table-II
Phenotype-Guided Therapy

Phenotype	Biomarkers	First-line Biologic
Allergic	IgE 30-700 IU/mL	Omalizumab
Eosinophilic	Blood eosinophils $\geq 150/\mu$ L	Anti-IL-5/IL-5R
T2-high + polyps	FeNO ≥ 25 ppb, eosinophils ≥ 150	Dupilumab
T2-low	Low biomarkers	Tezepelumab (or trial)

Table-III
Comparative Effectiveness of Asthma Biologics

Biologic (Target)	Exacerbation Reduction	FEV ₁ Improvement	Steroid-Sparing Effect	Onset of Action	Best Responder Profile
Omalizumab (IgE)	25-50% ¹¹	+0.15 L ¹²	Moderate (30-50% OCS reduction)	Up to 16 weeks	Allergic asthma (IgE 30-700 IU/mL)
Mepolizumab (IL-5)	50-60% ⁶	+0.10 L ⁶	Strong (50-70%)	4-8 weeks	Eosinophilic (≥ 150 cells/ μ L, ≥ 300 optimal)
Benralizumab (IL-5R α)	60-70% ⁶	+0.12 L ⁶	Strong (60-75%)	2-4 weeks	Eosinophilic (≥ 300 cells/ μ L)
Dupilumab (IL-4R α)	60-70% ⁷	+0.32 L ⁷	Very strong (50-80%)	2-4 weeks	T2-high + nasal polyps (FeNO ≥ 25 ppb)
Tezepelumab (TSLP)	50-60% ⁸	+0.23 L ⁸	Moderate (40-60%)	4-8 weeks	Greatest efficacy in T2-high; also effective in T2-low

Table-IV
Adverse Effects of Asthma Biologics

Biologic	Common AEs	Serious but Rare AEs	Monitoring Recommendations
Omalizumab (anti-IgE)	Injection-site reactions (20%), Headache (5%)	Anaphylaxis (0.1%), Arterial thromboembolism	Observe for 2h post 1st dose; monitor for thrombotic events ¹⁵
Mepolizumab/Reslizumab (anti-IL-5)	URI (15%), Pharyngitis (8%)	Herpes zoster reactivation, Eosinophilic granulomatosis	CBC (eosinophil count), Signs of vasculitis ¹⁶
Benralizumab (anti-IL-5R α)	Pyrexia (4%), Pharyngitis (6%)	Hypersensitivity (angioedema), Paradoxical eosinophilia	Monitor for eosinophilia if symptoms worsen ¹⁵
Dupilumab (anti-IL-4R α)	Injection-site reactions (10%), Conjunctivitis (8%)	Eosinophilic pneumonia, Keratitis	Ophthalmic exams if conjunctivitis persists ¹⁵
Tezepelumab (anti-TSLP)	Arthralgia (6%), Back pain (4%)	None significant reported ¹⁵	

Next-Generation Approaches in Asthma Biologics

The future of asthma biologics is rapidly evolving, with several promising next-generation therapies under investigation. Novel cytokine targets include IL-33 inhibitors (itepekimab) and IL-17 blockers (brodalumab), currently in phase 2/3 trials for severe asthma, particularly in patients with non-type 2 or mixed inflammation phenotypes²⁰. Beyond injectable biologics, oral small-molecule therapies such as JAK inhibitors (e.g., abrocitinib) are being explored for their potential to modulate multiple inflammatory pathways while offering improved convenience²¹. At the cutting edge, gene-editing technologies like CRISPR-Cas9 are in preclinical development, aiming to permanently silence key asthma-related genes (e.g., IL-4R α or TSLP)²². Additionally, bispecific antibodies targeting dual pathways (e.g., IL-5 + IL-13) and alarmin inhibitors beyond TSLP (e.g., IL-25) are expanding the therapeutic landscape. These innovations aim to address unmet needs in T2-low asthma, reduce treatment burden, and potentially offer disease-modifying effects through upstream immune modulation.

Unmet Needs and Future Directions in Asthma Biologics

Despite significant advances, critical unmet needs persist in severe asthma management. Foremost among these is the lack of approved therapies for T2-low asthma, which accounts for 30-50% of severe cases and remains poorly responsive to existing biologics. Current research is exploring novel targets such as IL-17, IL-23, and GM-CSF to address this neutrophilic-dominant phenotype. Another major challenge is the prohibitive cost of biologic therapies, driving investigations into biosimilars (e.g., omalizumab biosimilars in development) and dose-optimization strategies (e.g., extended-interval dosing of benralizumab) to improve accessibility²³. The future of asthma treatment lies in precision medicine, with emerging AI-driven algorithms that integrate multi-omics data (e.g., sputum transcriptomics, proteomics) with clinical biomarkers to predict optimal biologic selection and monitor real-time treatment response²⁴. Additional priorities include:

1. Early intervention trials are underway to determine if initiating biologics in patients

with moderate asthma can prevent or attenuate airway remodeling.

2. Dual-target biologics for patients with overlapping inflammatory pathways
3. Global equity initiatives to address disparities in biologic access

Conclusion

Biologics have redefined severe asthma management by enabling precision medicine. Current agents significantly reduce exacerbations and improve lung function, with emerging therapies expanding treatment options. Future research should focus on biomarkers, cost-effectiveness, and novel targets for non-T2 asthma.

References

1. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014 Feb;43(2):343-73. doi: 10.1183/09031936.00202013. PMID: 24337046.
2. Pelaia C, Crimi C, Vatrella A, Bruni A, Terracciano R, Savino R. New biologics for severe asthma: current evidence and future perspectives. *Expert Review of Respiratory Medicine*. 2022 Mar;16(3):351-63. doi:10.1080/17476348.2022.2043745.
3. Holgate ST, Casale TB, Wenzel S, Bousquet J, Deniz Y, Reisner C. Anti-immunoglobulin E treatment with omalizumab in allergic diseases. *Journal of Allergy and Clinical Immunology*. 2018 Feb;142(2):463-72. doi:10.1016/j.jaci.2018.06.010.
4. Busse WW, Maspero JF, Lu Y, Corren J, Hanania NA, Chipps BE, et al. Efficacy of omalizumab in severe allergic asthma: a systematic review and meta-analysis. *European Respiratory Journal*. 2019 May;53(5):1802196. doi:10.1183/13993003.02196-2018.
5. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *New England Journal of Medicine*. 2021 Sep 26;371(13):1198-207. doi:10.1056/NEJMoa1403290.

6. Bleecker ER, FitzGerald JM, Wechsler ME, Wu Y, Hirsch I, Goldman M, et al. Benralizumab reduces exacerbations in severe, uncontrolled asthma: results from the SIROCCO trial. *Lancet*. 2016 Nov 12;388(10056):2115-27. doi:10.1016/S0140-6736(16)31324-1.
7. Castro M, Corren J, Pavord ID, Maspero J, Wenzel S, Rabe KF, et al. Dupilumab efficacy in uncontrolled moderate-to-severe asthma. *New England Journal of Medicine*. 2021 Jun 28;378(26):2486-96. doi:10.1056/NEJMoa1804092.
8. Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, et al. Tezepelumab in adults with uncontrolled asthma. *New England Journal of Medicine*. 2022 Sep 8;387(10):866-77. doi:10.1056/NEJMoa2204973.
9. Pavord ID, Korn S, Howarth P, Bleecker ER, Buhl R, Keene ON, et al. Mepolizumab for severe eosinophilic asthma: a meta-analysis. *Lancet Respiratory Medicine*. 2022 Apr;10(4):354-66. doi:10.1016/S2213-2600(21)00507-7.
10. Agache I, Beltran J, Akdis C, Akdis M, Canelo-Aybar C, Canonica GW, et al. Long-term safety of biologics in asthma: a systematic review. *Allergy*. 2023 Feb;78(2):145-60. doi:10.1111/all.15568.
11. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2024 [Internet]. Available from: <https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Main-Report.pdf>
12. Wechsler ME, Ruddy MK, Pavord ID, Israel E, Rabe KF, Ford LB, et al. Efficacy and safety of itepekimab in patients with moderate-to-severe asthma. *New England Journal of Medicine*. 2023 Jul 13;389(2):165-76. doi:10.1056/NEJMoa2213082.
13. Rabe KF, Brusselle G, Pavord ID, Szeffler SJ, Busse WW, Maspero JF, et al. Emerging biologics for severe asthma: beyond anti-IL-5. *Lancet Respiratory Medicine*. 2023 Feb;11(2):166-80. doi:10.1016/S2213-2600(22)00441-4.
14. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, et al. Dupilumab reduces nasal polyp burden in patients with chronic rhinosinusitis. *New England Journal of Medicine*. 2019 Jul 4;381(1):55-63. doi:10.1056/NEJMoa1902049.
15. Pelaia C, Heffler E, Crimi C, Brussino L, De Blasio F, Carpagnano GE, et al. Interleukin-5 inhibition in severe eosinophilic asthma: a systematic review. *Journal of Asthma and Allergy*. 2022;15:789-803. doi:10.2147/JAA.S338928.
16. Wechsler ME, Colice G, Griffiths JM, Almqvist G, Skärby T, Piechowiak T, et al. SOURCE: a phase 3 trial evaluating reslizumab after omalizumab failure. *Journal of Allergy and Clinical Immunology: In Practice*. 2021 Aug;9(8):3104-15. doi:10.1016/j.jaip.2021.03.044.
17. National Heart, Lung, and Blood Institute. Guidelines for the diagnosis and management of asthma (EPR-3) [Internet]. 2023. Available from: <https://www.nhlbi.nih.gov/health-topics/guidelines-for-diagnosis-management-of-asthma> [cited 2023 Nov 15].
18. Namazy J, Cabana MD, Scheuerle AE, Thorp JM, Chen H, Carrigan G, et al. The Xolair Pregnancy Registry (EXPECT): the safety of omalizumab use during pregnancy. *Journal of Allergy and Clinical Immunology*. 2015 Feb;135(2):407-12. doi:10.1016/j.jaci.2014.08.025.
19. Wang E, Wechsler ME, Tran TN, Heaney LG, Jones RC, Menzies-Gow AN, et al. Characterization of severe asthma worldwide: data from the International Severe Asthma Registry. *Chest*. 2023 Mar;163(3):583-96. doi:10.1016/j.chest.2022.08.2226.
20. Brightling CE, Gaga M, Inoue H, Li J, Maspero J, Wenzel S, et al. Effectiveness of fevipiprant in reducing exacerbations in patients with severe asthma (LUSTER-1 and LUSTER-2): two phase 3 randomised controlled trials. *Lancet Respiratory Medicine*. 2021 Jan;9(1):43-56. doi:10.1016/S2213-2600(20)30412-2.

21. Moss RB, Corren J, Pavord ID, Wechsler ME. The role of small molecules and biologics in the management of severe asthma. *J Allergy Clin Immunol Pract*. 2022 Mar;10(3):799-810. doi: 10.1016/j.jaip.2021.12.031.
22. Gauvreau GM, O'Byrne PM, Boulet LP, Wang Y, Cockcroft D, Bigler J, et al. Effects of an anti-TSLP antibody on allergen-induced asthmatic responses. *New England Journal of Medicine*. 2023 Jun 15;388(24):2247-58. doi:10.1056/NEJMoa2212895.
23. Israel E, Cardet JC, Carroll JK, Fahy JV, Fuhlbrigge AL, Henderson AG, et al. Reliever-triggered inhaled glucocorticoid in Black and Latinx adults with asthma. *New England Journal of Medicine*. 2023 Jun 1;388(22):2039-50. doi:10.1056/NEJMoa2216063.
24. Pavord ID, Chanez P, Criner GJ, Kerstjens HAM, Korn S, Lugogo N, et al. Mepolizumab for eosinophilic chronic obstructive pulmonary disease. *New England Journal of Medicine*. 2023 Sep 7;389(10):911-23. doi:10.1056/NEJMoa2208208.

CASE REPORT

Mycotic Pseudoaneurysm Mimicking Community-Acquired Pneumonia: A Rare Diagnostic Vigilance

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Abstract:

Mycotic pseudoaneurysm (infected pseudoaneurysm) rarely complicates the presentation of community-acquired pneumonia, which leads to diagnostic challenges. In this case report, we describe a 66-year-old male who presented with fever, breathlessness and hemoptysis. Initial workup with clinical findings and chest x-ray suggested a diagnosis of community-acquired pneumonia. However, CECT followed by CT pulmonary angiogram confirmed the presence of a pseudoaneurysm in the background of pneumonia. This case report highlights that pseudoaneurysm complicating pneumonia can be associated with a rare cause of hemoptysis.

Keywords: Mycotic pseudoaneurysm, Community-acquired pneumonia, CT Pulmonary angiogram

[Chest Heart J. 2024; 48(2) : 115-119]

Introduction:

Pulmonary artery pseudoaneurysms (PAPs) are uncommon but associated with high mortality. If left untreated, lesions can enlarge, rupture, and lead to exsanguination and death. May be congenital (rare) or acquired (mostly associated with cardiovascular disease). Other acquired causes are infection (mycotic pseudoaneurysm), neoplasm, trauma, iatrogenic, etc. Mycotic pseudoaneurysm (or infected pseudoaneurysm) is an infectious arteritis, leading to the destruction of the arterial wall with the formation of a blind, saccular outpouching contiguous with the arterial lumen.

Mycotic aneurysms arising from the pulmonary arteries are rare; only a few cases have been reported. This case report highlights the diagnostic dilemma encountered in a 66-year-old male who initially presented with the clinical features of community-acquired pneumonia and was treated conservatively, but as his coughing up of blood was not responding to the treatment, further workup was done to find out the cause of his hemoptysis. We came across the evidence of pseudoaneurysm by CT pulmonary angiogram and to determine the cause of this pseudoaneurysm, we did a histopathological examination of the surrounding

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Submission on: 19 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>

tissue of the aneurysm, which ultimately resulted in a conclusion of infective or mycotic pseudoaneurysm. This case mainly focuses on the fact that a complaint like hemoptysis should be investigated thoroughly.

Case Summary:

A 66-year-old male from Dohar, who worked as a truck driver, presented with increased shortness of breath for 1 month, coughing up of blood for 1 month, and fever for 7 days. The history of cough dates back 3 years; it persisted throughout the day and night, sometimes with mucoid or mucopurulent sputum production with no seasonal or diurnal variation, and was not aggravated on exposure to cold, dust or fumes. For the last month, cough had increased in intensity and was associated with coughing up blood. He experienced coughing up blood for several episodes, each episode contained about 15 ml (3 tsf blood), bright red in colour, mixed with sputum. There was no history of massive blood loss or hemodynamic instability. He also complained of fever for 7 days, which was high grade and continued; the highest recorded temperature was 103°F and associated with chills and rigor. Fever subsided after taking antipyretics and was not associated with an evening rise of temperature or night sweats. He also gave a history of unintentional and undocumented weight loss, evident by the loosening of his clothes. He had no history of chest pain, nor did he show signs of connective tissue disease or previous history of pulmonary TB infection. His medical history suggested he was diabetic for 15 years and was on oral anti-diabetic medication with good control. He was a smoker and smoked 30 pack

years and had no history of substance abuse or pet exposure. Family medical history was unremarkable. He was up-to-date on all vaccinations, including the COVID-19 booster dose.

Upon examination, the patient appeared ill and dyspneic, showing signs of anemia. Vitals showed a temperature of 103.0°F, pulse 110 b/min, respiratory rate 24 breaths/min, and SpO₂: 96%.

Respiratory assessment was consistent with the findings of right-sided consolidation.

Laboratory tests showed anemia with neutrophilic leucocytosis, along with elevated ESR and chest x-ray showed right-sided consolidation. Sputum culture revealed growth of *Klebsiella*. A contrast-enhanced CT scan showed an ill-defined soft tissue mass lesion in the lower lobe of right lung, which took contrast. Being doubtful about the lesion, we further approached with a CT pulmonary angiogram, which showed a heterogeneous soft tissue lesion involving the middle and lower lobes of the right lung having internal necrosis and pseudoaneurysm within it. The lung window showed areas of consolidation around the soft tissue lesion and few enlarged mediastinal and right hilar lymph nodes raised the suspicion of malignancy. Fiberoptic bronchoscopy showed a normal endobronchial tree and BAL cytology revealed 80% neutrophils. As there was a pseudoaneurysm within the mass, we approached with CT-guided FNAB from the surrounding solid heterogeneous soft tissue lesion to exclude the possibility of malignancy and reviewed the FNAB material for histopathology from two different labs. Both reports came back negative for malignancy. Both reports suggested an inflammatory lesion.

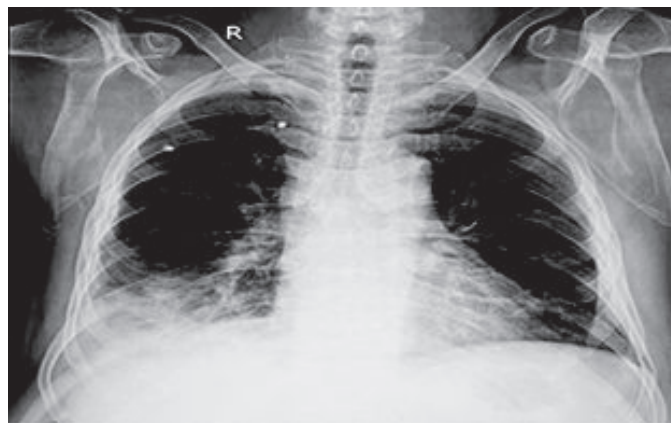


Figure-1: Chest X-ray showing Right sided consolidation

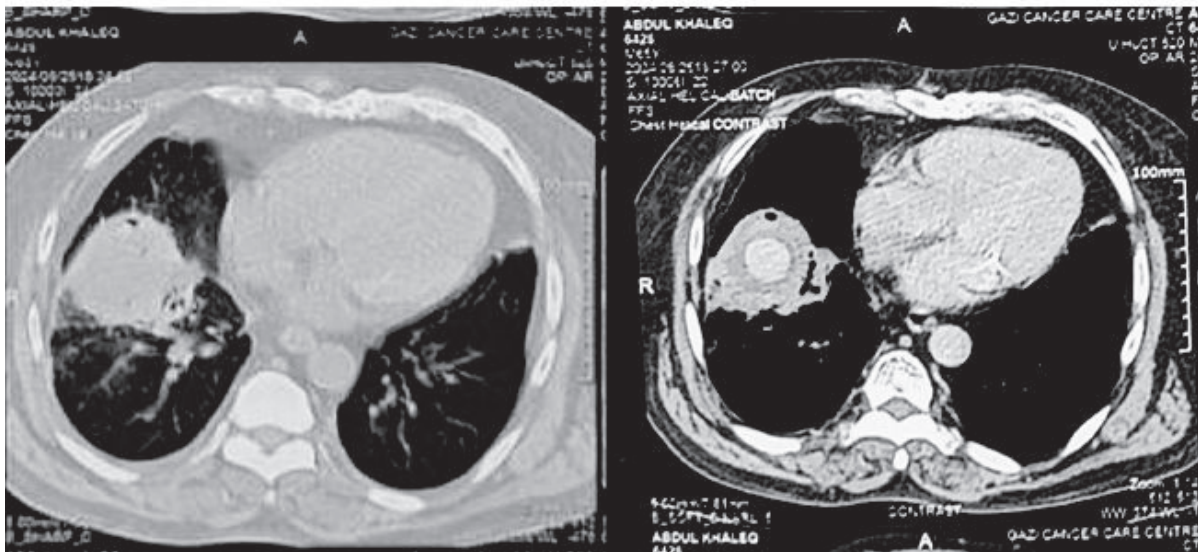
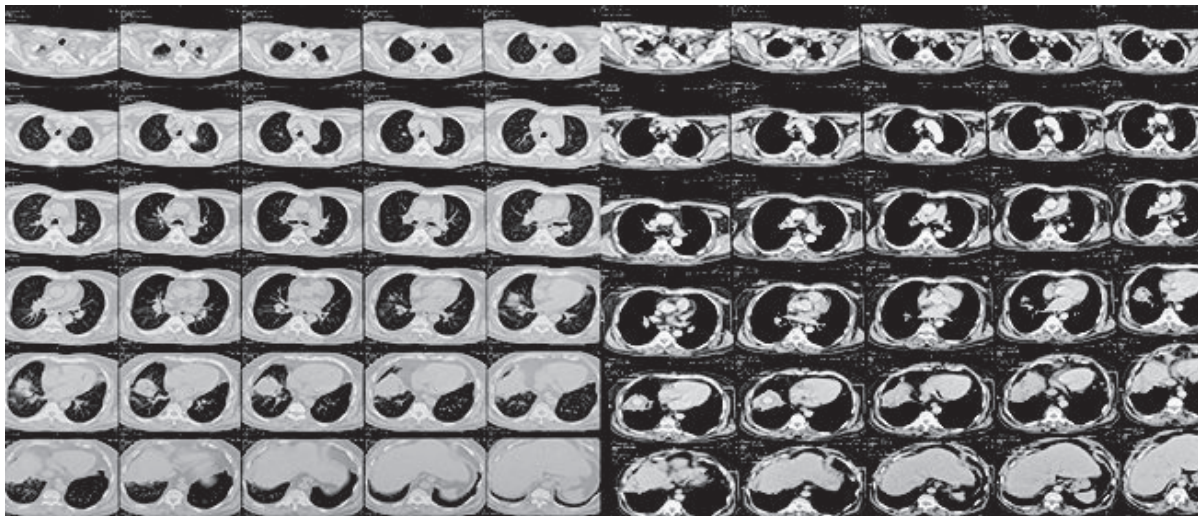


Figure 2: CT Scan of chest: Right sided mass lesion with a round contrast enhanced well circumscribed lesion within the mass

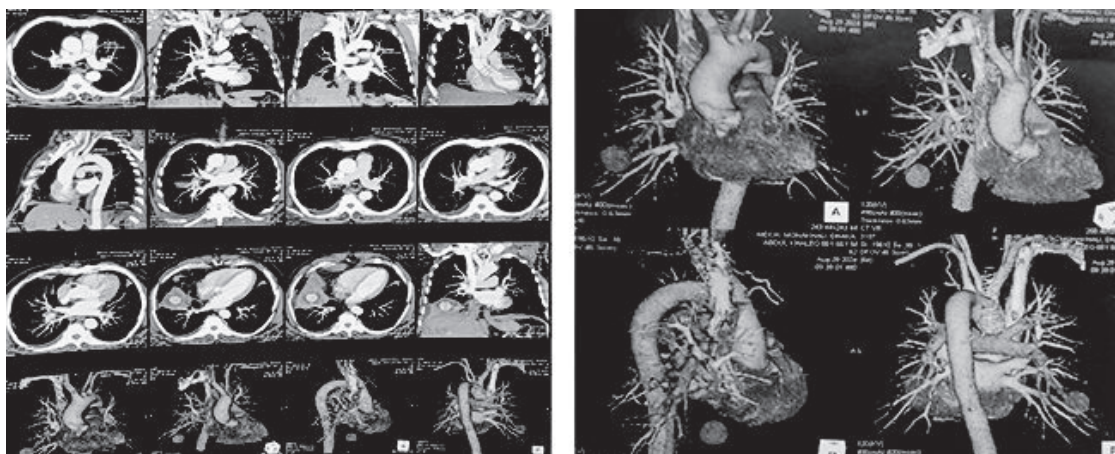


Figure 3: CT Pulmonary Angiogram: Suggestive of mass lesion involving middle and lower lobes of right lung having internal necrosis and pseudo-aneurysm of segmental branch of pulmonary artery within it.

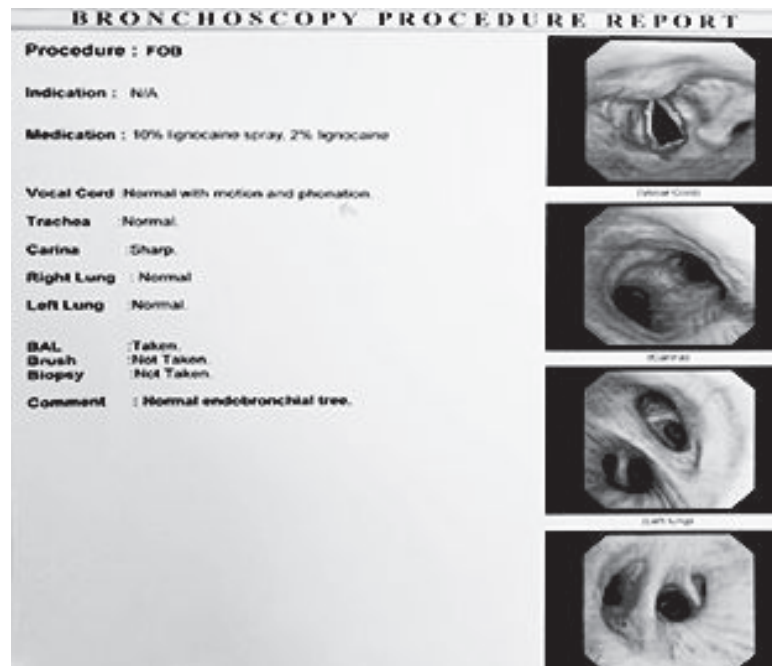


Figure 4: Fiberoptic bronchoscopy shows normal endobronchial tree

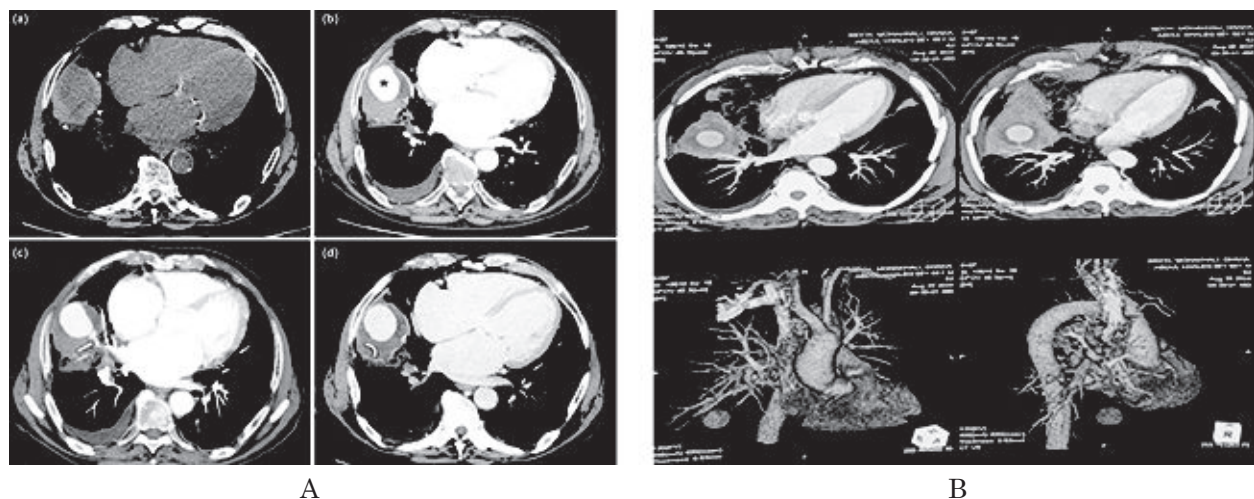


Figure 5 : A. Collected from a international case report. B. CT pulmonary angiogram finding of presenting case

Discussion:

Aneurysms are true aneurysms and false aneurysms (pseudoaneurysms). True aneurysms contain all three layers of the aortic wall (intima, media, and adventitia). In contrast, pseudoaneurysms have less than three layers by the adventitia or peri-adventitial tissues. Pseudoaneurysms are vascular abnormalities that lack a complete arterial wall

Mycotic pseudoaneurysm (or infected pseudoaneurysm) is an infectious arteritis, leading to the

destruction of the arterial wall with the formation of a blind, saccular outpouching contiguous with the arterial lumen. Mycotic aneurysms arising from the pulmonary arteries are rare; only a few cases have been reported. Here mycotic denotes saccular shape, not fungal origin.

Chest radiograph may show nonspecific focal lung consolidation, a solitary pulmonary nodule, or mass. There may be pleural effusion.

Contrast enhance CT scan usual findings are central enhancement within a hematoma or lung

consolidation. Other findings include an enhancing mass next to a pulmonary artery, thrombus within a dilated pulmonary artery, and an enhancing nodule with a low attenuation halo.

CT Pulmonary angiogram is diagnostic, shows the anatomy and communication with the pulmonary artery and provides a road map for treatment by embolization.

Mycotic aneurysms arising from the pulmonary arteries are rare; only a few cases have been reported. *Staphylococcus* and *Streptococcus* species are the most common causative pathogens. Mycotic aneurysms are seldom clinically apparent unless as a sequela of adverse procedural complications. They carry high morbidity and mortality if not treated expeditiously.

Embolization of the affected vessel is the mainstay of treatment. Percutaneous embolization is a minimally invasive alternative to surgical treatment. Transcatheter embolization with stainless steel coils, platinum coils, or detachable balloons is a practical, effective, and safe therapeutic option

Conclusion:

Mycotic pseudoaneurysm is a rare vascular pathology creating a diagnostic challenge with differentials such as pulmonary mass or mediastinal mass, an infected collection or conglomerate nodal disease.

Mycotic (or infected) pseudoaneurysm can rupture spontaneously causing life threatening situation which may be prevented by early management such as surgery, stenting or embolization.

Reference:

1. Jesinger RA, Thoreson AA, Lamba R. Abdominal and pelvic aneurysms and pseudoaneurysms: Imaging review with clinical, radiologic, and treatment correlation. *Radiographics*. 2013;33:E71–96. doi: 10.1148/rg.333115036. [DOI] [PubMed] [Google Scholar]
2. Saad NE, Saad WE, Davies MG, Waldman DL, Fultz PJ, Rubens DJ. Pseudoaneurysms and the role of minimally invasive techniques in their management. *Radiographics*. 2005;25(Suppl 1):S173–89. doi: 10.1148/rg.25si055503. [DOI] [PubMed] [Google Scholar]
3. Aftab S, Uppaluri SA. Mycotic-pseudoaneurysm of the aortic isthmus secondary to salmonella infection causing a diagnostic dilemma. *J Radiol Case Rep*. 2019;13:17–27. doi: 10.3941/jrcr.v13i4.3571. [DOI] [PMC free article] [PubMed] [Google Scholar]
4. Warshauer DM, Archer RK, Selzman CH, Tamaddon HS, Mauro MA. Case 115: Aortic pseudoaneurysm from penetrating superior vena cava stent. *Radiology*. 2007;243:901–4. doi: 10.1148/radiol.2433040944. [DOI] [PubMed] [Google Scholar]
5. Guo Y, Bai Y, Yang C, Wang P, Gu L. Mycotic aneurysm due to *Salmonella* species: Clinical experiences and review of the literature. *Braz J Med Biol Res*. 2018;51:e6864. doi: 10.1590/1414-431x20186864. [DOI] [PMC free article] [PubMed] [Google Scholar]
6. Lee WK, Mossop PJ, Little AF, Fitt GJ, Vrazas JI, Hoang JK, et al. Infected (Mycotic) aneurysms
7. Bin Hsu R, Lin FY, Chen RJ, Hsueh PR, Wang SS. Antimicrobial drug resistance in salmonella-infected aortic aneurysms. *Ann Thorac Surg*. 2005;80:530–6. doi: 10.1016/j.athoracsur.2005.02.046. [DOI] [PubMed] [Google Scholar]
8. Fisk M, Peck LF, Miyagi K, Steward MJ, Lee SF, Macrae MB, et al. Mycotic aneurysms: A case report, clinical review and novel imaging strategy. *QJM*. 2012;105:181–8. doi: 10.1093/qjmed/hcq240. [DOI] [PubMed] [Google Scholar]
9. Pirvu A, Bouchet C, Garibotti FM, Hauptert S, Sessa C. Mycotic aneurysm of the internal carotid artery. *Ann Vasc Surg*. 2013;27:826–30. doi: 10.1016/j.avsg.2012.10.025. [DOI] [PubMed] [Google Scholar]
10. Hot A, Mazighi M, Lecuit M, Poiree S, Viard JP, Loulergue P, et al. Fungal internal carotid artery aneurysms: Successful embolization of an *Aspergillus*-associated case and review. *Clin Infect Dis*. 2007;45:e156–61. doi: 10.1086/523005. [DOI] [PubMed] [Google Scholar]

CASE REPORT

Multifocal Giant Cell Tumor of the Ribs Presenting with Chest Pain and Fever: A Rare Case

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Abstract

Giant cell tumor of bone (GCTB) is an uncommon, usually benign tumor, which can be locally aggressive. It mostly affects long bone, rib involvement is rare & having multiple rib lesions is very unusual. We report the case of a 47 years old man who presented with chest pain & fever. Initial chest imaging showed opacities along both side of the chest wall. Further tests revealed multifocal GCTB affecting several ribs.

Keywords: Giant cell tumor, bone tumor, ribs, lytic lesion.

[Chest Heart J. 2024; 48(2) : 120-123]

Introduction

Giant cell tumor of bone (GCTB) is a rare tumor that is often benign but may be aggressive¹. It accounts for about 5% of all bone tumors and 20% of benign tumors^{1,2}. GCTB usually affects the meta-epiphyseal region of long bones, particularly in the distal femur, proximal tibia, and distal radius². It mostly occurs in young adults aged 20 to 40 years^{2,3}. Involvement of flat bones like the ribs is rare³, and multifocal rib lesions are exceedingly rare, making up less than 1% of cases^{4,5}. We report a unique case of multifocal GCTB affecting several ribs, which presented with severe chest pain and other systemic symptoms.

Case Presentation

A 47-year-old otherwise healthy male was admitted at National Institute of Diseases of the Chest & Hospital (NIDCH) with severe chest pain, more intense on the left side, along with fever lasting

15 days and generalized body aches. He did not have trauma, cough, weight loss, or any prior chronic illnesses. During the examination, vital signs were mostly normal; however, there was localized tenderness and mild warmth over the left anterior chest wall. No lymphadenopathy or respiratory distress was observed.

A chest X-ray revealed bilateral pleural-based opacities. Laboratory tests showed normocytic normochromic anemia, an elevated ESR, leukocytosis (11,490/cmm), and increased serum creatinine levels (2.61 mg/dL). Other tests, including random blood sugar and liver function, returned normal results.

A CT scan of the chest showed multiple irregular, expansive lytic lesions impacting the lateral aspects of several ribs, mainly on the left side. The lung tissue appeared normal.

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Submission on: 28 May, 2024

Accepted for Publication: 16 June, 2024

Available at <http://www.chabjournal.org>



Figure 1: *Chest x-ray showing bilateral pleural based opacity*

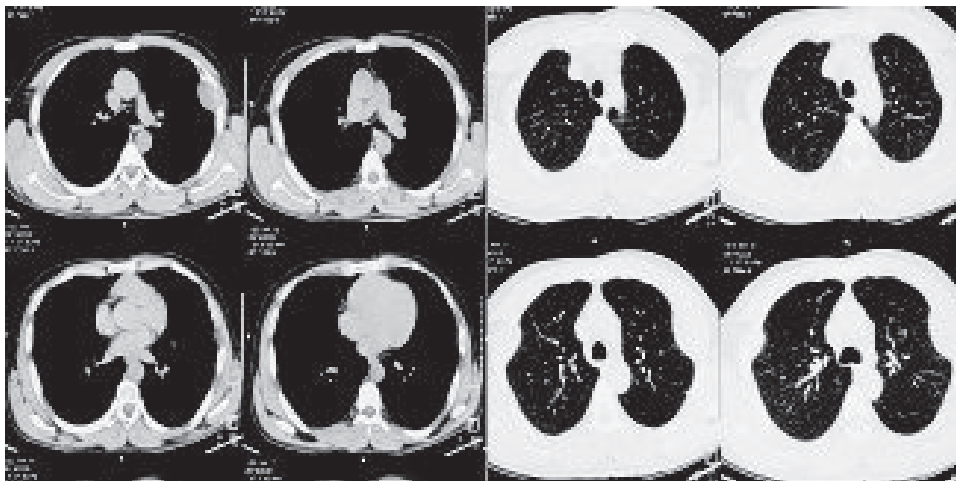


Figure 2: *CT scan of the chest*

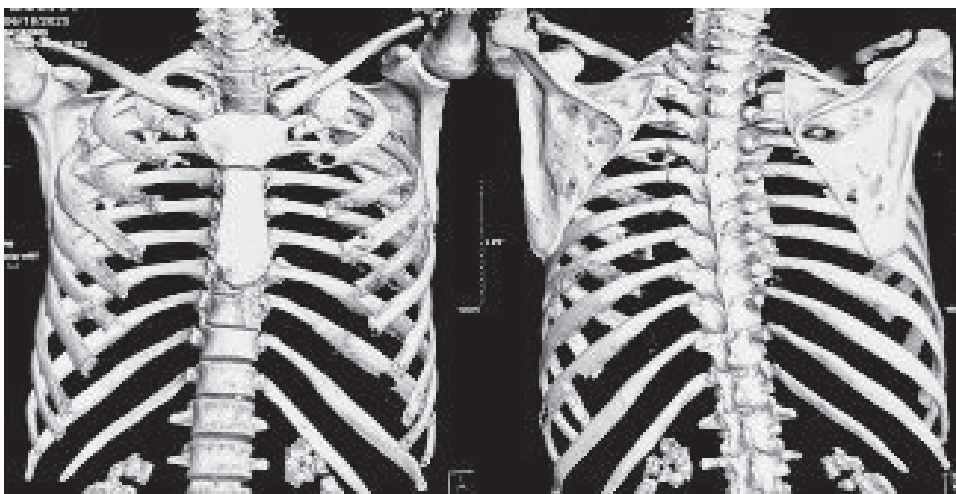


Figure 3: *Bony reconstruction of the rib lesions*

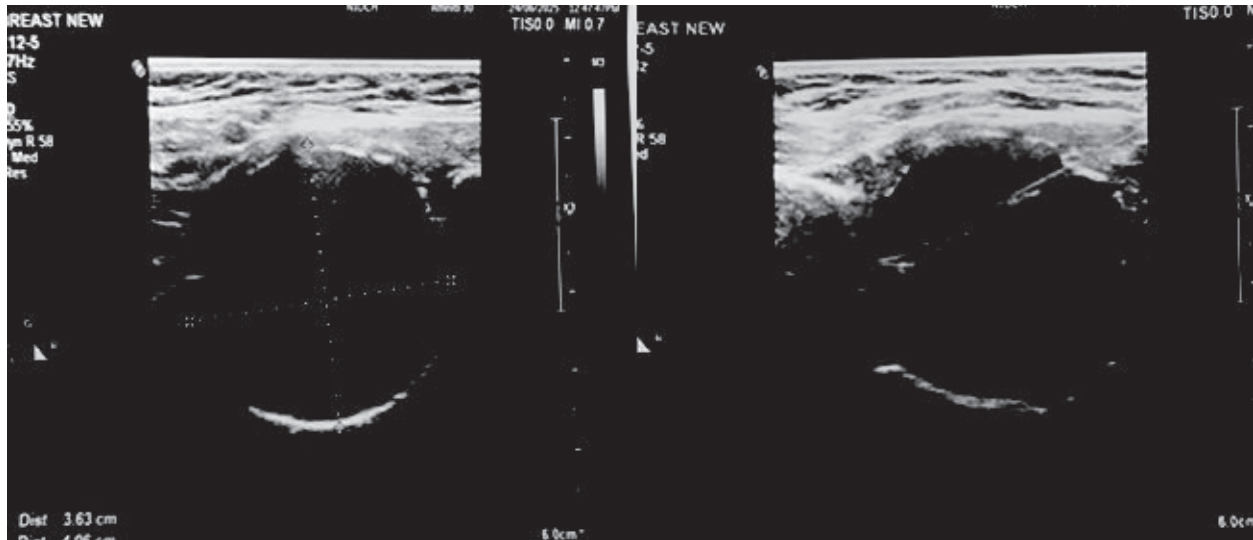


Figure 3: *USG guided aspiration from lesion*

An ultrasound-guided core biopsy from the left sided rib lesion confirmed the giant cell tumor of bone. This histopathology revealed many multinucleated giant cells distributed evenly among mononuclear stromal cells, which were spindle or ovoid and arranged in a storiform pattern.

Discussion

We present an uncommon case of multifocal giant cell tumor of bone (GCTB) affecting the ribs in a 47-year-old man who presented with chest pain and fever. GCTB constitutes about 5% of all primary bone tumors and roughly 20% of benign bone tumors¹. It most commonly occurs in the meta-epiphyseal areas of long bones like the distal femur, proximal tibia, and distal radius. The highest incidence is seen in individuals aged 20 to 40 years² of age. Rib involvement is very rare, appearing in less than 1% of cases⁴, and multifocal rib occurrences are even more unusual⁵.

The pathogenesis of GCTB involves the interaction between neoplastic stromal cells and osteoclast-like giant cells. The stromal cells express receptor activator of nuclear factor-kappa B ligand (RANKL), which encourages osteoclast differentiation and bone loss. This activity accounts for the tumor's locally destructive nature⁶. Although GCTB is classified as benign, it can behave aggressively, leading to destruction of the cortex, soft-tissue growth, recurrence, and lung metastases in up to 5% of patients⁷. The chance of

recurrence is strongly influenced by the surgical method, with wide excision associated with a lower recurrence rate compared to simple curettage².

Clinical signs of rib GCTB often non specific. Patients might feel localized pain, swelling, or tenderness, but systemic symptoms like fever are rare and can mislead into thinking it is an infectious or pleural pathology^{3,4}. In our case, the fever and raised ESR initially pointed to an inflammatory process, delaying the identification of a bone tumor. Similar issues with diagnosis have been noted in previous reports of rib GCTB⁵.

Radiology is crucial for diagnosis. While regular X-rays can show lytic lesions, these may be less clear in the ribs. CT scans provide better details of cortical damage, number of lesions, and any soft-tissue involvement. Three-dimensional images help with surgical planning^{5,8}. In this situation, CT scans clearly indicated multiple rib lesions while sparing the lung tissue, suggesting a primary bone issue.

Confirming the diagnosis through histopathology is important. Under the microscope, GCTB shows many multinucleated osteoclast-like giant cells among mononuclear stromal cells, often arranged in a storiform pattern^{1,6}. These characteristics were seen in our patient's biopsy.

The differential diagnosis for lytic rib lesions includes metastatic cancer, multiple myeloma, aneurysmal bone cysts, brown tumors related to hyperparathyroidism, and chronic osteomyelitis^{6,8}.

Therefore, careful consideration of clinical, imaging, and histological findings is essential for an accurate diagnosis.

Managing rib GCTB is challenging. Complete surgical removal is the best option, with wide resection lowering the chance of recurrence². For cases that cannot be surgically treated, systemic therapy with denosumab, a monoclonal antibody aimed at RANKL, has shown promise in shrinking tumors, easing symptoms, and can facilitate in subsequent surgeries^{6,9}. A recent systematic review from 2025 confirmed that denosumab consistently provides clinical and imaging benefits across different dosing methods, with generally mild side effects, highlighting its effectiveness as a supportive treatment for GCTB¹⁰.

Radiation therapy may be an option for lesions that cannot be removed surgically, but it is usually avoided due to the risk of sarcomatous transformation⁷. The prognosis depends on factors such as the completeness of the surgical excision, the lesion's location, and whether metastasis present or not. GCTBs in flat bones often show up later and present a higher recurrence risk compared to those in long bones^{4,5}. Our case highlights the need to include GCTB in the differential diagnosis for chest wall pain and fluid in the pleura. It also emphasizes the urgency of imaging and biopsy for prompt diagnosis and treatment.

Conclusion

This case highlights a rare multifocal presentation of GCTB in the ribs, accompanied by chest pain and fever. It emphasizes the need to consider bone tumors when diagnosing pleuritic chest pain and pleural abnormalities found on imaging. Early imaging and biopsy are essential for prompt diagnosis and treatment.

References

1. Sobti A, Agrawal P, Agarwala S, Agarwal M. Giant cell tumor of bone – an overview. *Arch Bone Jt Surg*. 2016;4(1):2–9.
2. Klenke FM, Wenger DE, Inwards CY, Rose PS, Sim FH. Giant cell tumor of bone: risk factors for recurrence. *ClinOrthopRelat Res*. 2011;469(2):591–599. doi:10.1007/s11999-010-1501-7
3. Park IH, Lee SY, Kim HY, et al. Giant cell tumor of the rib: a rare location. *J Korean Med Sci*. 2004;19(2):308–310.
4. Lee CH, Chung HW, Park JH, et al. Multifocal giant cell tumor of bone: radiologic and pathologic findings in two cases. *Korean J Radiol*. 2001;2(3):170–175.
5. Brien EW, Mirra JM, Kessler S, et al. Benign giant cell tumor of bone with pulmonary metastases. *ClinOrthopRelat Res*. 1997;(337):256–270.
6. Chakarun CJ, Forrester DM, Gottsegen CJ, et al. Giant cell tumor of bone: review, mimics, and new developments in treatment. *Radiographics*. 2013;33(1):197–211.
7. Thomas DM, Skubitz KM. Giant cell tumor of bone. *CurrOpinOncol*. 2009;21(4):338–344.
8. Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. *J Bone Joint Surg Am*. 1987;69(1):106–114.
9. Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. *Lancet Oncol*. 2010;11(3):275–280.
10. Barreto BG. Denosumab regimens in the treatment of giant cell tumor of bone: a systematic review. *World J Orthop*. 2025;16(3):102–110. doi:10.5312/wjo.v16.i3.102

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