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Ca-125: A Useful Marker to Distinguish Pulmonary Tuberculosis from Bacterial Pneumonia

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Abstract

Background: Ca-125 is a large molecular-weight glycoprotein synthesized by different cells originating from the coelomic epithelium. Although classically it has been used to monitor the course of ovarian epithelial cancer, there are other established circumstances associated with high serum Ca -125 levels and pulmonary tuberculosis is one of them. Diagnosing pulmonary tuberculosis, which is not bacteriologically positive often very challenging. Because many procedures are available for such cases but they are of limited use because some of them are lengthy or expensive or need sophisticated equipment, highly skilled personnel, etc. Serum CA-125 is a rapid, relatively inexpensive investigation. **Objective:** The present study aimed to assess the role of CA-125 in distinguishing pulmonary TB from bacterial pneumonia. **Methods:** This analytical cross-sectional study was conducted in the Department of Medicine, Dhaka Medical College Hospital for the period of March 2018 to September 2020.100 pulmonary tuberculosis patients were taken in group I, and 100 bacterial pneumonia patients were taken in group II according to selection criteria. Informed written consent was taken from each of the participants. All were subjected to detail clinical and demographic history along with thorough physical examination. Relevant investigations were done including serum CA-125. All final data were collected in the semi-structured and pretested case record form. After data collection, data were checked for errors, and analysis was done. **Results:** In this study, the mean CA-125 value was 62.29 (SD±31.51) IU/mL in group I(pulmonary tuberculosis). In group II (bacterial pneumonia) mean value was 22.95(±8.25) IU/mL. The mean value of CA-125 was significantly higher (p-value <0.001) in group I patients compared to group II. About 59.0% of patients in group I had a high level of serum CA-125 which had a significant difference from group II (p<0.001). ROC analysis of CA-125 in the diagnosis of patients with active pulmonary tuberculosis showed a cut-off value of ≥31.7 IU/mL had sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy of 72%, 87%, 84.7%, 75.7%, 5.54%, 0.321%, and 79.5% respectively. **Conclusion:** This study's findings stated that serum CA-125 may be a useful marker in distinguishing PTB from bacterial pneumonia. Therefore, further study with a more generalized study population is recommended.

Keywords:- Ca-125, Glycoprotein, Caulomic epithelium, Pulmonary tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by bacilli belonging to the genus Mycobacterium. There are two forms of tuberculosis: (a) pulmonary tuberculosis (PTB), which accounts for 80% of all cases of

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tuberculosis, and is the infectious form of the disease; and (b) less common, non-infectious, extra-pulmonary tuberculosis (EPTB) which can affect any part of the body other than the lungs, e.g. lymph nodes, spine, pericardium, pleura, joints, genital urinary tract, and abdomen.[1] Pulmonary tuberculosis is further classified as either sputum smear-positive or sputum smear-negative. A patient with both pulmonary and extra-pulmonary tuberculosis should be classified as a case of pulmonary tuberculosis because it is infectious.[1] Tuberculosis remains a major health problem globally. It is one of the top 10 causes of death worldwide. According to World Health Organization in 2017,[2] 10 million people suffered from TB, and 1.6 million died from the disease (including 0.3 million people with HIV). In 2017, an estimated 1 million children became ill with TB and 230000 children died of TB (including children with HIV-associated TB). According to WHO Global TB Report 2016, Bangladesh is one of the world's 30 high TB burden countries. About 73, 000 people die annually due to Tuberculosis. The Highest incidence rates of tuberculosis are found in developing countries like South-East Asia and Western Pacific regions (56%).[3] In Bangladesh70% of patients diagnosed under the national tuberculosis program are new smear-positive patients, and 3% are relapsed. Rest 27% are smear-negative pulmonary and extrapulmonary patients, which is very low than expected (50-55%).[4] Pulmonary tuberculosis (PTB), is diagnosed mainly by its symptoms, chest radiography, sputum smear microscopy, and culture of M. tuberculosis [5]. Sputum smear microscopy is inexpensive and simple, and people can be trained to do it relatively quickly and easily. In addition, the results are available within hours. The sensitivity of the sputum smear microscopy test is 50%-70%.[6] Microscopic examination is performed with the Ziehl-Neelsen (ZN) staining. it is an operator-dependent technique, requires trained personnel, and is also time-consuming as at least 100 microscopic fields need to be observed for at least 15 minutes.[7] In the case of both pulmonary TB and HIV co-infection, the detection rate can be even lower.[8] With light Emitting Diode (LED) fluorescence microscopy (FM) about 10 % more positive smears can be detected compared to ZN.[9] However, in many cases of pulmonary TB, acid-fast bacilli stains in sputum samples may be negative or respiratory specimens may not be available. Culture is the gold standard for TB diagnosis and drug-resistant testing. The sensitivity of Mycobacterium culture is between 43% to 83%. Positive cultures for MTB confirm the diagnosis of TB disease. Commercially two types of broth culture systems; liquid and solid media are available. Culture in liquid media takes 4-14 days and 3-6 weeks in solid media. Culture needs specialized laboratories and skilled personnel which are often unavailable in most TB-endemic regions.[10] The polymerase chain reaction (PCR) has limited use in developing areas because of the high cost and the lack of special equipment and professional staff.[11,12] Expert MTB/RIF, a highly sensitive

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and specific rapid, automated molecular test for the combined detection of tuberculosis and rifampicin resistance. In a meta-analysis, the pooled sensitivity and pooled specificity of MTB /RIF for pulmonary tuberculosis were 90.4% and 98.4% respectively. The sensitivity and specificity of detecting RIF resistance were 94.1% and 97.0%. For extrapulmonary tuberculosis, the overall pooled sensitivity was 80.4% and the specificity was 86.1%.[13] But wide utilization is not still possible in low-income countries.[14] There are molecular methods for TB diagnosis. But the high cost, sophisticated equipment, or requirement for highly skilled personnel have precluded them from routine use, especially in low-income countries.[15] Different biochemical parameters like various markers of cellular activity, acute phase reactants, and enzymes have also been studied to use as helpful tools for this purpose.[16] In recent years, serum tumor markers have become a standard clinical method for tumor screening. Cancer antigen 125 is a high molecular weight glycoprotein (200 KDa). It was identified on the surface of the ovarian carcinoma cell line OVCA 433. Ca -125 is most consistently elevated in epithelial ovarian cancer, but can be elevated in some gynecologic (endometrial, fallopian tube) and non-gynecologic (pancreatic, breast, colon, and lung) cancers.[17] Ca-125 levels have been found high in patients with pulmonary and extrapulmonary tuberculosis, including pleural, peritoneal, pelvic, milliary, and intra-abdominal disease.[18] In pulmonary TB, it was claimed by Yilmaz et al. (2001)[19] that raised levels of Ca 125 can significantly increase the likelihood of tuberculosis activity. Fortun et al. (2009)[20] proposed the tumor marker Cancer antigen 125 as a useful diagnostic tool for tuberculosis. He also showed the diagnostic value of Ca-125 to differentiate pulmonary tuberculosis from other pulmonary infections by using a cut-off value of Ca-125 of 32.5 IU/ml, with sensitivity, specificity, positive predictive value, and negative predictive value of 68.6%, 77.8%, 66.7%, and 79%, respectively. Said et al. (2013)[21] found that at a serum Ca 125 level of 34.6 U/ml as a cut-off value, it had sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of 81.4%, 95%, 95.6%, 79.2%, and 87.2%, respectively, among patients with active pulmonary TB. Then another study reported that the serum levels of CA125, CA199, and CEA in PTB were higher in pulmonary tuberculosis than those in the normal population and also showed CA-125 has good diagnostic performance for pulmonary tuberculosis (Jingjing et al. 2016).[22] These results from different studies provided a clue that tumor markers had potential clinical value for the diagnosis of PTB. There is only one study in Bangladesh showing that the CA-125 level was significantly higher in positive sputum for AFB patients than in negative patients. That study showed that serum CA-125 may be used as a marker for the diagnosis of active pulmonary tuberculosis.[23] But there is no study in Bangladesh showing the role of CA-125 to differentiate pulmonary tuberculosis from other

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respiratory infections. Thus, the purpose of the present study was to assess the role of CA-125 as a useful marker to distinguish pulmonary TB from bacterial pneumonia.

Objectives

General Objective

To evaluate the status of CA-125 as a useful marker to distinguish pulmonary tuberculosis from bacterial pneumonia.

Specific Objectives

- To compare the levels of CA-125 among pulmonary TB and bacterial pneumonia.
- To determine a cut-off value of CA-125 to distinguish pulmonary tuberculosis from bacterial pneumonia.
- To determine the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios of the calculated cut-off value of CA-125.

MATERIAL AND METHODS

This was Hospital based cross-sectional analytical study. The patients were selected purposively. A total of 200 patients were included in this study- group I and group II, 100 pulmonary tuberculosis patients were taken in group I and 100 bacterial pneumonia patients in group II. The study was conducted in the Department of Medicine, Dhaka Medical College Hospital. Dhaka Bangladesh From March 2018 to September 2020. (but actual enrollment started after ERC clearance in November 2019.

Inclusion Criteria

Group I

- Patient's age was 18 to 65 years.
- Sputum smear microscopy positive for acid-fast bacilli (AFB) or Xpert MTB/RIF positive and
- Radio-logically, lung parenchymal abnormalities-Diffuse patchy opacity/consolidation /cavitary lesion, etc and
- Clinical symptoms of active pulmonary TB - cough for 3 weeks or more, hemoptysis, fever, loss of appetite, weight loss, night sweats (Any two)

Group II

- Patient's age was 18 to 65 years.
- Radiological evidence of consolidation and
- Clinical symptoms of pneumonia, cough, fever, expectoration-mucopurulent, hemoptysis, (rusty color), pleuritic chest pain (Any two) and
- With or without sputum smear positive for bacteria or culture positive, and
- Sputum smear-negative for acid-fast bacilli (AFB) or Xpert MTB/RIF negative.

Exclusion Criteria

- History of previous pulmonary or extrapulmonary TB or ongoing TB treatment
- Any known condition which might increase serum CA-125 level-pregnancy, menstruation, Known malignancy in the body, benign gynecological lesions, pelvic inflammatory disease (PID), patients with known liver, renal or cardiac diseases, any known pulmonary disease other than pneumonia or PTB.

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RESULTS

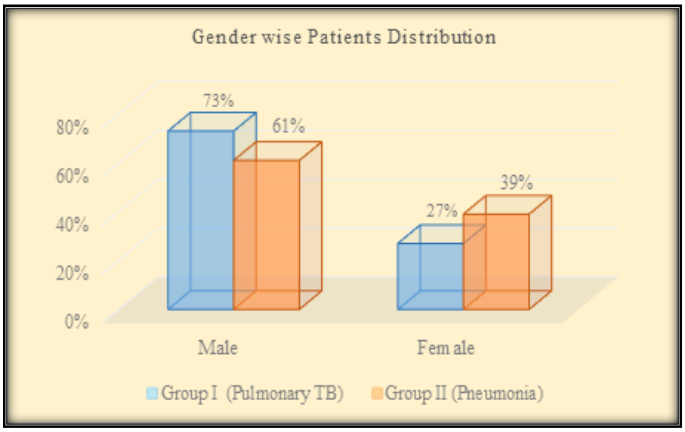

Figure 1: Bar chart showed sex-wise participants. (N=200)

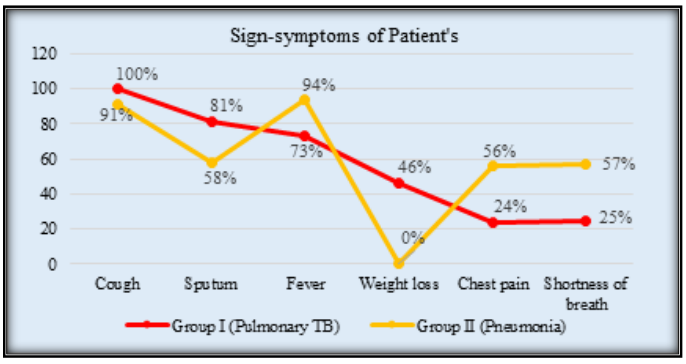

Figure 2: Line chart showed Sign-symptoms of Patients. (N=200)

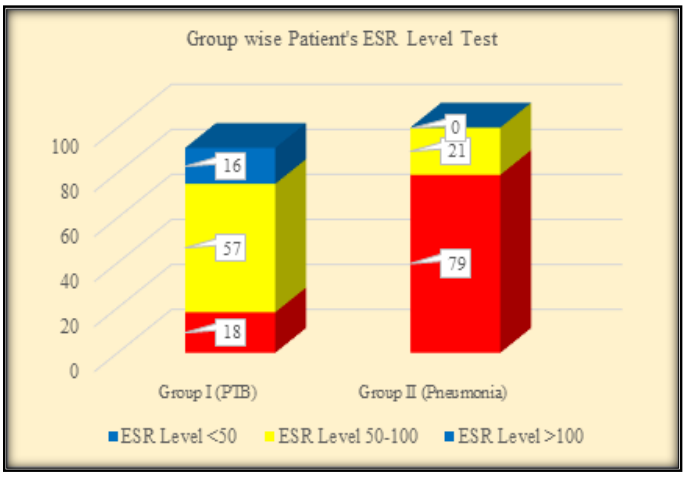

Figure 3: Erythrocyte sedimentation rate (ESR) level among the groups (N=200).

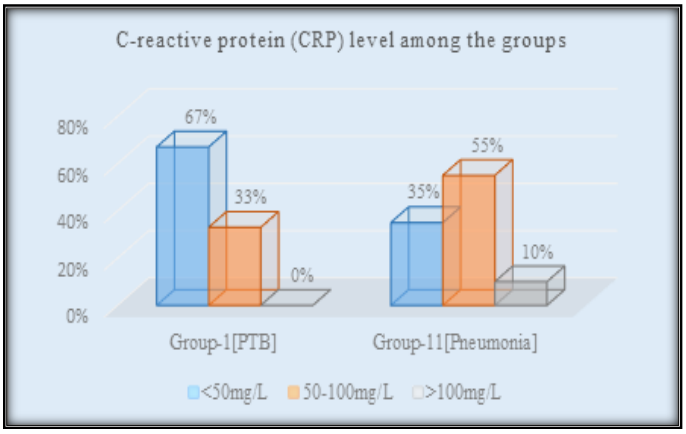

Figure 4: C-reactive protein (CRP) level among the groups (N=200)

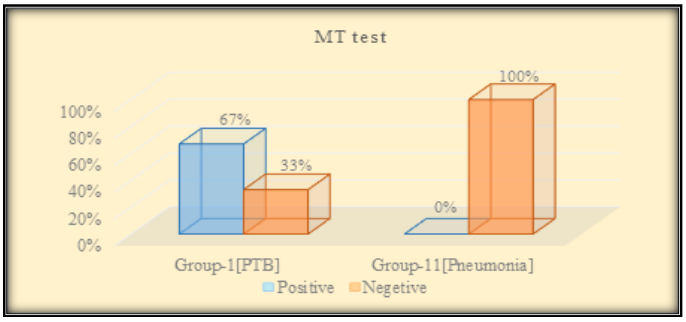

Figure 5: Mantoux test level in different groups of the study population (N=200)

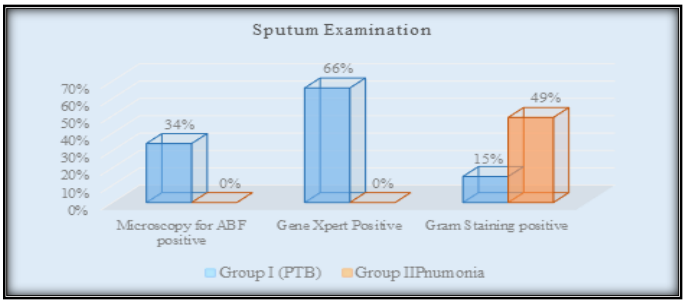

Figure 6: Sputum examination among different groups of the study population (N=200)

About 34% of group I patients had positive sputum smear microscopy examination for AFB, 66% had positive Xpert MTB/RIF and 15% had positive gram staining. In group II 49% had positive sputum Gram staining.

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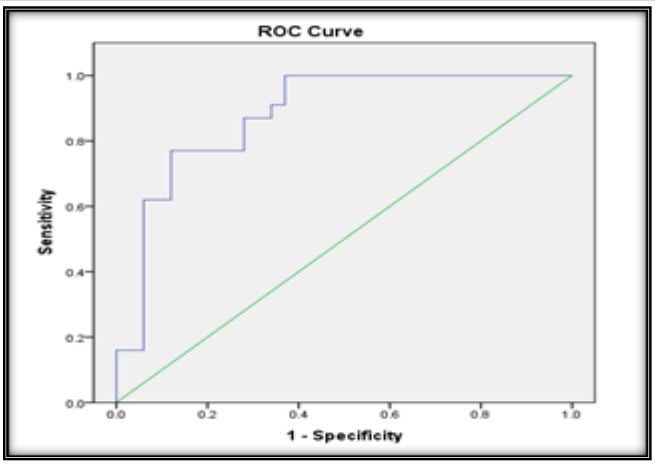

Figure 7: ROC analysis of CA 125 in the diagnosis of patients with active pulmonary tuberculosis.

Table 1: Distribution of study population according to age group (N=200)

Age Group	Group I (Pulmonary TB) n(%)	Group II (Pneumonia) n(%)	P-value
18-30 yrs.	18(18.0%)	0	<0.001
31-40 yrs.	25(25.0%)	9(9.0%)	
41-50 yrs.	30(30.0%)	22(22.0%)	
51-60 yrs.	21(21.0%)	41(41.0%)	
>60 yrs.	6(6.0%)	28(28.0%)	
Mean age (years)	42.59±12.73	54.02±9.49	

Table 2: Distribution according to occupation (N=200)

Occupation	Group I (Pulmonary TB) n(%)	Group II (Pneumonia) n(%)
Housewife	15(15.0%)	29(29.0%)
Service holder	30(30.0%)	27(27.0%)
Businessman	21(21.0%)	19(19.0%)
Farmer	16(16.0%)	15(15.0%)
Unemployed	9(9.0%)	10(10.0%)
Student	9(9.0%)	0(0.0%)

Table 3: Distribution of study population according to socio-economic status (N=200)

Socio-economic status	Group I (Pulmonary B) n(%)	Group II (Pneumonia) n(%)
low income	46(46.0%)	41(41.0%)
Middle income	51(51.0%)	54(54.0%)
High income	3(3.0%)	5(5.0%)

Table 4: Sign-symptoms of study Population (N=200)

Clinical features	Group I (Pulmonary TB) n(%)	Group II (Pneumonia) n(%)
Cough	100(100.0%)	91(91.0%)
Sputum	81(81.0%)	58(58.0%)

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Fever	73(73.0%)	94(94.0%)
Weight loss	46(46.0%)	0(0.0%)
Chest pain	24(24.0%)	56(56.0%)
Shortness of breath	25(25.0%)	57(57.0%)

Table 5: X-ray findings in the study population (N=200)

X-ray findings	**Group I (Pulmonary TB) n(%)**	**Group II (Pneumonia) n(%)**
Chest X-ray findings		
Patchy opacity	40(40.0%)	0(0.0%)
Consolidation in different lobe	22(22.0%)	100(100.0%)
Cavitary lesion	7(7.0%)	0(0.0%)
Upper lobe consolidation	28(28.0%)	0(0.0%)
Others	3(3.0%)	0(0.0%)
Additional Chest X-ray findings		
Pleural effusion	10(10.0%)	45(45.0%)
Collapse	8(8.0%)	0(0.0%)
Lymphadenopathy	20(20.0%)	0(0.0%)

Table 6: Comparison between the 2 groups according to serum CA-125 values (N=200)

	CA-125 level (IU/L)	**CA-125 range (min-max)**	**P value**
Group I (Pulmonary TB)	62.29±31.51	16.60-130.0	<0.001
Group II (Bacterial pneumonia)	22.95±8.25	2.60-37.40	

AUC	**Std. Error**	**P-value**	**Asymptotic 95% CI**	
			Lower Bound	**Upper Bound**
0.880	0.025	<0.001	0.831	0.928
*AUC: Area under the curve; CI: Confidence Interval				

ROC analysis of CA-125 in the diagnosis of patients with active pulmonary tuberculosis found an AUC of 0.880 (95% CI 0.831-0.928) which was statistically significant (p<0.001). A cut-off value measured ≥31.7 U/mL showed 72% sensitivity and 87% specificity.

Table 7: Cross-tabulation of Serum CA-125 with pulmonary TB and bacterial pneumonia based on derived cut-off value.

Serum CA-125 level (U/mL)	**Pulmonary TB**		**Total**
	Yes	**No**	
≥31.7(U/mL)	True Positive 72	False Positive 13	All patient (TP+FP) 85
<31.7 (U/mL)	False Negative 28	True Negative 87	All patient (FN+TN) 115
	All patients with EV (TP+FN) 100	All patients without EV (FP+TN) 100	200

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Among 100 cases a cut-off value of serum CA-125 of ≥31.7 U/mL could detect truly 72 cases of Pulmonary Tuberculosis.

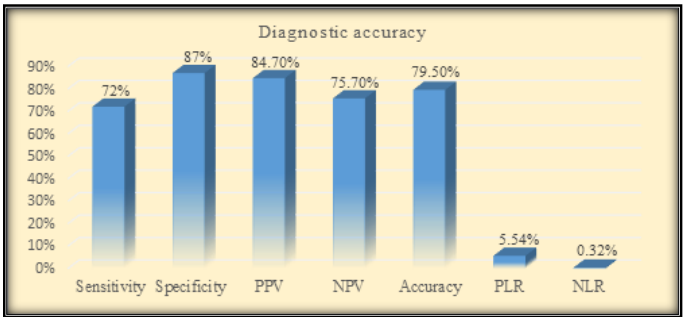

Figure 8: Diagnostic accuracy of Serum CA-125 to distinguish pulmonary TB from bacterial pneumonia.

A cut-off value of Serum CA-125≥ 31.7 U/mL showed sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy72%, 87%, 84.7%, 75.7%, 5.54%, 0.321%, and 79.5% respectively.

DISCUSSION

According to World Health Organization (2011)[24] many people have had undetected tuberculosis (TB) for a long time. late detection of PTB increases the risk of the disease transmission to the community, also results in poor health outcomes, or causes physical, and mental distress and economic hardship to the individual and their family. The Global TB burden is declining slowly. It could be expedited by programs focusing on early diagnosis and treatment. Globally remarkable efforts are being made to accelerate the development and expansion of new diagnostic technologies. However, diagnosing pulmonary tuberculosis remains dependent upon sputum smear and culture, chest radiography, and clinical sign symptoms. Currently, 57% of global tuberculosis patients are being diagnosed bacteriologically.[25] However, in some cases of pulmonary TB, Acid Fast Bacilli stains in sputum samples may be negative or respiratory specimens may not be available, and other methods have to be used to establish the diagnosis of TB.[15] The tumor marker Cancer antigen-125 (CA-125) has been studied as a useful diagnostic tool for tuberculosis and its role to differentiate pulmonary tuberculosis from other pulmonary infections has also been studied.[20] The current study aimed to detect if there is any role of tumor marker CA-125 as a tool in distinguishing pulmonary tuberculosis from bacterial pneumonia. In this study, the total number of respondents was 200.Among them, 100 patients with pulmonary tuberculosis (PTB), the majority of respondents were aged between 41-50 years (30.0%) followed by 25% at 31-40 years with a mean age of 42.59±12.73 years. Among 100 pneumonia patients, the majority were in the age group of 51-60 years (41.0%) followed by 28% in >60 years with a mean age of 54.02±9.49 years. A hospital-based study in India found that about 72.5% of patients with PTB were above 40 years of age [26]. Another study in India showed that 61.7% patients of with pulmonary tuberculosis were within the age group of 15 - 34 years.[28] Among infected persons, the incidence of tuberculosis was highest during late adolescence and early

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adulthood the reasons are unclear.[29] The majority of patients in this study in both pulmonary TB (73.0%) and pneumonia (61.0%) were male. In a previous study, the differences in sociodemographic characteristics in two periods, from the very beginning of the 21st century and 10 years after, were examined. In both observed periods, male people suffered from tuberculosis more frequently.[29] Among hospitalized pneumonia patients studied by[30] found the majority of patients were male. The majority of patients were service holders in group I (30.0%) and housewife in group II (29.0%). Most of the patients belonged to a middle-income family in our study, 51.0% and 54.0 % respectively in group I and group II. Cough was the predominant clinical feature found in 100% of patients, followed by 81% sputum, 73% fever, and 46% weight loss. Sajith et al. (2015) found in their study about clinical features of tuberculosis that cough with expectoration is prevalent in 96.5% of patients followed by weight loss (80.7%), fever (73.7%), and loss of appetite (54.4%). ESR was in the level of 50-100 mm in 1st hour in 67% of PTB cases,15% had >100 mm and in pneumonia, it was only 21% had ESR in 50-100 mm. Mandal and Chavan (2016)[31] found ESR was elevated in 87 (87%) and normal in 26 (26%) of PTB patients. The mean ESR in all patients was 67.6 mm/hr. 55.0% of pneumonia patients had CRP levels between 50-100 mg/L compared to 33% in PTB. 92% of CAP patients had elevated CRP with a median value of 65 mg/L found in a study by Lagerström, Engfeldt, and Holmberg (2006).[32] About 67% had Mantoux test positive in PTB cases with 100% negative in the pneumonia group. Sputum examination revealed that 34% had sputum smear microscopy positive for AFB, and 66% had sputum Xpert MTB/RIF positive for AFB in the PTB group. X-ray findings showed that 40.0% had patchy opacity, 28.0% had upper lobe consolidation, and 100% of patients with pneumonia had consolidation in different lobes. In the current study, it was found that mean CA-125 levels were significantly higher (p-value <0.001) among group I that is in pulmonary tuberculosis (62.29±31.51 U/mL) compared to bacterial pneumonia group (22.95±8.25U/mL). About 59% of PTB cases had a high level of CA-125 level (≥46 U/mL) while among pneumonia patients, 100% had a normal CA-125 level (<46 U/mL). A similar study by Mohammad et al. (2016)[33] found significantly higher mean CA-125 value in pulmonary TB patients (65.58±6977 U/mL) compared to the pneumonia group (18.36 ± 8.89, P=0.004), which is to some extent close to the value in the present study. In Said et al. (2013)[21] study It was found that mean Ca 125 levels were significantly higher in pulmonary tuberculosis (93.5 ± 138.9 U/ml) compared to the pneumonia group (B1=31.2 ± 34.2, P=0.03). This value is much higher than the present study, probably due to extent of radiological changes in the lungs and different methods of measuring CA-125.As Said et al. (2013)[21] showed a significant correlation between radiological extensive disease and increased levels of CA-125 (r = 0.56, P = 0.003).

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Besides different methods of measuring CA-125 can result in inconsistency of CA125 levels.[34] On the other hand, Kim et al. (2010)[35] study showed a lower mean value of CA-125 in patients with active pulmonary TB (54.5± 22.4) lower than in our study. This may be due to the difference in ways of the diagnosis of tuberculous patients. They depend on sputum culture while in this research; we depended on sputum smear-probably with a higher bacillary load than culture. ROC analysis of CA-125 in the diagnosis of patients with active pulmonary tuberculosis found that, at a serum CA-125 of ≥31.7 U/mL as a cut-off value, it had sensitivity, specificity, positive and negative predictive values, positive and negative Likelihood ratios, and diagnostic accuracy of 72%, 87%, 84.7%, 75.7%, 5.54%, 0.321%, and 79.5% respectively. For estimation of the activity of TB, Yilmaz et al. (2001)[36] found a sensitivity and specificity of Ca 125 to be 97.5% and 100%, respectively at a 31 U/mL cut-off point. Fortún et al. (2009)[20] found a cut-off value of CA-125 for TB diagnosis of 32.5 IU/mL, with sensitivity, specificity, positive predictive value, and negative predictive value of 68.6%, 77.8%, 66.7%, and 79%, respectively. Said et al (2013)[21] found the sensitivity and specificity of Ca-125 to be 81.4% and 95%, respectively, at a 34.6 U/ml cut-off point. Mohammad et al. (2016)[33] showed that at a serum CA-125 level of 21.05 U/mL as a cut-off value, CA-125 had sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of 82.5%,72.5%, 77.3%, 83.3%, and 80.0% respectively.

CONCLUSIONS

The present study seems to conform to the results of other similar studies that, serum CA-125 levels in patients with active pulmonary tuberculosis are significantly higher than those observed in patients with pneumonia. So serum CA-125 level measurement may guide the clinicians as a useful marker to differentiate pulmonary tuberculosis from bacterial pneumonia in suspected cases when AFB stain of respiratory samples is negative or not available. Therefore, further study is necessary to get a more precise result and further recommendations.

Limitations

This was a single-center study. Sputum smear microscopy for Gram stain and/or culture could not be done in all pneumonia patients. The sample size was small.

Recommendation

Further study with a more generalized study population is recommended. Serum CA-125 level measurement may help clinicians by acting as a useful marker to differentiate pulmonary tuberculosis from bacterial pneumonia when sputum or respiratory samples are negative for AFB or not available.

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REFERENCES

1. Alffenaar JWC, Stocker SL, Forsman LD, Garcia-Prats A, Heysell SK, Aarnoutse RE, et al. Clinical standards for the dosing and management of TB drugs. Int J Tuberc Lung Dis. 2022;26(6):483-499. doi: 10.5588/ijtld.22.0188.
2. Akkerman OW, Duarte R, Tiberi S, Schaaf HS, Lange C, Alffenaar JWC, et al. Clinical standards for drug-susceptible pulmonary TB. Int J Tuberc Lung Dis. 2022;26(7):592-604. doi: 10.5588/ijtld.22.0228.
3. Mohapatra PR, Mishra B, Dutta A, Bhuniya S. Responding to WHO´s 4-month regimen for drug-susceptible pulmonary TB. Int J Tuberc Lung Dis. 2022;26(9):898-899. doi: 10.5588/ijtld.22.0313.
4. Banu S, Rahman MT, Uddin MK, Khatun R, Ahmed T, Rahman MM, et al. Epidemiology of tuberculosis in an urban slum of Dhaka City, Bangladesh. PLoS One. 2013;8(10):e77721. doi: 10.1371/journal.pone.0077721.
5. Nahid P, Pai M, Hopewell PC. Advances in the diagnosis and treatment of tuberculosis. Proc Am Thorac Soc. 2006;3(1):103-10. doi: 10.1513/pats.200511-119JH.
6. Srikanth P, Kamesh S, Daley P. Bleach optimization of sputum smear microscopy for pulmonary tuberculosis. Indian J Tuberc. 2009;56(4):174-84.
7. Zingue D, Weber P, Soltani F, Raoult D, Drancourt M. Automatic microscopic detection of mycobacteria in sputum: a proof-of-concept. Sci Rep. 2018;8(1):11308. doi: 10.1038/s41598-018-29660-8.
8. Padmapriyadarsini C, Narendran G, Swaminathan S. Diagnosis & treatment of tuberculosis in HIV co-infected patients. Indian J Med Res. 2011;134(6):850-65. doi: 10.4103/0971-5916.92630.
9. Hossain MD, Ahmed JU, Rahim MA, Musa AK, Latif ZA. Bangladesh national guidelines on the management of tuberculosis and diabetes mellitus co-morbidity (summary). Indian J Endocrinol Metab. 2016;20(6):853-857. doi: 10.4103/2230-8210.192898.
10. Jaroenram W, Kampeera J, Arunrut N, Sirithammajak S, Jaitrong S, Boonnak K, et al. Ultrasensitive detection of Mycobacterium tuberculosis by a rapid and specific probe-triggered one-step, simultaneous DNA hybridization and isothermal amplification combined with a lateral flow dipstick. Sci Rep. 2020;10(1):16976. doi: 10.1038/s41598-020-73981-6.
11. Afrasiabian S, Mohsenpour B, Bagheri KH, Sigari N, Aftabi K. Diagnostic value of serum adenosine deaminase level in pulmonary tuberculosis. J Res Med Sci. 2013;18(3):252-4.
12. Saw SH, Tan JL, Chan XY, Chan KG, Ngeow YF. Chromosomal rearrangements and protein globularity changes in Mycobacterium tuberculosis isolates from cerebrospinal fluid. PeerJ. 2016;4:e2484. doi: 10.7717/peerj.2484.
13. Chang K, Lu W, Wang J, Zhang K, Jia S, Li F, et al. Rapid and effective diagnosis of tuberculosis and rifampicin resistance with Xpert MTB/RIF assay: a meta-analysis. J Infect. 2012;64(6):580-8. doi: 10.1016/j.jinf.2012.02.012.
14. Trébucq A, Enarson DA, Chiang CY, Van Deun A, Harries AD, Boillot F, et al. Xpert® MTB/RIF for national tuberculosis programs in low-income countries: when, where and how? Int J Tuberc Lung Dis. 2011;15(12):1567-72. doi: 10.5588/ijtld.11.0392.
15. Foulds J, O'Brien R. New tools for the diagnosis of tuberculosis: the perspective of developing countries. Int J Tuberc Lung Dis. 1998;2(10):778-83.
16. Ameglio F, Giannarelli D, Cordiali-Fei P, Pietravalle M, Alemanno L, Paone G, et al. Use of discriminant analysis to assess disease activity in pulmonary tuberculosis with a panel of specific and nonspecific serum markers. Am J Clin Pathol. 1994;101(6):719-25. doi: 10.1093/ajcp/101.6.719.
17. Bast RC Jr, Xu FJ, Yu YH, Barnhill S, Zhang Z, Mills GB. CA 125: the past and the future. Int J Biol Markers. 1998;13(4):179-87. doi: 10.1177/172460089801300402.
18. Fortún J, Martín-Dávila P, Méndez R, Martínez A, Norman F, Rubi J, et al. Ca-125: a useful marker to distinguish pulmonary tuberculosis from other pulmonary infections. Open Respir Med J. 2009;3:123-7. doi: 10.2174/1874306400903010123.
19. Yilmaz A, Ece F, Bayramgürler B, Akkaya E, Baran R. The value of Ca 125 in the evaluation of tuberculosis activity. Respir Med. 2001;95(8):666-9. doi: 10.1053/rmed.2001.1121.
20. Elias J, Kew MC. Evaluation of CA 125 as a serum marker of hepatocellular carcinoma. Int J Cancer. 1990;46(5):805-7. doi: 10.1002/ijc.2910460510.
21. Zhao P, Yu Q, Zhang A, He F, Xu S, Chen L. Serum CA-125 for the diagnosis of pulmonary tuberculosis: a systematic review and meta-analysis. BMC Infect Dis. 2021;21(1):1091. doi: 10.1186/s12879-021-06772-7.
22. Ma J, Xia D, Hu J, Fu R, Xu L, Zhang Y, et al. Predictive Role of Serum Tumor Markers in Diagnosis of

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Page no- 357-368 | Section- Research Article (Internal Medicine)

Pulmonary Tuberculosis. Iran J Public Health. 2016;45(4):435-40.
23. Fortún J, Martín-Dávila P, Méndez R, Martínez A, Norman F, Rubi J, et al. Ca-125: a useful marker to distinguish pulmonary tuberculosis from other pulmonary infections. Open Respir Med J. 2009;3:123-7. doi: 10.2174/1874306400903010123.
24. Ameglio F, Giannarelli D, Cordiali-Fei P, Pietravalle M, Alemanno L, Paone G, et al. Use of discriminant analysis to assess disease activity in pulmonary tuberculosis with a panel of specific and nonspecific serum markers. Am J Clin Pathol. 1994;101(6):719-25. doi: 10.1093/ajcp/101.6.719.
25. Mahajan M, Singh NP, Gadre DJ, Talwar V, Gupta HC, Agarwal DS. Detection of IgM antibodies in pulmonary tuberculosis by ELISA using A60 antigen. J Commun Dis. 1996;28(3):176-80.
26. Giri PA, Deshpande JD, Phalke DB. Prevalence of Pulmonary Tuberculosis Among HIV Positive Patients Attending Antiretroviral Therapy Clinic. N Am J Med Sci. 2013;5(6):367-70. doi: 10.4103/1947-2714.114169.
27. Mondal MN, Nazrul HM, Chowdhury MR, Howard J. Socio-demographic factors affecting knowledge level of Tuberculosis patients in Rajshahi City, Bangladesh. Afr Health Sci. 2014;14(4):855-65. doi: 10.4314/ahs.v14i4.13.
28. Khazaei S, Nematollahi S, Doosti-Irani A, Zahiri A, Mofarrah-Zat A, Ayubi E, et al. Spatio-Temporal Analysis of Tuberculosis in Hamadan Province, West of Iran, from 1992 to 2013. Tanaffos. 2019;18(1):18-24.
29. Narasimhan P, Wood J, Macintyre CR, Mathai D. Risk factors for tuberculosis. Pulm Med. 2013;2013:828939. doi: 10.1155/2013/828939.
30. Shah BA, Singh G, Naik MA, Dhobi GN. Bacteriological and clinical profile of Community acquired pneumonia in hospitalized patients. Lung India. 2010;27(2):54-7. doi: 10.4103/0970-2113.63606.
31. Ukpe IS, Southern L. Erythrocyte sedimentation rate values in active tuberculosis with and without HIV co-infection. S Afr Med J. 2006;96(5):427-8.
32. Lagerström F, Engfeldt P, Holmberg H. C-reactive protein in diagnosis of community-acquired pneumonia in adult patients in primary care. Scand J Infect Dis. 2006;38(11-12):964-9. doi: 10.1080/00365540500388826.
33. Mohammad OI, Okab AA, El Behisy MM, Sudhom FGT. Value of CA-125 in diagnosis and assessment of severity of active pulmonary tuberculosis. Egypt J Chest Dis Tuberc. 2016;65(1):205-209.
34. Weiland F, Fritz K, Oehler MK, Hoffmann P. Methods for identification of CA125 from ovarian cancer ascites by high-resolution mass spectrometry. Int J Mol Sci. 2012;13(8):9942-9958. doi: 10.3390/ijms13089942.
35. Kim SY, Hong Y, Choi CM, Oh YM, Lee SD, Kim WS, et al. Elevated serum CA-125 levels in patients with non-tuberculous mycobacterial lung disease. Respirology. 2010;15(2):357-60. doi: 10.1111/j.1440-1843.2009.01686.x.
36. Andréjak C, Lescure FX, Douadi Y, Laurans G, Smail A, Duhaut P, et al. Non-tuberculous mycobacteria pulmonary infection: management and follow-up of 31 infected patients. J Infect. 2007;55(1):34-40. doi: 10.1016/j.jinf.2007.01.008.

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