Original Research Article

CBNAAT Study of Extra-Pulmonary Tuberculosis among Population of North Andhra Pradesh

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Abstract
Background & Objectives: Extra pulmonary tuberculosis (EPTB) constitutes 15 to 20% of total cases of tuberculosis in India. It is high in incidence among HIV and Pediatric group and involves almost all systems of the body. CBNAAT (Cartridge-based nucleic acid amplification test) is of definitive value in its diagnosis. The present study aims at knowing the prevalence of EPTB among the population of Visakhapatnam of North Andhra.

Material & Methods: 12,372 cases of EPTB out of total cases (old & new) of 67,017 are studied from the data at District Tuberculous Center, Visakhapatnam for the period 2007 to Aug 2018.

Results & Discussion: FNAC samples of lymph nodes and others reported highest (177) among EPTB followed by pleural effusion (28) and pus & abscess (30) showing similar and bronchial wash (26). In the present study EPTB showed overall prevalence of 18.80 similar to Indian average of 15 to 20%. PTB: EPTB is 4:1 in males and 2:1 in females showing more in incidence in the latter. Hence the target group for EPTB is more of female population as they are vulnerable due to anaemia, malnutrition and low immunity.

Conclusions: Though the emphasis is more on PTB case finding, EPTB is also significant and has to be paid attention in the control of tuberculosis.

Keywords: EPTB, CBNAAT, prevalence, percentage, ratio, tuberculosis.

Introduction
Tuberculosis still remains a thorn in our sole despite intense efforts to control it. Even today India has the highest7 TB burden accounting for 1.9 million cases out of 9.1 million globally. Extra pulmonary tuberculosis (EPTB) involves almost every organ system in the body. Its burden ranges from 15 to 20 % of all TB cases among HIV –Ve patients and about 40 to 50% in HIV +Ve new TB patients. EPTB has significant impact on the people and the economy. Diagnosis is difficult. Latest 6Gene-Xpert (CBNAAT) has revolutionised the diagnosis of TB particularly EPTB.
Visakhapatnam city is situated in North Andhra Coastal area (comprising the districts of Srikakulam, Vizianagaram and Visakhapatnam in Southern India). Visakhapatnam has a population of about 45.5 lakhs with 15% tribal. Most of the city population are migrants and industrial pollution is a matter of concern in this part of the state which may be a contributing factor for the high incidence of tuberculosis relatively. EPTB cases are noticed at the famous 1200 bedded King George Hospital (KGH). Visakhapatnam is the central point of receiving samples for CBNAAT study of Tuberculosis esp. EPTB.

Present Study
It is an observational study of the data collected from the District Tuberculous Center (DTC) of Visakhapatnam, District in North Andhra which caters to the population of the three districts Srikakulam, Vizianagaram and Visakhapatnam. About 12,825 new cases of EPTB are identified among the total old and new cases of 67,017 from 2007 to Aug 2018 from the pooled data of DTC. Tabulated and calculated on excel sheet and the relevant health status indicators are derived as per bio statistics.

Limitations
Factors like HIV status, Diabetes, Anaemia, alcohol, smoking, pollution, slum area problem and co-morbid conditions like COPD, CKD, CANCER etc. are not part of the present study due to the paucity of data. The emphasis is on the highly sensitive Cbnaat diagnostic result of the cases of EPTB.

Material and Methods
The material for the study is obtained with permission from the district tuberculous officer, Visakhapatnam. The method adopted is the tabulation and calculation on the excel sheet at the research center of GIMSR. The bio-statistician is consulted to adopt the relevant statistical methods applied wherever necessary. The health status
Bio-Statistics

Certain relevant health status indicators like prevalence, incidence, PTB-EPTB ratio, case fatality rate, relapse rate, failure rate and default rate are calculated as per the formulae though the emphasis is made on prevalence of EPTB.

Table: 1 Case Profile Data 2007 – 2014

| YEAR | AREA   | NEW SPUTUM +VE | NEW SPUTUM -VE | NEW EPTB +VE | RELAPSES | FAILURE | TAD | OTHERS | TOTAL CASES |
|------|--------|----------------|----------------|--------------|----------|---------|-----|--------|-------------|
| 2007 | URBAN  | 916            | 509            | 533          | 170      | 22      | 30  | 74     | 2254        |
|      | RURAL  | 1167           | 638            | 357          | 209      | 11      | 17  | 83     | 2488        |
|      | TRIBAL | 478            | 137            | 46           | 42       | 9       | 7   | 4      | 723         |
| Total:|        | 2561           | 1284           | 936          | 421      | 42      | 54  | 161    | 5465        |
| 2008 | URBAN  | 880            | 591            | 549          | 108      | 15      | 61  | 74     | 2278        |
|      | RURAL  | 1155           | 537            | 412          | 201      | 17      | 53  | 93     | 2468        |
|      | TRIBAL | 486            | 246            | 98           | 68       | 13      | 16  | 4      | 932         |
| Total:|        | 2521           | 1374           | 1059         | 377      | 45      | 130 | 171    | 5678        |
| 2009 | URBAN  | 894            | 535            | 434          | 170      | 16      | 26  | 75     | 2151        |
|      | RURAL  | 1199           | 633            | 410          | 254      | 28      | 60  | 94     | 2698        |
|      | TRIBAL | 504            | 176            | 77           | 82       | 3       | 6   | 9      | 857         |
| Total:|        | 2597           | 1344           | 921          | 506      | 47      | 92  | 178    | 5706        |
| 2010 | URBAN  | 852            | 593            | 426          | 200      | 25      | 30  | 90     | 2216        |
|      | RURAL  | 1191           | 651            | 431          | 211      | 35      | 43  | 121    | 2683        |
|      | TRIBAL | 504            | 219            | 77           | 79       | 17      | 7   | 22     | 925         |
| Total:|        | 2547           | 1463           | 934          | 490      | 77      | 80  | 233    | 5824        |
| 2011 | URBAN  | 921            | 521            | 438          | 199      | 26      | 34  | 104    | 2243        |
|      | RURAL  | 1232           | 556            | 386          | 222      | 44      | 44  | 124    | 2608        |
|      | TRIBAL | 543            | 219            | 102          | 77       | 4      | 8   | 25     | 978         |
| Total:|        | 2696           | 1296           | 926          | 498      | 74      | 86  | 253    | 5829        |
| 2012 | URBAN  | 877            | 426            | 489          | 143      | 11      | 21  | 117    | 2084        |
|      | RURAL  | 1294           | 573            | 391          | 175      | 20      | 32  | 116    | 2601        |
|      | TRIBAL | 624            | 340            | 142          | 63       | 10      | 20  | 20     | 1219        |
| Total:|        | 2795           | 1339           | 1022         | 381      | 41      | 73  | 253    | 5904        |
| 2013 | URBAN  | 947            | 397            | 494          | 165      | 20      | 25  | 89     | 2137        |
|      | RURAL  | 1284           | 463            | 370          | 171      | 12      | 27  | 115    | 2442        |
|      | TRIBAL | 536            | 216            | 116          | 73       | 9      | 16  | 21     | 987         |
| Total:|        | 2767           | 1076           | 980          | 409      | 41      | 68  | 225    | 5566        |
| 2014 | URBAN  | 946            | 404            | 478          | 247      | 28      | 29  | 127    | 2259        |
|      | RURAL  | 1347           | 527            | 382          | 248      | 15      | 32  | 107    | 2658        |
|      | TRIBAL | 679            | 150            | 145          | 81       | 15      | 38  | 24     | 1132        |
| Total:|        | 2972           | 1081           | 1005         | 576      | 58      | 99  | 258    | 6049        |

Relapse= reporting TB after complete treatment.
Failure = Sputum +ve in the middle of treatment.
TAD = Treatment after default.
### Table: 2

| YEAR | REGION  | POPULATION AT RISK | NEW EPTB CASES | PREVALENCE RATE/1 LAKH |
|------|---------|--------------------|-----------------|-------------------------|
| 2015 | URBAN   | 27,69,383          | 660             | 23.83                   |
|      | RURAL   | 19,77,979          | 304             | 15.37                   |
|      | TRIBAL  | 10,15,082          | 150             | 14.78                   |
| TOTAL : |        | 57,62,444          | 1,114           | 19.33                   |
| 2016 | URBAN   | 21,78,359          | 768             | 35.26                   |
|      | RURAL   | 15,89,463          | 341             | 21.45                   |
|      | TRIBAL  | 6,72,621           | 156             | 23.19                   |
| TOTAL : |        | 44,40,443          | 1,265           | 28.49                   |
| 2017 | URBAN   | 21,93,299          | 732             | 33.37                   |
|      | RURAL   | 16,00,368          | 398             | 24.87                   |
|      | TRIBAL  | 6,77,242           | 184             | 27.17                   |
| TOTAL : |        | 44,70,909          | 1,314           | 29.39                   |
| Aug-18 | URBAN  | 21,93,299          | 580             | 26.44                   |
|       | RURAL   | 16,00,368          | 238             | 14.87                   |
|       | TRIBAL  | 6,77,242           | 78              | 11.52                   |
| TOTAL : |        | 44,70,909          | 896             | 20.04                   |
| TOTAL : |        | 4,589              | 24.31           |                         |

### Table: 3

| YEAR | POPULATION AT RISK | CASES OLD & NEW | PREVALENCE |
|------|--------------------|-----------------|------------|
| 2007 | 4069450            | 5465            | 134.29     |
| 2008 | 4112740            | 5678            | 138.06     |
| 2009 | 4155178            | 5706            | 137.32     |
| 2010 | 4202021            | 5824            | 138.60     |
| 2011 | 4240606            | 5829            | 137.46     |
| 2012 | 4318579            | 5904            | 136.71     |
| 2013 | 4349045            | 5566            | 127.98     |
| 2014 | 4351557            | 6049            | 139.01     |
| 2015 | 5762444            | 6073            | 115.00     |
| 2016 | 4440443            | 6076            | 144.46     |
| 2017 | 4470909            | 5614            | 134.80     |
| 2018 | 4470909            | 3233            | 74.36      |
| TOTAL old & new cases : | 67017 |
Table 4

EPTB CASE STATISTICS FROM 2007 TO AUG 2018 OF VISAKHAPATNAM DISTRICT

| YEAR | NEW CASES | EPTB OUT OF NEW CASES | EPTB % OUT OF NEW CASES | TOTAL CASES (OLD & NEW) | EPTB % OF TOTAL CASES |
|------|-----------|-----------------------|-------------------------|--------------------------|-----------------------|
| 2007 | 4781      | 936                   | 19.58                   | 5465                     | 17.12                 |
| 2008 | 4954      | 1059                  | 21.37                   | 5678                     | 18.67                 |
| 2009 | 4862      | 921                   | 18.94                   | 5706                     | 16.14                 |
| 2010 | 4944      | 934                   | 18.89                   | 5824                     | 16.04                 |
| 2011 | 4918      | 926                   | 18.82                   | 5829                     | 15.88                 |
| 2012 | 5156      | 1022                  | 19.82                   | 5908                     | 17.30                 |
| 2013 | 4823      | 980                   | 20.31                   | 5566                     | 17.60                 |
| 2014 | 5058      | 1005                  | 19.86                   | 6049                     | 16.61                 |
| 2015 | 5079      | 1114                  | 21.93                   | 6073                     | 18.34                 |
| 2016 | 5096      | 1265                  | 24.82                   | 6086                     | 20.78                 |
| 2017 | 4759      | 1314                  | 27.61                   | 5614                     | 23.40                 |
| Aug-18 | 2799  | 896                   | 32.00                   | 3233                     | 27.71                 |
| Total | 57229 | 12372 | 22.00 | 67017 | 18.80 |

Table 5

GENDER DISTRIBUTION OF PTB & EPTB AND THE RATIO

| YEAR | SEX   | PTB  | EPTB  | EPTB % | PTB : EPTB |
|------|-------|------|-------|--------|------------|
| 2015 | MALE  | 2672 | 547   | 20.47  | 4.88 : 1   |
|      | FEMALE| 1293 | 567   | 43.85  | 2.28 : 1   |
|      | TOTAL | 3965 | 1114  | 28.10  | 3.56 : 1   |
| 2016 | MALE  | 2587 | 635   | 24.55  | 4.07 : 1   |
|      | FEMALE| 1244 | 630   | 50.64  | 1.97 : 1   |
|      | TOTAL | 3831 | 1265  | 33.02  | 3.03 : 1   |
| 2017 | MALE  | 2441 | 683   | 27.98  | 3.57 : 1   |
|      | FEMALE| 1004 | 631   | 62.85  | 1.59 : 1   |
|      | TOTAL | 3445 | 1314  | 38.14  | 2.52 : 1   |
| 2018 | MALE  | 1860 | 706   | 37.96  | 2.63 : 1   |
|      | FEMALE| 917  | 643   | 70.12  | 1.43 : 1   |
|      | TOTAL | 2777 | 1349  | 48.58  | 2.06 : 1   |

CBNAAT Data

EPTB – CBNaat samples at DTC & KGH – from 2016 TO 2018

- 2016: 240 samples
- 2017: 492 samples
- 2018: 905 samples
- Total: 1637 samples
EPTB – CBNaat samples at District Hospital – RJY from 2017, 2018

2017 – Total samples - 112
  RIF – Sensitive - 46
  RIF – Resistant - 2

2018 - Total samples - 178
  RIF – Sensitive - 59
  RIF – Resistant - 2

The above data from Rajahmundry (RJY), AP shows Rifampcin resistance of 4.34 in 2017 and 3.39 in 2018.

Table: 6

| SAMPLE TYPE                        | CBNAAT TESTED | RIFAMPCIN SENSITIVE | RIFAMPCIN RESISTANT |
|-----------------------------------|---------------|---------------------|---------------------|
| FNAC (LYMPH NODE, THYROID, PAROTID, BREAST, TUMOURS etc.) | 622           | 177                 | 8                   |
| PLEURAL EFFUSION                  | 265           | 28                  | 1                   |
| PUS & ABSCESS                     | 123           | 30                  | 3                   |
| ASCITIC FLUID                     | 123           | 4                   | 0                   |
| BONE & JOINT                      | 102           | 15                  | 1                   |
| CSF                               | 135           | 4                   | 1                   |
| GASTRIC LAVAGE                    | 135           | 3                   | -                   |
| BRONCHIAL WASH                    | 94            | 26                  | 1                   |
| ENDO METRIAL                      | 9             | 1                   |                     |
| BIOPSY                            | 26            | 2                   | 0                   |
| HYDROCELE FLUID                   | 2             | -                   | -                   |
| DRAIN SITE FLUID                  | 1             | -                   | -                   |
| TOTAL :                           | 1637          | 290                 | 15                  |

The above Chnaat sample data is collected from two main centers, DTC & KGH. Rifampcin resistance is 5% of total TB samples tested +Ve with Chnaat.
Diagram – 1:

Bar Diagram showing the RIF sensitive and resistant on Cbnaat – Frequency distribution

Table: 7

| RIFAMPCIN RESISTANCE - IN INDIA - 2016                  |
|--------------------------------------------------------|
| NEW TB CASES                                           | 20% |
| IN PREVIOUSLY TREATED TB PATIENTS                       | 67% |
| IN NOTIFIED TB PATIENTS                                 | 41% |

Results

Detailed case profile data of PTB & EPTB is shown in Table-1 for the period 2007 to 2014. As per table – 2, the prevalence of EPTB among urban, rural and tribal areas of Visakhapatnam shows an increasing trend from 2015 to Aug 2018, rate ranging from 19.33 in 2015 to 29.39 in 2017. The average prevalence for the period 2015 to 2018 is 24.31 per one lakh population. The overall prevalence of total TB including PTB plus EPTB from 2007 to 2018 is about 135(Table – 3). EPTB percentage of total cases (Old & New) is about 18.80% for the period 2007 to 2018(Table-4). Hence, the EPTB share of total TB cases is similar to Indian average of 15 to 20%. Table – 5 shows the PTB : EPTB gender ratio in males is about 4:1 but in females it is 2:1 for the period of study 2015 to 2018. The CBNAAT diagnostic results confine to 2 to 3 years for 2016,2017,2018, as this Gene-Xpert has come into force recently throughout India, yet not spread widely. The present sample study shows EPTB of lymph node (FNAC) maximum in occurrence followed by abscess and pleural taking next. The Rifampcin resistance in the present study population is 4 – 5% (Table-6) far less than Indian average (Table-7). The bar diagram-1 gives a telltale picture of Rifampcin sensitivity pattern of different diseases of EPTB. Out of total 1637 samples received for Cbnaat testing at DTC and KGH, 290 are +Ve for EPTB Rifampcin sensitive and 15 resistant, sample size is increasing gradually. Which shows the improved awareness among medical personnel towards the definitive diagnosis of tuberculosis. This trend shows better compliance of the treatment of tuberculosis esp. EPTB. The Cbnaat profile when compared Visakhapatnam to another center Rajahmundry shows similar trend. Hence the pattern is almost same in the state of Andhra Pradesh.
Pradesh. The failure rate and the default rate of all cases of TB from 2007 to 2014 is 16% and 1.5% respectively, and the case fatality rate maintains at 1.5% for the period 2015 to 2018.

Discussion
Often EPTB diagnosis depends upon strong clinical suspicion by the doctor. Surprisingly, most of the clinicians/specialists are not aware of importance of the high sensitive genetic test like the Cbnaat. General feeling medical fraternity is TB means PTB but EPTB is no less common and it is very high even upto 50% among HIV +ve people effected with TB due to reactivation as the immunity is compromised in them. Surgical implications of EPTB is an important consideration as ATT may cure the disease but leaves the residual sequelae like adhesions of intestines, obstruction to CSF flow, lung fibrosis, bone loss etc. EPTB is often clinical than epidemiological. Other Studies: As per Pooja Singh Gour retrospective study in 2017 in North India of 552 patients, 252 are EPTB cases which are more common in female gender in the age group 31 to 40 years, and in males between 41 to 50 years. Co-infection is often reported with diabetes and HIV and only 12% are retreatment cases which is 24% in PTB. MDR is more often reported with PTB. Pleural followed by lymph node is the pattern of EPTB in their study and even in the present study FNAC is followed by abscess and pleural equally. Another recent study by Anita Velingker from Goa for the period 2013 to 2015 of 1,598 cases revealed 31% incidence of EPTB cases with 47% among HIV +ve with diabetes. Here also pleural is followed by lymphatic in the incidence maximum among 30 to 50 years age group.

Conclusions
The prevalence of EPTB maintains a plateau without much fluctuations over years as per the present study. The case burden is more in the society as they are not suspected and not referred to Cbnaat centers. With the establishment of more and more of Gene-Xpert machines network all over the areas, EPTB case load can cross the tip of the iceberg coming to the surface. Provision has to be made in RNTCP in this aspect. There is no separate emphasis on EPTB control by the RNTCP. Hence all the hospitals (both private & govt) have to be directed by the G.O.I. to tackle cases of EPTB in co-ordination with the control agencies. EPTB resulting in surgery has to be done free of cost or at gross concession at all private hospitals. A special provision has to be made through the health insurance scheme. It has to be made compulsory for all private hospitals to purchase Gene-Xpert so that more cases of EPTB can be diagnosed and the drug treatment can be provided by the govt. nodal agencies.

Conflict Of Interest: Nil
Financial Support: Nil

Acknowledgement
Our sincere thanks to the DTCO, Visakhapatnam for furnishing the data for the study and the issue of permission to conduct research. Also the service rendered by the DEOs Venkatarao o/o DTC and Srinivasaraao Nammi GIMSR and also the STLS Mr. Gopi are well appreciated.

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