

## Extrapulmonary tuberculosis in pediatric patients- A matter to worry??MRI

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**Abstract**

**Introduction:** Tuberculosis(TB) is still a major problem worldwide, it is estimated that, one third of the world population is affected with TB. Extrapulmonary TB accounts for 10-15% of tuberculosis worldwide. Pediatric TB is ignored mainly due to the fact that BCG vaccine will provide protection. Cartridge Based Nucleic Acid Amplification Test (CBNAAT) gives results in 4-5 hours and is therefore widely used. **Aims and objectives:** 1.To study the age and sex distribution of pediatric patients suspected to have extra pulmonary tuberculosis.2.To detect tuberculosis in extra pulmonary samples in pediatric patients by GeneXpert.3.To detect the rifampicin resistance in these cases.4.To evaluate the co-occurrence of HIV with tuberculosis in these cases.**Material and methods:** Retrospective study was conducted from 1<sup>st</sup> January 2016 to 31<sup>st</sup> December 2020. GeneXpert was done on all the clinically suspected cases of extrapulmonary tuberculosis. **Results:** Cerebrospinal fluid (CSF), Gastric lavage and Pleural fluid were the major samples received (31.15%, 29.91% and (22.94%) respectively. Majority of suspected patients were from less than 3 years age group (54.92%). Minimum age found was 1.5 month child. Males predominated females in clinically suspected cases M:F ratio was 1.37:1. 86.47% negative by GeneXpert and 12.29% were positive. Rifampicin sensitive were 8.61%, Resistant were 0.82%. In positive cases female outnumbered males. 3.28% pus samples were positive, 2.46% CSF was positive. There was no co-infection of HIV with Tuberculosis in our study. **Conclusion:** We found a rise in cases of extrapulmonary tuberculosis as compared to our previous study. This may be due to proper detection of cases, interaction with clinicians and encouraging them to send the suspected samples in microbiology department. CSF samples constituted 31.15% of total sample. This alarm us the increase in meningeal tuberculosis cases.

**Key words:** CSF, extrapulmonary, GeneXpert, less than 3 years, Rifampicin

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**Introduction**

Tuberculosis (TB), an infectious disease caused by Mycobacterium tuberculosis, has an estimated global annual incidence of 9.6 million with 2.2 million cases in India according to World Health Organization (WHO) Global TB Report (2015)[1]. India, China and the Russian Federation accounted for 45% of all estimated MDR/RR-TB cases (henceforth to be called as MDR-TB). India, one of the countries with high burden of TB, has an estimated 79,000 MDR-TB cases among notified pulmonary TB cases[2]. Extrapulmonary tuberculosis (EP-TBC) is observed more frequently in children compared with adults because the risk of lympho-hematogen spread is high, especially in young children[3]. Lymph nodes are the most common site of involvement followed by pleural effusion and virtually every site of the body can be affected[4]. Diagnosing EPTB is challenging due to its varied clinical presentations and paucibacillary nature of the disease[5]. Culture by conventional methods takes time. This delays initiation of anti-tuberculosis treatment leads to transmission of tuberculosis in the community and increase risk of spread of Tuberculosis. GeneXpert MTB/RIF assay (Cepheid Inc., CA, USA) marks an important development in the field of rapid molecular TB diagnostics[6,7]. It detects rifampicin resistance also. It is simple, rapid, cost effective and doesn't require technical expertise[8]. So, we have used CBNAAT/GeneXpert system for the detection of extrapulmonary tuberculosis in pediatric patients.

**Aims and objectives**

1. To study the age and sex distribution of pediatric patients suspected to have extra pulmonary tuberculosis.
2. To detect tuberculosis in extra pulmonary samples in pediatric patients by GeneXpert.
3. To detect the rifampicin resistance in these cases.
4. To evaluate the co-occurrence of HIV with tuberculosis in these cases.

**Material and methods**

- **Study Design:** Retrospective study.
- **Setting:** Department of Microbiology, Government Medical College, Dhule.
- **Study Period:** 1<sup>st</sup> January 2016 to 31<sup>st</sup> December 2020(5 years).
- **Sample size-** 244
- **Inclusion criteria-** Patients suspected to have extrapulmonary tuberculosis below 18 years.
- **Procedure-** Samples like pleural fluid, ascitic fluid, urine, Broncho-alveolar lavage (BAL), brain abscesses, Cerebrospinal Fluid(CSF), Fine needle aspiration cytology(FNAC) sample, Gastric lavage, lymph node aspirate, pus, synovial fluid were collected depending upon the site of infection. The samples were categorized according to MDR suspect criteria. The samples were subjected to GeneXpert MTB/ RIF manufactured by Cepheid, France for the detection of M. tuberculosis and then rifampicin resistance in them. GeneXpert MTB/RIF is a cartridge based nucleic acid amplification technique which includes semi quantitative, nested real time PCR in vitro diagnostic test for the detection of MTBC DNA in sputum samples or concentrated sediments prepared from induced or expectorated sputum. Rifampicin resistance associated mutations of the rpoB gene in the samples.

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**Results**

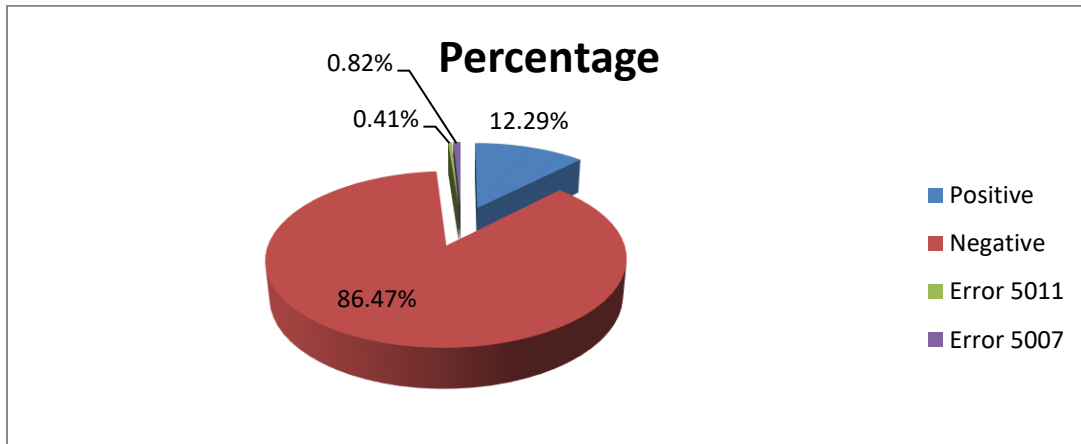
Total 244 samples were received from clinically suspected extrapulmonary tuberculosis cases. The distribution of samples is as follows-

**Table 1: Extrapulmonary samples received for GeneXpert**

S.no	Sample	N	Percentage(%)
1.	Pleural fluid	56	22.94
2.	<b>CSF</b>	<b>76</b>	<b>31.15</b>
3.	Gastric lavage	73	29.91
4.	Urine	2	0.82
5.	Ascitic fluid	5	2.05
6.	Bronchoalveolar lavage	1	0.41
7.	Brain abscesses	1	0.41
8.	Fine needle aspiration cytology sample	1	0.41
9.	Lymph node aspirate	8	3.29
10.	Pus	18	7.38
11.	Synovial fluid	3	1.23
	<b>Total</b>	<b>244</b>	<b>100%</b>

**Table 2: Age and sex distribution in extrapulmonary samples received**

S.no	Age group	Males n( % )	Females n( % )
1.	Birth- 3 years	72(29.51)	62(25.41)
2.	4-6 years	27(11.06)	10(4.10)
3.	7-9 years	12(4.91)	10(4.10)
4.	10-12 years	20(8.20)	5(2.05)
5.	13-15 years	5(2.05)	7(2.87)
6.	16-18 years	5(2.05)	9(3.69)
	<b>Total(244)</b>	<b>141(57.78)</b>	<b>103(42.22)</b>



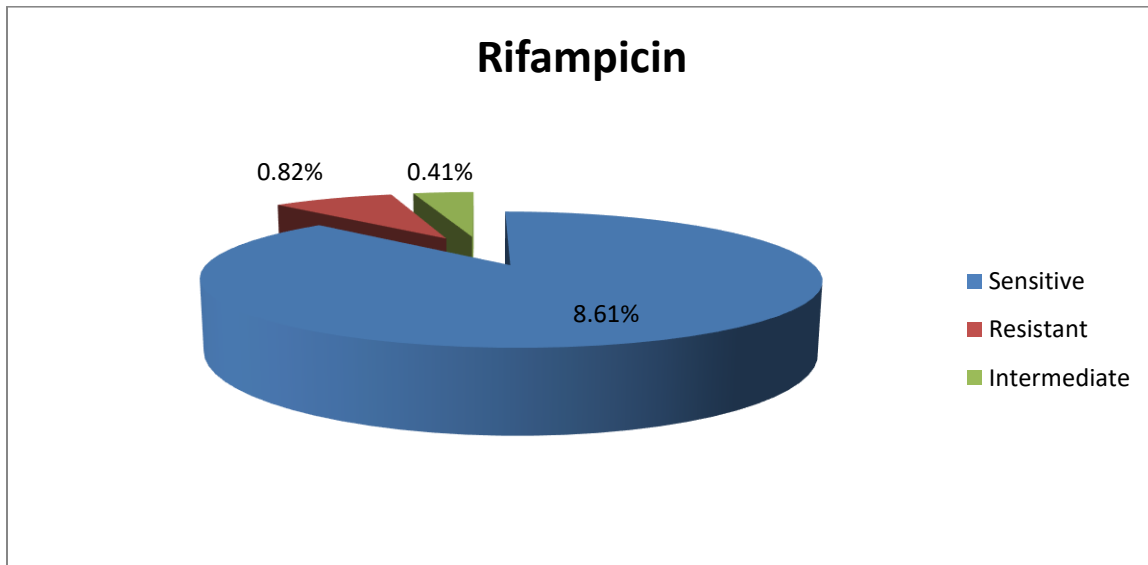
**Fig 1: Total number of positive and Negative cases on CBNAAT**

**Table 3: Extrapulmonary samples Positive for GeneXpert**

S.no	Sample	N	Percentage(%)
1.	Pleural fluid	4	1.64%
2.	<b>CSF</b>	<b>6</b>	<b>2.46%</b>
3.	Gastric lavage	4	1.64%
4.	Urine	0	0%
5.	Ascitic fluid	1	0.41%
6.	Bronchoalveolar lavage	0	0%
7.	Brain abscesses	0	0%
8.	Fine needle aspiration cytology sample	1	0.41%
9.	Lymph node aspirate	5	2.04%
10.	Pus	8	3.28%
11.	Synovial fluid	1	0.41%
	<b>Total</b>	<b>30</b>	<b>12.29%</b>

**Table 4: Age and sex distribution in positive extrapulmonary samples**

S.no	Age group	Males n( % )	Females n( % )
1.	Birth- 3 years	8(3.28%)	3(1.23%)
2.	4-6 years	2(0.82%)	0(0%)
3.	7-9 years	2(0.82%)	0(0%)
4.	10-12 years	0(0%)	4(1.65%)
5.	13-15 years	0(0%)	6(2.46%)
6.	16-18 years	1(0.41%)	4(1.65%)
	<b>Total(30)</b>	<b>13(5.33%)</b>	<b>17(6.99%)</b>

**Fig 2: Rifampicin Sensitive, resistant and intermediate cases by CBNAAT**

In our study, we didn't find correlation of HIV and TB.

### Discussion

In our study, 31.15% clinically suspected extrapulmonary samples were CSF followed by Pleural fluid(22.94%) followed by Gastric lavage(29.91%). Very few samples of Broncho alveolar lavage, brain abscesses, urine, Ascitic fluid, Lymph node aspirate, pus, synovial fluid were received.

Similar results were found in the study of Yeshi Metaferia et al in which CSF was major sample was CSF(52.1%).<sup>9</sup> In the studies of Kumar et al fine needle aspiration cytology (FNAC) constituted the major sample[1]. In the study of Kandi et al, lymph node aspirate was major sample(19%) whereas in the case of Lawn et al, 5% CSF were received[2]. The difference may be due to different sites involved, different presentations of patients, presence of experienced staff to take out CSF. According to Maou Shui Wang, increasing trend was observed in the proportion of tuberculous lymphadenitis amongst childhood TB, as compared to previous studies where BCG vaccination was regarded as the most common cause of tuberculous lymphadenitis in children[10].

In our study, most of the suspected cases were from birth to third year of age(54.92%) and males were affected more than females M:F ratio being 1.37:1. In the study conducted by Kumar et al also, 47.60% were from less than 5 years age group and males suspected were 67.30% and females were 32.70%[1]. In the study done by Sunilkumar et al, there was no significant difference in gender. Females suspected were 51% and males were 48%[11]. The difference in age may be due to, mother to child transmission through placenta during pregnancy and delivery. The other reason could be, lack of knowledge regarding precautions to be taken in tuberculosis positive patient during handling the child.

In our study, samples positive by GeneXpert were 12.29%, negative were 86.47%, Error 5011 was found in 0.41% and error 5007 was found in 0.82%. In the study conducted by Kasat et al, positivity was

15.06% which is quite close to our study.<sup>8</sup> In the study by Lawn et al, Saurabh Jain et al and Phuljhele et al, 14.11%, 18.5% and 30% respectively were positive for tuberculosis[12-14]. Increase in occurrence of extrapulmonary TB may be due lack of proper knowledge, not taking adequate precautions, increase in detection rate and suspicion by physician.

In our study, out of 12.29% samples that were positive, 3.28% was pus, 2.46% CSF, Lymph node aspirate 2.04% and 1.64% pleural fluid. In the study conducted by Saurabh Jain et al, pus was positive in 43.7%, pus in 27% and cervical lymph node aspirate in 16.6%[13]. In the study conducted by Kumar A et al, FNAC was most common and most positive sample followed by CSF pleural fluid and ascetic fluid[1]. They have not mentioned about the pus sample. Gour Sanjay M et al found Pleural fluid 49.81% most common sample followed by lymph node 40%, and pus 37.73%[15].

In our study females were more affected than males(6.99% females as compared to 5.33% males). This could be due to ignorance of female child after birth, anaemia and malnutrition. Brain et al, Mulualem et al and Poojasingh et al also females were more affected than males(54%, 76%, 69% respectively)[16-18]. Birth to third year age group was hit the most by tuberculosis. It might be due to fact that, BCG might provide protection, this may led to lack of detection of cases.

In our study Rifampicin resistance was seen in 8.61% cases. In the study by Saurabh Jain et al, Gour Sanjay et al, Pragati Rao et al, Deewan et al and Tripathi et al, it was 6.74%, 6.38%, 13.55%, 25% and 53% respectively[13,15, 19-20]. Increase in Rifampicin resistance may be due to missing the doses, increase in exposure to Multidrug resistant patients, lack of follow up. In the study of our hospital by Lilani et al, which was done on pulmonary as well as extrapulmonary samples, the prevalence of extrapulmonary TB was 1.08%[22]. So, increase in number of cases were seen in present study. We had

received only CSF, gastric lavage and pleural fluid during that study. So, in this study the number of sample has increased and type of sample has also increased. In that males were more affected as compared to females. So, change in trend of gender was observed in present study.

### Conclusion

There was rise in cases of extrapulmonary tuberculosis as compared to our previous study in Northern Maharashtra. CSF was the major sample that was collected which alarms us regarding increasing cases of meningeal tuberculosis. Increase in detection rate, close suspicion of extrapulmonary cases is must as they have bizarre presentation most of the times. Proper contact with clinicians is need of the day. GeneXpert detects TB in 4-5 hours along with rifampicin resistance hence it still continues to be used widely.

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