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CLINICAL DISCRIMINATION BETWEEN TUBERCULOUS AND MALIGNANT PLEURAL EFFUSIONS: AN ANALYSIS BASED ON BIOMARKERS AND SOCIODEMOGRAPHIC CHARACTERISTICS

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Abstract:

Background: Many times, it is difficult to differentiate between malignant & tubercular pleural effusion because of some common symptoms in both diseases. The present study was aimed to differentiate these two-disease based on pleural fluid biomarkers & some sociodemographic factors.

Material & methods: The present hospital based cross-sectional study was conducted in Government medical college Akola, Maharashtra. Total 50 study subjects were studied during in time period. 25 cases of Microbiologically confirmed Tuberculosis & 25 cases of malignancy confirmed on cytology were selected randomly from medicine ward & their pleural fluid sample were sent in pathology department for further evaluation. Comparison between these two were done on the basis of sociodemographic profile & pleural fluid biomarkers like pH, LDH, TLC, ADA, glucose, protein etc. P values were calculated to know the statistical significant difference between two diseases.

Results: Sociodemographic profile like age, weight & personal habits like smoking, alcohol consumption, biomass fuel exposure also Pleural fluid biomarkers like pleural fluid ADA, TLC, glucose were found statistically significant with diagnosis of TB or malignancy.

Conclusion: Sociodemographic profile & Pleural fluid biomarkers like pleural fluid ADA, TLC, glucose, protein can be considered as a tool to differentiate malignant from tubercular pleural effusion.

Key words: Pleural effusion, biomarkers, tuberculosis, malignancy.

INTRODUCTION

Tubercular & malignant pleural effusion are most common types of exudative pleural effusion. Prompt discrimination between two diseases is far most important for early intervention & treatment. Because of the immunological response to tubercular bacteria and a smaller number of TB bacilli, many times it is very difficult for microbiological confirmation.[1]

Similarly, a major hindrance in diagnosing malignant effusions is the presence of false negative cytological results in about 40% of cases.[2] Needle biopsy of the pleura has a low sensitivity in detecting malignancy and thoracoscopy, which can be a definitive procedure for both tuberculosis and neoplasm, is invasive and not widely available.[3]

Ideally the gold standard for diagnosis of tubercular pleural effusion is its microbiological confirmation in pleural fluid but because of paucibacillary nature of the disease it is always not practical to do so. Thus, doing some supportive investigations like pleural fluid biomarkers like ADA, LDH, pleural fluid glucose & protein levels etc are always reliable to distinguish tubercular from malignant effusion. [4]

While considering a potent biomarker in TB pleural effusion, ADA is considering as effective biomarker for diagnosis of TB. ADA is a purine-degrading enzyme present in profusion in tubercular pleural effusions and it is rapid & inexpensive assay. ADA level above 40 IU is commonly considered as the diagnostic cut-off for EPTB. A 2019meta-analysis including 174 publications with 27009 patients reported a high pooled sensitivity (92%) and specificity (90%) for pleural fluid ADA in diagnosing EPTB[5]

Considering above facts the present cross sectional study was planned to study the biomarkers as a distinguishing factor for tubercular & malignant pleural effusion.

MATERIALS & METHODS

The present hospital based cross-sectional study was conducted in the department of General Medicine of Government medical college Akola in Maharashtra state. The above study was conducted during period March 2016 to January 2017.

Total 50 cases of pleural effusion diagnosed on x ray were included in the study. Among that 25 microbiologically confirmed cases i.e. pleural fluid on CBNAAT suggestive of MTB detected were compared with 25 cytologically confirmed malignant pleural effusion cases retrospectively. Patients with exudative pleural effusion having either TB or malignancy with ready to give consent to participate in study were included in the study while transudative pleural effusion cases or inconclusive cases on cytology & having both TB & malignancy were excluded from study.

Pleural fluid sample was sent for biomarkers like ADA, LDH, pleural fluid glucose, protein & pleural fluid biochemistry etc. Also, on predesigned pretested questionnaire with complete sociodemographic information including personal habits were recorded.

Data was entered in Microsoft excel & statistical analysis was done using SPSS trial version 21 software. Results were explained in tabular format. Chi square test was applied for qualitative data and students t test was applied for quantitative data to calculate p value. P value less than 0.05 was considered as statistically significant.

RESULTS

Table No.1: Distribution of study subjects according to age.

Age group (In	Diagnosis	Total

years)	Tuberculosis	Malignancy	
<30	08 (32%)	02 (08%)	10 (20%)
31-40	03 (12%)	00 (00%)	03 (6%)
41-50	04 (16%)	06 (24%)	10 (20%)
51-60	05 (20%)	05 (20%)	10 (20%)
>61	05 (20%)	12 (48%)	17 (34%)
Total	25(100%)	25 (100%)	50 (100%)
(X^2=9.882, DF=4, P value=0.04246)			

The mean age of cases with TB was 44.28 ± 16.59 years while those with malignancy mean age were 57.52 + 12.65 years. The mean difference of age was statistically significant (P=0.002631). TB was observed in younger age group while malignancy was common in elderly age group and p value was statistically significant.

Figure: Distribution of study subjects according to age.

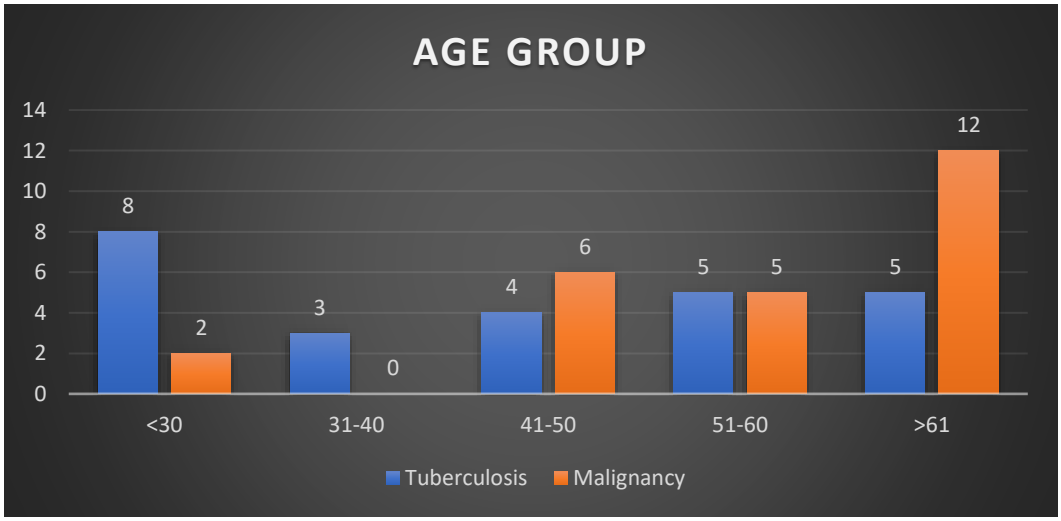


Table No.2: Distribution of study subjects according to Gender

Age group (In years)	Diagnosis		Total
	Tuberculosis	Malignancy	
Male	18 (72%)	11 (44%)	29 (58%)
Female	07 (28%)	14(56%)	21 (42%)
Total	**25 (100%)**	**25 (100%)**	**50 (100%)**
(X^2=4.023, DF=1, P value=0.02244)			

In tuberculosis more than half patients were male (72%) while in malignancy both genders were equally involved with slightly high in females. The statistical difference between gender and above mentioned two diseases were statistically significant.

Table No.3: Distribution of study subjects according to BMI

Weight	Diagnosis		Total
	Tuberculosis	Malignancy	

Underweight	11 (44%)	06 (24%)	17 (34%)
Normal	12 (48%)	14 (56%)	26 (52%)
Overweight	02 (8%)	05 (20%)	07 (14%)
Total	**25 (100%)**	**25 (100%)**	**50 (100%)**
(X^2=2.678, DF=2, P value=0.2621)			

In tuberculosis 44% study subjects were underweight while in malignancy 24% study subjects were underweight. But the statistical difference was not significant.

Table No.4: Distribution of study subjects according to personal habits

personal habits	Diagnosis		Total	P value
	Tuberculosis	Malignancy		
Smoker				
Non-Smoker	20 (80%)	10 (40%)	30(60%)	
Smoker	03 (12%)	12 (48%)	15 (30%)	0.01149
Ex-Smoker	02 (8%)	03 (12%)	05 (10%)	
Tobacco Addiction				
Absent	13 (52%)	13 (52%)	26 (52%)	
Present	09 (36%)	11 (44%)	20 (40%)	0.5488
Ex-Tobacco Chewer	03 (12%)	01 (4%)	04 (8%)	
Alcohol Consumption				
Non-Alcoholic	17 (68%)	16 (64%)	33 (66%)	
Alcoholic	07 (28%)	06 (24%)	13 (26%)	0.5749
Ex-Alcoholic	01 (4%)	03 (12%)	04 (8%)	
Biomass Fuel Exposure	21 (84%)	16 (64%)	37 (74%)	0.1235
Absent	04 (16%)	09 (36%)	13 (26%)	
Present				

Active smokers with tobacco addiction were found more in malignancy patients however tuberculosis cases were more alcoholic than malignant cases. None of the habit except smoking were statistically significant to show any difference between two diseases.

Table No.5: Distribution of study subjects according to plural fluid analysis

	Diagnosis		P value
	Tuberculosis	Malignancy	
Pleural fluid pH	7.46 ± 0.23	7.46± 0.27	0.9999
Pleural fluid LDH (IU/L)	922.52±584.526	640.96±628.5546	0.02244
Pleural fluid glucose (mg/dL)	65.32±27.91	89.08± 40.76	0.009130
Pleural fluid protein(g/dL)	5.15 ± 0.81	4.544±1.07	0.04228
Pleural fluid TLC	928.4±782.3468	444.72 ± 588.44	0.01707

(cells/cumm)			
Pleural fluid ADA	59.31± 19.26	12.88± 6.15	0.000000400

Pleural fluid LDH, ADA, Protein, TLC were statistically significant high in Tubercular pleural effusion. While pleural fluid glucose was higher in malignant pleural effusion. Pleural fluid LDH, ADA, Protein, glucose was showing statistically significant difference between two diseases.

DISCUSSION

In present study pleural fluid biomarkers such a pleural fluid ADA, LDH, Glucose, Protein was found to be statistically significant for differentiating tubercular from malignant pleural effusion.

Pleural fluid ADA levels>40 U can be considered as tubercular effusion but should not be interpreted in isolation, as high levels are not exclusively found in Tuberculosis [6,7]. In fact, very high levels (>250 U·L−1) are uncommon in Tuberculosis, and should prompt consideration ofan alternative diagnosis such as lymphoma or bacterial empyema.[8]

In a retrospective study by Wang J et al, comparing72 tuberculous effusions to 47 parapneumonic effusions in a high TB endemic area, a pleural LDH/ADAratio of <16.2 was found to reliably identify tuberculous effusions, with a sensitivity and specificity of93.6% and 93.1%, respectively.[9]

TB pleural effusions are typically straw-coloured exudates [10]. Fluid lactate dehydrogenase (LDH) and protein are elevated in over 75% of cases, and fluid glucose may be low compared with serum.[11] These similar findings were found in the present study.

While considering socio demographic profile, in this study age and smoking habit was considered as statistically significant. Similarly, many studies concludes that age and smoking were most powerful predictor for discriminating tubercular from malignant pleural effusion. [12,13]

Thus, these biomarkers and some sociodemographic factors can give the clinicians a glimmer to diagnose the correct disease and can aid them to facilitate early intervention and treatment for the same.

CONCLUSION

Biochemical pleural biomarkers such as ADA, LDH, glucose, protein, along with age and smoking habits are potent discriminating factors to distinguish tubercular from malignant pleural effusion.

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