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Extra-pulmonary tuberculosis (EPTB): Study of clinico-demographic profile, and comparison of microbiological diagnostic modalities with special emphasis on role of CBNAAT in detecting rifampicin resistance in fluid specimens

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Abstract
The purpose of our study was to evaluate the place of CBNAAT in the diagnosis of extra-pulmonary TB in fluid specimens, and also detecting drug resistance in comparison to the Gold Standard - MGIT Bactec Culture.
Material and Methods: In prospective observational study of 2 yrs. among 165 EPTB cases, we studied the clinical presentation, compared the results of microbiological diagnostic modalities (ZN smear, CBNAAT, MGIT Culture) and evaluated the drug resistance.
Statistics: Used Chi square test via software STATA 15 and calculated p value.
Results: The positivity rate of CBNAAT (31.30%) was higher than ZN smear (23.92%), which was in turn higher than MGIT culture (9.9%) and CBNAAT was able to detect Rifampicin resistance in 16.66% EPTB cases.
Conclusion: We concluded that, the role of CBNAAT in fluid specimens should not be undermined and should be preferred over the "Gold standard" MGIT culture.

Keywords: extra-pulmonary tuberculosis (EPTB), Cartridge based nucleic acid amplification test (CBNAT), Mycobacteria growth indicator tube (MGIT), Ziehl Neelsen (ZN) staining, rifampicin resistance

Introduction
As per evidence based INDEX TB guidelines, the committe laid "Conditional recommendations" for use of Cartridge-based nucleic acid amplification test (CBNAAT) in diagnosis of Lymph Node TB and CNS TB, and "Strong recommendation" against the use of CBNAAT in diagnosis of Pleural TB. This led us to re-evaluate the reasons behind such strong recommendations against its use especially in pleural TB cases, and review the older recommendations.

Material and Methods
After obtaining the approval from ethical committee and consent from participant subjects, we conducted a prospective observational study over a period of 2 yr. among 165 cases of clinically suspected extra-pulmonary TB cases above the age of 18 yrs. in our tertiary care centre. Among all these suspected EPTB cases we, initially studied the clinical presentation and demographic profile. Further we subjected all the fluid specimens to microbiological modalities (ZN Smear, CBNAAT, MGIT Bactec culture). We tabulated and compared the results of microbiological modalities and evaluated the Rifampicin resistance in these cases. Lastly we studied the correlation between microbiological diagnostic modalities and their radio-histopathological findings.

Statistical analysis
The data collected from 165 cases using proforma was tabulated and organized in Microsoft excel sheet. From this data master chart was prepared and tables were designed using

different variables. The data from these tables was then analysed using Chi square test via software STATA 15 and p value was calculated for different groups and the difference among the groups was quoted as to be either significant or insignificant. Finally the different microbiological diagnostic modalities were compared with culture as gold standard and their correlation with radio-histopathological findings was studied.

Observations and Results

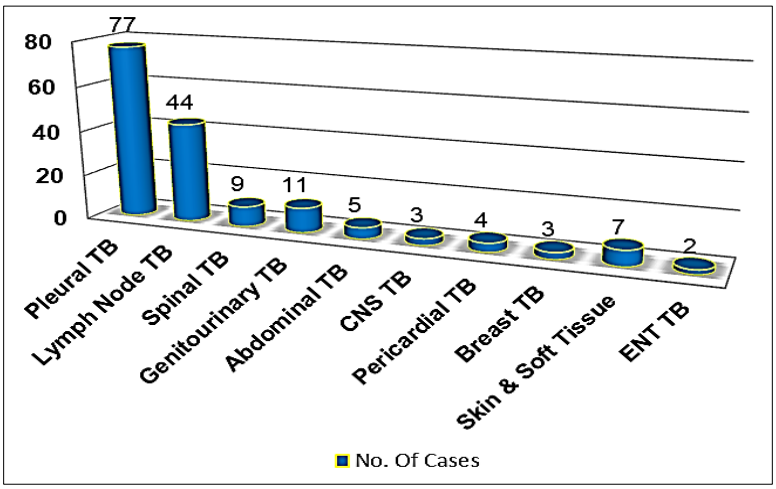

Fig 1: Presentation and distribution of different types of EPTB

Figure 1 shows presentation and distribution of 165 cases of EPTB in to 10 different groups based on system involved.

Table 1: Types of EPTB and age distribution

Age group Type of EPTB	18-28 yr. [n = 71] (%)	29-38 yr. [n = 31] (%)	39-48 yr. [n = 19] (%)	49-58 yr. (n = 11) (%)	59-68 yr. [n = 17] (%)	69-78 yr. [n = 12] (%)	79-88 yr. [n = 4] (%)
Pleural TB [n = 77]	19 (26.76)	16 (51.61)	9 (47.36)	10 (90.91)	10 (58.82)	9 (75)	4 (100)
LN TB [n = 44]	27 (38.03)	7 (22.58)	5 (26.32)	1 (9.09)	4 (23.53)	0 (0)	0 (0)
Spine TB [n = 9]	5 (7.04)	1 (3.23)	1 (5.26)	0 (0)	0 (0)	0 (0)	0 (0)
GU TB [n = 11]	9 (12.68)	1 (3.23)	1 (5.26)	0 (0)	0 (0)	0 (0)	0 (0)
Abdominal TB [n = 5]	4 (5.63)	0 (0)	0 (0)	0 (0)	1 (5.88)	0 (0)	0 (0)
CNS TB [n = 3]	0 (0)	1 (3.23)	1 (5.26)	0 (0)	0 (0)	1 (8.33)	0 (0)
Pericardial TB [n = 4]	1 (1.41)	2 (6.45)	0 (0)	0 (0)	1 (5.88)	0 (0)	0 (0)
Breast TB [n = 3]	2 (2.82)	1 (3.23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SS TB [n = 7]	4 (5.63)	0 (0)	2 (10.52)	0 (0)	1 (5.88)	0 (0)	0 (0)
ENT TB [n = 2]	0 (0)	2 (6.45)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total n/165 (%)	71 71/165 (43.03)	31 31/165 (18.78)	19 19/165 (11.51)	11 11/165 (6.66)	17 17/165 (10.30)	12 12/165 (7.27)	4 4/165 (2.42)

Pearson chi square = 64.14, p value = 0.16.

Table 1 shows the types of EPTB in different age categories.

Table 2: Types of EPTB on the basis of gender

Type of EPTB	Male [n = 95] (%)	Female [n = 70] (%)	Total [N = 165] (%)
Pleural TB [n = 77]	60/95 (63.15)	17/70 (24.28)	77/165 (46.66)
LN TB [n = 44]	14/95 (14.74)	30/70 (42.86)	44/165 (26.66)
Spine TB [n = 9]	7/95 (7.37)	2/70 (2.86)	9/165 (5.45)
GU TB [n = 11]	2/95 (2.11)	9/70 (12.86)	11/165 (6.66)
Abdominal TB [n = 5]	3/95 (3.16)	2/70 (2.86)	5/165 (3.03)
CNS TB [n = 3]	2/95 (2.11)	1/70 (1.43)	3/165 (1.82)
Pericardial TB [n = 4]	2/95 (2.11)	2/70 (2.86)	4/165 (2.42)
Breast TB [n = 3]	0 (0)	3/70 (4.29)	3/165 (1.82)
SS TB [n = 7]	4/95 (4.21)	3/70 (4.28)	7/165 (4.24)
ENT TB [n = 2]	1/95 (1.05)	1/70 (1.43)	2/165 (1.21)
Total n/165 (%)	95 95/165 (57.57%)	70 70/165 (42.42%)	165 165/165 (100%)

Pearson chi square = 37.16, p value <0.001 (Statistically significant)

Table 2 shows types of EPTB with respect to gender.

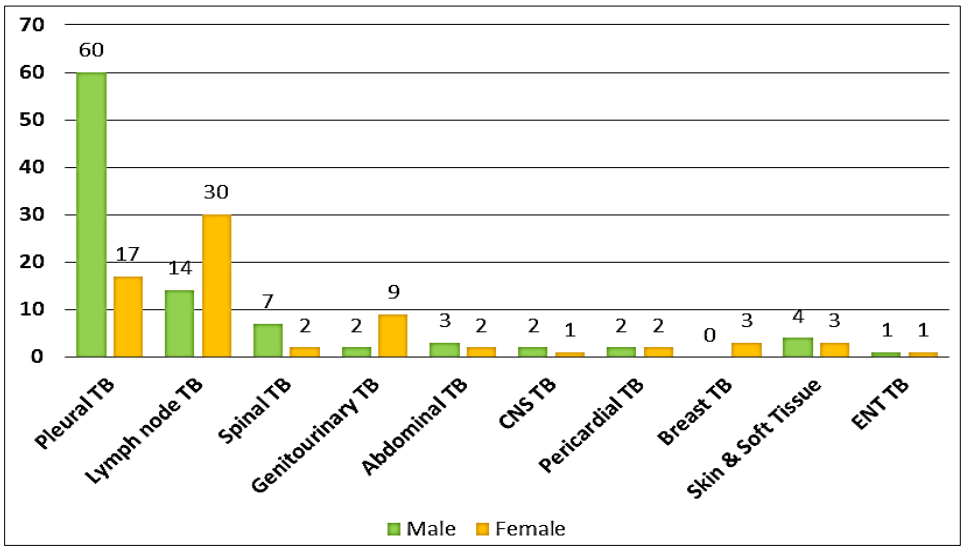

Fig 2: Distribution of different types of EPTB on basis of gender

Figure 2 shows that pleural TB (M = 60, F = 17), spine TB (M = 7, F = 2), abdominal TB (M = 3, F = 2), CNS TB (M = 2, F = 1), skin and soft tissue TB (M = 4, F = 3) were more common in male sex, whereas lymph node TB (M = 14, F = 30), genitourinary TB (M = 2, F = 9), breast TB (M = 0, F = 3), were more in female sex. However pericardial TB (M = 2, F = 2) and ENT TB (M = 1, F = 1) showed no sex predilection.

Table 3: Types of EPTB and area of residence

Type of EPTB	Rural [n = 106] (%)	Urban [n = 59] (%)	Total [N = 165] (%)
Pleural TB [n = 77]	45/106 (42.45%)	32/59 (54.24)	77/165 (46.66)
LN TB [n = 44]	32/106 (30.19)	12/59 (20.34)	44/165 (26.66)
Spine TB [n = 9]	5/106 (4.72)	4/59 (6.78)	9/165 (5.45)
GU TB [n = 11]	8/106 (7.55)	3/59 (5.08)	11/165 (6.66)
Abdominal TB [n = 5]	2/106 (1.89)	3/59 (5.08)	5/165 (3.03)
CNS TB [n = 3]	2/106 (1.89)	1/59 (1.69)	3/165 (1.82)
Pericardial TB [n = 4]	4/106 (3.77)	0 (0)	4/165 (2.42)
Breast TB [n = 3]	1/106 (0.94)	2/59 (3.39)	3/165 (1.82)
SS TB [n = 7]	6/106 (5.66%)	1/59 (1.69)	7/165 (4.24)
ENT TB [n = 2]	1/106 (0.94)	1/59 (1.69)	2/165 (1.21)
Total n/165 (%)	106 106/165 (64.24%)	59 59/165 (35.76%)	165 165/165 (100%)

Pearson chi square = 7.51, p value = 0.58.

Table 3 shows the distribution of EPTB on the basis of area of residence.

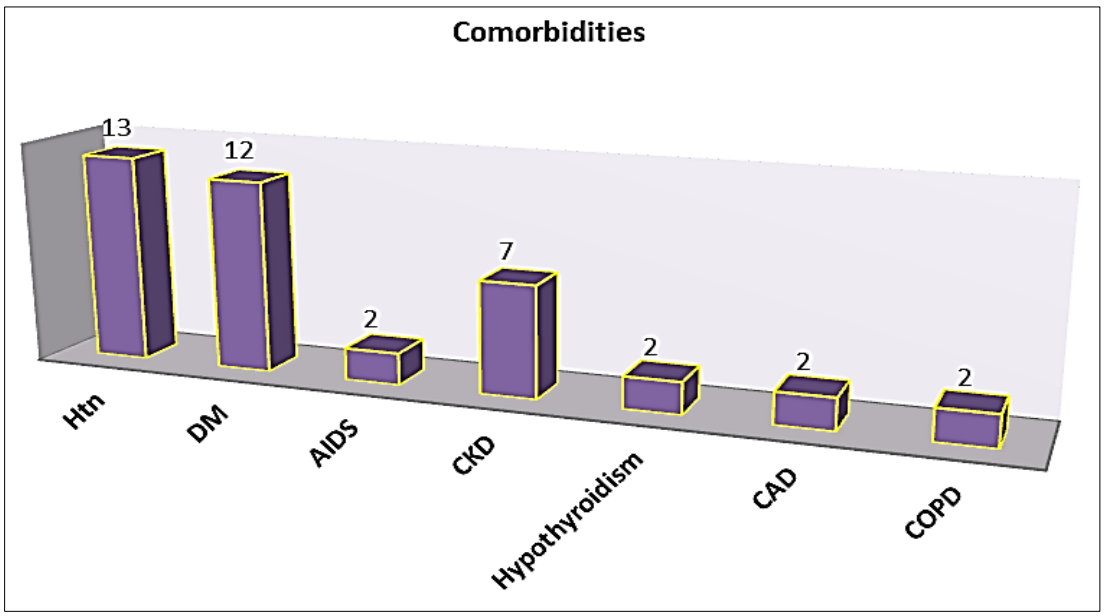

Fig 3: EPTB v/s Comorbidities

Figure 3 shows that co-morbidities commonly associated with EPTB are HTN, DM, CKD.

Table 4: Type of EPTB v/s History of previously T/T PTB or EPTB

Type of EPTB	Old T/t PTB [n = 3] (%)	Old T/t EPTB [n = 18] (%)	Total [N = 165] (%)
Pleural TB [n = 77]	3/77 (3.89)	1/77 (1.29)	77/165 (46.66)
LN TB [n = 44]	0	9/44 (20.45)	44/165 (26.66)
Spine TB [n = 9]	0	2/9 (22.22)	9/165 (5.45)
GU TB [n = 11]	0	1/9 (11.11)	11/165 (6.66)
Abdominal TB [n = 5]	0	0	5/165 (3.03)
CNS TB [n = 3]	0	0	3/165 (1.82)
Pericardial TB [n = 4]	0	0	4/165 (2.42)
Breast TB [n = 3]	0	2/3 (66.66)	3/165 (1.82)
SS TB [n = 7]	0	3/7 (42.85)	7/165 (4.24)
ENT TB [n = 2]	0	0	2/165 (1.21)
Total n/165 (%)	3 3/165 (1.81%)	18 18/165 (10.90%)	165 165/165 (100%)

Table 4 shows that out of the 165 cases, 3 cases (1.81%) had previous history of treatment for pulmonary tuberculosis and 18 cases (10.90%) had previous history of treatment for extra-pulmonary tuberculosis.

Table 5: Type of EPTB and systemic symptoms

Type of EPTB	Systemic symptoms					
Pleural TB [n = 77]	Fever	Cough	Chest pain	Dyspnea		
	49/77 (63.63)	61/77 (79.22)	56/77 (72.72)	36/77 (46.75)		
LN TB [n = 44]	Fever	Swelling	Single	Multiple	Tenderness	Sinus
	20/44 (45.45)	40/44 (90.90)	39/44 (88.63)	5/44 (11.36)	15/44 (34.09)	4/44 (9.09)
Spine TB [n = 9]	Fever	Back pain	Deformity	Abscess	Neuro. Deficit	
	5/9 (55.55)	8/9 (88.88)	3/9 (33.33)	6/9 (66.66)	2/9 (22.22)	
GU TB [n = 11]	Fever	Lower Abd pain	Urinary symptoms	Menstrual symptoms	Infertility	
	3/11 (27.27)	4/11 (36.36)	2/11 (18.18)	4/11 (36.36)	7/11 (63.63)	
Abdominal TB [n = 5]	Fever	Abd. Pain	Distension	Vomiting	Diarrhea	Jaundice
	4/5 (80.00)	4/5 (80.00)	5/5 (100.0)	4/5 (80.00)	1/5 (20.00)	2/5 (40.00)
CNS TB [n = 3]	Fever	Headache	Vomiting	Alter. sensorium	Seizures	Neck rigidity
	2/3 (66.66)	2/3 (66.66)	1/3 (33.33)	3/3 (100.0)	1/3 (33.33)	2/3 (66.66)
Pericardial TB [n = 4]	Fever	Cough	Chest pain	Dyspnea	Orthopnea	
	3/4 (75.00)	3/4 (75.00)	3/4 (75.00)	3/4 (75.00)	3/4 (75.00)	
Breast TB [n = 3]	Fever	Lump	Pain	Ulceration	Discharge	
	2/3 (66.66)	2/3 (66.66)	3/3 (100.0)	1/3 (33.33)	2/3 (66.66)	
SS TB [n = 7]	Fever	Plaque	Discoloration	Ulceration	Discharge	
	6/7 (85.71)	2/7 (28.57)	1/7 (14.28)	2/7 (28.57)	1/7 (14.28)	
	Cough	Chest pain	Dyspnea			
	5/7 (71.42)	5/7 (71.42)	5/7 (71.42)			
ENT TB [n = 2]	Fever	Sore Throat	Hoarseness	Swelling	Dysphagia	
	1/2 (50.00)	1/2 (50.00)	1/2 (50.00)	1/2 (50.00)	1/2 (50.00)	

Table 5 shows the different systemic symptoms associated with different types of EPTB and their corresponding incidence

Table 6: Type of EPTB v/s AFB smear result

Type of EPTB	AFB smear + ve [n = 39] (%)	AFB Smear – ve [n = 124] (%)	AFB smear not done [n = 2] (%)	Total number [N = 165] (%)
Pleural TB [n = 77]	6/39 (15.38)	71/124 (57.25)	0	77/165 (46.66)
LN TB [n = 44]	24/39 (61.53)	20/124 (16.12)	0	44/165 (26.66)
Spine TB [n = 9]	1/39 (2.56)	8/124 (6.45)	0	9/165 (5.45)
GU TB [n = 11]	1/39 (2.56)	8/124 (6.45)	2/165 (1.21)	11/165 (6.66)
Abdominal TB [n = 5]	1/39 (2.56)	4/124 (3.22)	0	5/165 (3.03)
CNS TB [n = 3]	0	3/124 (2.41)	0	3/165 (1.82)
Pericardial TB [n = 4]	0	4/124 (3.22)	0	4/165 (2.42)
Breast TB [n = 3]	2/39 (5.12)	1/124 (0.80)	0	3/165 (1.82)
SS TB [n = 7]	2/39 (5.12)	5/124 (4.03)	0	7/165 (4.24)
ENT TB [n = 2]	2/39 (5.12)	0	0	2/165 (1.21)
Total n/165 (%)	39 39/163 (23.92%)	124 124/163 (76.07%)	2 2/165 (1.21%)	165 165/165 (100%)

Pearson chi square = 74.32, p value <0.001

Table 6 shows that out of 166 cases subjected to ZN smear examination, (39/163) 23.92% patients tested positive for AFB smear test. Among the smear positive cases, Maximum number of patients were found in the Lymph node TB (24/39) 61.53% and pleural TB (6/39) 15.38%. Statistically significant difference was found in between the groups. (p value <0.001).

Table 7: Type of EPTB v/s Xpert MTB (CBNAAT/GENEXPERT) result

Type of EPTB	MTB detected [n = 36] (%)	MTB Not detected [n = 79] (%)	MTB Not done [n = 50] (%)	Total number [N = 165] (%)
Pleural TB [n = 77]	18/36 (50.00)	59/79 (74.68)	0	77/165 (46.66)
LN TB [n = 44]	9/36 (25.00)	2/79 (2.53)	33/50 (66.00)	44/165 (26.66)
Spine TB [n = 9]	3/36 (8.33)	4/79 (5.06)	2/50 (4.00)	9/165 (5.45)
GU TB [n = 11]	2/36 (5.55)	3/79 (3.79)	6/50 (12.00)	11/165 (6.66)
Abdominal TB [n = 5]	0	3/79 (3.79)	2/50 (4.00)	5/165 (3.03)
CNS TB [n = 3]	0	2/79 (2.53)	1/50 (2.00)	3/165 (1.82)
Pericardial TB [n = 4]	0	3/79 (3.79)	1/50 (2.00)	4/165 (2.42)
Breast TB [n = 3]	2/36 (5.55)	0	1/50 (2.00)	3/165 (1.82)
SS TB [n = 7]	2/36 (5.55)	3/79 (3.79)	2/50 (4.00)	7/165 (4.24)
ENT TB [n = 2]	0	0	2/50 (4.00)	2/165 (1.21)
Total n/165 (%)	36 36/115 (31.30%)	79 79/115 (68.69%)	50 50/165 (30.30%)	165 165/165 (100%)

Pearson chi square = 105.73, p value <0.001

Table 7 shows that on Xpert MTB testing, MTB was detected in 36/115 (31.30%) cases, and not detected in 79/115 (68.69%) cases. Out of the 36 cases diagnosed to be MTB detected, 83.33% (30/36) cases were sensitive to rifampicin and 16.66% (6/36) cases were resistant to rifampicin. Maximum number of patients in whom MTB was detected belonged to Pleural TB (18/36) 50.00%. P value was found to be statistically significant (p value <0.001).

Table 8: Type of EPTB v/s MGIT culture result

Type of EPTB	Culture growth seen [n = 11] (%)	Culture no growth [n = 100] (%)	Culture not done [n = 54] (%)	Total number [N = 165] (%)
Pleural TB [n = 77]	9/11 (81.82)	68/100 (68.00)	0	77/165 (46.66)
LN TB [n = 44]	2/11 (18.18)	9/100 (9.00)	33/54 (61.11)	44/165 (26.66)
Spine TB [n = 9]	0	7/100 (7.00)	2/54 (3.70)	9/165 (5.45)
GU TB [n = 11]	0	2/100 (2.00)	9/54 (16.66)	11/165 (6.66)
Abdominal TB [n = 5]	0	2/100 (2.00)	3/54 (5.55)	5/165 (3.03)
CNS TB [n = 3]	0	2/100 (2.00)	1/54 (1.85)	3/165 (1.82)
Pericardial TB [n = 4]	0	3/100 (3.00)	1/54 (1.85)	4/165 (2.42)
Breast TB [n = 3]	0	2/100 (2.00)	1/54 (1.85)	3/165 (1.82)
SS TB [n = 7]	0	5/100 (5.00)	2/54 (3.70)	7/165 (4.24)
ENT TB [n = 2]	0	0	2/54 (3.70)	2/165 (1.21)
Total n/165 (%)	11 11/111 (9.90%)	100 100/111 (90.09%)	54 54/165 (32.72%)	165 165/165 (100%)

Pearson chi square = 100.47 *P*<0.001

Table 8 shows that on MGIT culture, out of 111 cases, only 11 cases, (11/111) 9.90% cases were seen to have growth, whereas in (100/111) 90.09% cases, no growth was seen. Of the 11 cases with Culture growth, Pleural TB cases constituted (9/11) 81.82% and Lymph node TB constituted (2/11) 18.18%. The difference between the groups was found to be statistically significant.

Table 9: Comparison of microbiological diagnostic modalities

	Smear + VE (n)	CBNAAT + VE (n)	MGIT growth (n)
Pleural TB [n = 77]	6	18	9
LN TB [n = 44]	24	9	2
Spine TB [n = 9]	1	3	0
GU TB [n = 11]	1	2	0
Abdominal TB [n = 5]	1	0	0
CNS TB [n = 3]	0	0	0
Pericardial TB [n = 4]	0	0	0
Breast TB [n = 3]	2	2	0
SS TB [n = 2]	2	2	0
ENT TB [n = 2]	2	0	0
Total n/165 (%)	39 39/163 23.92	36 36/115 31.30	11 11/111 9.90

Table 9 depicts different types of EPTB, and shows comparison of various microbiological diagnostic modalities with culture as gold standard.

Discussion

Presentation and distribution of different types of EPTB: The distribution of different types of EPTB was Pleural TB (77/165) 46.66%, Lymph node TB (44/165) 26.66%, Genitourinary TB (11/165) 6.66%, Spine TB (9/165) 5.45%, Skin and Soft Tissue TB (7/165) 4.24%, Abdominal TB (5/165) 3.03%, Pericardial TB (4/165) 2.42%, CNS TB (3/165) 1.81%, Breast TB (3/165) 1.81%, and ENT TB (2/165) 1.21%. As per this distribution, most common type of EPTB was Pleural TB followed by Lymph node TB, whereas least common type of EPTB was ENT TB. These Findings were similar to that of the study conducted by Gaur PS *et al*. [1] with 252 EPTB cases, which showed that the most common type of EPTB was pleural TB 138/252 (54.76%), followed by lymph node TB 88/252 (34.92%). Similarly in a study conducted by Velingker A *et al*. [2] with 492 EPTB cases, the most common type of EPTB was pleural TB 194/492 (39.43%), followed by lymph node TB 136/492 (27.64%).

Types of EPTB and age distribution: Maximum number of EPTB patients (71/165) 43.03% belonged to age group of 18-28 yrs., whereas minimum number of patients (4/165) 2.42% belonged to age group of 79-88 yrs. The results showed statistically insignificant p value. These Findings were similar to that of the study conducted by Gaur PS *et al*. [1] in 252 EPTB cases, where the majority of cases (105/252, 41.7%) belonged to 31 - 40 yr. age group and least number of cases (26/252, 10.3%). Similar results were found in study conducted by Shrivastava AK *et al*. [3] among 130 EPTB patients, where the age group of 20-39 years had the highest proportion (54/130, 41.53%) of EPTB cases, while lowest proportion (7/130, 5.38%) was observed in the geriatric age group > 60 years. Further in study conducted by Aravind *et al*. [4] in 151 cases, the majority of cases 55/151 (36.42%) belonged to age group of 21 to 30 years and the mean age of the sample was 38.9 years with a SD of 16.5 years.

Types of EPTB on the basis of gender: In our study EPTB cases were more common in male sex (57.57%) compared to female sex (42.42%). On comparing different types of EPTB on the basis of gender, the results showed statistically significant difference, (p value <0.001). These Findings were similar to that of the study conducted by Shrivastava AK *et al*. [3] where they found that out of 130 EPTB patients, 53.84% were males, 46.15% were females, with Male to female ratio of 1.16:1. Similarly in study conducted by Aravind *et al*. [4] among 151 cases showed a male sex predominance with 78.7% males and 21.3% females. Also in study conducted by Tiwari VK *et al*. [5] among 108 EPTB cases, 62 cases (57.4%) were males and 46 cases (42.5%) were females, which concluded male preponderance.

Types of EPTB and area of residence: Majority of the patient belonged to rural area (64.24%) compared to urban area (35.76%). However, No statistically significant difference was found in between the groups. This was similar to that of the study conducted by Shrivastava AK *et al*. [3] where 62.30% patients were belong to urban areas and only 37.69% belong to rural areas. Also in study conducted by Pang Y *et al*. [6] they found that most of the EPTB patients belonged to rural areas.

EPTB and associated co-morbidities: In our study most common comorbidity among EPTB patients was Hypertension (13/165) 7.87%, followed by Diabetes mellitus (12/165) 7.27%, and Chronic kidney disease (7/165) 4.24%. However these findings were not in accordance with that of the study conducted by Gaur PS *et al*. [1] among 252 EPTB cases, where DM was present in 16.7% cases. Similarly in the study conducted by Shrivastava AK *et al*. [3] in 130 EPTB patients, they found that 7.69% had DM and was most commonly associated.

Type of EPTB v/s History of previously treated PTB or EPTB: In our study out of the 165 cases, 3 cases (1.81%) had previous history of treatment for pulmonary tuberculosis and 18 cases (10.90%) had previous history of treatment for extra-pulmonary tuberculosis. This finding was not in accordance with the results of study conducted by Aravind *et al*. [4] which showed that 17.22% of the sample population had past history of pulmonary tuberculosis and this was significantly higher compared to our study.

Type of EPTB and systemic symptoms: In our study pleural TB findings were similar to that of the study conducted by Cohen LA *et al*. [7] which stated that the most frequent symptoms in pleural TB are non-productive cough (70%), which is usually non-productive, and pleuritic chest pain (70%). Lymph node TB findings were similar to that of the study conducted by Gandhare A *et al*. [8] which stated that the most common presentation in lymph node TB was single, non-tender lymphadenopathy, and fever was seen in 20 - 50%, whereas sinus formation was relatively rare. Spinal TB findings were similar to that of the study conducted by Garg RK *et al*. [9] which stated that back pain was the most common presenting feature. Genitourinary TB findings were similar to that of the study by Hemal AK *et al*. [10] which stated that the association of tuberculosis and pelvic disease most frequently presented as infertility, lower abdominal pain, and altered menstrual pattern. Abdominal TB findings were similar to that of the study conducted by Underwood MJ *et al*. [11] in 24 abdominal TB cases in which the most common presenting complaint was abdominal pain in (21/24) 88%, followed by weight loss in (18/24) 75%, anorexia in (15/21) 62%, and night sweats in (13/24) 54%. CNS TB findings were similar to that quoted by PN Sutlas *et al*. [12] which stated that adults with tuberculous meningitis (TBM) present with the classic symptoms of fever, headache, neck stiffness and altered sensorium. Pericardial TB findings were in accordance with that of the study conducted by BM Mayosi *et al*. [13] which stated that chest pain, cough, and dyspnea were the common presenting features. Skin and Soft tissue TB findings were in accordance with the observations of Wang SH *et al*. [14] which stated that SS TB had a varied presentation. ENT TB findings were in accordance with that conducted by Michael RC *et al*. [15] which stated that ENT TB typically presents with hoarseness, odynophagia, and dysphagia along with loss of weight and loss of appetite. Overall fever (95/165) 57.57% was the most common constitutional symptom

associated with EPTB and night sweat (27/165) 16.36% was the least common.

Type of EPTB and ZN smear staining: In our study, out of 165 cases, 163 cases were subjected to ZN staining and in 2 cases it could not be done. Of the 163 cases, Smear for AFB was positive in 23.92% (39/163) and negative in 75.07% (124/163) cases. In the study conducted by Siddiqui MAM *et al*. [16] with 100 EPTB specimens, subjected to ZN staining, ZN smear positivity was found to be 5%. Also in study conducted by Bagdia *et al*. [19] where 108 EPTB specimens were subjected to ZN smear examination, ZN smear positivity was found to be 9.28%, both of these studies had ZN smear positivity lower than that of our study. Type of EPTB and Xpert MTB/RIF assay or PCR: Of the 165 cases of EPTB, Total of 115 cases were subjected to Xpert MTB (CBNAAT/Genexpert) and 50 cases were those in whom Xpert MTB could not be done. Of the 115 cases, MTB was detected in (36/115) 31.30% cases and MTB was not detected in (79/115) 68.69% cases. Thus Positivity rate of Xpert MTB/RIF assay was 31.30%, which was higher than the positivity rate of ZN smear i.e., 23.92%. These findings were in accordance with the study conducted by Munir MK *et al*. [17] in 403 EPTB specimens to assess the value of GeneXpert in diagnosis in comparison with ZN smear microscopy and culture, where they found that the positivity rate of ZN smear was 67.5%, of GeneXpert was 77.4% and of culture 85.1%. Similarly in the study conducted by Li Y *et al*. [18] in 420 EPTB specimens to evaluate the performance of Xpert MTB/RIF assay, the positivity rate of the Xpert MTB/RIF assay was found to be 18.4% (76/414), which was higher than culture (16.4%, 68/414) and AFB smear (9.2%, 38/414). Another study supporting our findings was that conducted by Bagdia *et al*. [19] where out of the 58 EPTB specimens subjected to ZN Staining, Genexpert and MGIT Culture, the positivity of Gene Xpert was 15.38% (8/58), of culture 12.06% (7/58), and of ZN stain 5.17% (3/58). Further in our study out of the 36 cases diagnosed to be MTB detected, 83.33% (30/36) cases were sensitive to rifampicin and 16.66% (6/36) cases were resistant to rifampicin. Maximum number of patients in whom MTB was detected belonged to Pleural TB (18/36) 50.00%.

Type of EPTB and MGIT culture: Of the 165 cases of EPTB, Total of 111 cases were subjected to MGIT Culture and 54 cases were those in whom MGIT Culture could not be done. Of the 111 cases, culture growth was seen in (11/111) 9.09% cases and growth was not seen in (100/111) 90.09% cases. The culture positivity in our study was 9.90%, which was lower than that of ZN smear positivity (23.92%). These findings were in contrast to the results of the study conducted by Siddiqui MAM *et al*. [16] in 100 EPTB specimens to compare conventional diagnostic modalities, where they found that the positivity of PCR was 70%, BACTEC culture 15% and ZN smear 5%. Similarly in the study conducted by Munir MK *et al*. [17] the culture positivity was 18.46%, which was considerably higher in comparison to the ZN smear positivity of 3.85%. Also in the study conducted by Bagdia *et al*. [19] in 108 EPTB specimens, culture positivity was 20.61%, which was higher than ZN smear positivity of 9.28%. Further in our study, out of the 11 EPTB cases with culture growth, (9/11) 81.82% were constituted by pleural TB and (2/11) 18.18% were constituted by lymph node TB. The difference between the groups was found to be statistically significant. (Pearson chi square = 100.47, $P<0.001$).

From our study we found that, the overall positivity rate of Xpert MTB/RIF was (36/115) 31.30%, with maximum proportion in pleural TB (61.54%) followed by lymph node TB (20.51%), which was higher than the overall positivity rate of ZN smear was (39/163) 23.92% and MGIT Culture was (11/111) 9.9%.

Conclusion

1. For Microbiological confirmation in fluid specimens, The Role of CBNAAT should not be undermined and should be preferred over the "Gold Standard" MGIT Culture and labelled as the "Platinum" of 21st Century.
2. Earlier detection of Rifampicin Sensitive cases with CBNAAT compared to the time taking Gold Standard helps in quicker diagnosis, Earlier Treatment initiation and prevents Loss to follow up and avoids treatment failure.
3. Earlier detection of Rifampicin resistant in newly diagnosed EPTB cases helps in earlier initiation of Drug Resistant TB Regimen, which in turn led to better treatment outcome and Quality of life.

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