

PERFORMANCE OF GENEXPERT IN THE DIAGNOSIS OF TUBERCULOSIS IN CHILDREN IN COMPARISON WITH SMEAR MICROSCOPY AND MGIT CULTURE AND DETECTION OF DRUG RESISTANT CASES AT HMC, PESHAWAR

Ambreen Ahmed, Islam Gul Afridi, Muhammad Idrees, Ansaar Hussain

ABSTRACT

Objectives: To determine the performance of Genexpert in detecting *Mycobacterium Tuberculosis* in children compared with microscopy and MGIT culture and determining the sensitivity pattern of *Mycobacterium Tuberculosis* in children at Hayatabad Medical Complex, Peshawar.

Study Design: This is cross-sectional observational study.

Duration and Place: This study was carried out from 1st January, 2019 to 31st December, 2019 at Pediatric B Unit, Hayatabad Medical Complex, Peshawar.

Materials and Methods: Data was extracted from the database of TBC Center, Hayatabad Medical Complex, Peshawar. It was analyzed with descriptive statistics using SPSS Version 26 and the results were presented in figures.

Results: 274 patients were included in the study. 121 (44.16%) were females and 153 (55.84%) were males. The mean age was 9.77 ± 3.92 years having a range of 1-15 years. 205 had pulmonary disease while 69 patients had extra pulmonary disease. Among those with pulmonary disease 97 were females and 105 were males. Among extra pulmonary cases 24 were females and 45 were males. Smear microscopy was positive in 14 cases, culture was positive in 16 cases and Genexpert was positive in 37 cases. In the cases in whom tuberculosis was detected by Genexpert, 30 (24 females 6 males) had pulmonary disease while 7 patients (6 females 1 male) had extra pulmonary disease. Drug resistance was detected in one patient showing resistance to Rifampicin, Isoniazid, Pyrazinamide and Ofloxacin and sensitivity to Ethambutol, Amikacin, Kanamycin, Moxifloxacin and Capreomycin.

Conclusions: The performance of genexpert is far better than microscopy and culture for the diagnosis of tuberculosis in children and in detecting multidrug resistant disease.

Key Words: Genexpert, tuberculosis, children, rifampicin resistance

INTRODUCTION

Tuberculosis is an important cause of morbidity and mortality that affected 10 million people in 2018 all over the world, with 44% of them in South-East-Asia.¹ Children 15 years of age or younger account for 11% of the global disease burden and 14% of the mortality.^{2,3}

Due to paucibacillary nature of the disease and difficulties in obtaining good quality samples, diagnosis of tuberculosis in children is challenging.⁴ Moreover, conventional investigations either have low sensitivity and specificity like chest radiography and smear microscopy, or are unavailable, difficult to perform, time consuming and costly like isolation by culture.⁵

Department of Pediatrics, Children B Unit, Hayatabad Medical Complex, Peshawar, Pakistan

.....

Address for correspondence:

Islam Gul Afridi

Department of Pediatrics, Children B Unit, Hayatabad Medical Complex, Peshawar, Pakistan
E-mail: igafridi4@gmail.com
Cell: 03339213936

To overcome these problems WHO has recommended the use of rapid molecular diagnostic technique GeneXpert as a first-line investigation in the evaluation of tuberculosis in resource-poor countries.⁶

The purpose of this study is to evaluate the performance of Genexpert in comparison with smear microscopy and MGIT culture in the diagnosis of tuberculosis in children and detection of drug resistant cases at HMC Peshawar.

MATERIALS AND METHODS

This cross-sectional, descriptive study was carried out at Pediatric B Unit, Hayatabad Medical Complex, Peshawar from 1st January, 2019 to 31st December, 2019. Data was collected on an Excel spreadsheet from the database of TBC Center, Hayatabad Medical Complex, Peshawar after verbal consent from the concerned authority. All samples sent for GeneXpert analysis from patients 18 years old or younger were included in the study while those above 18 years were excluded. Non-probability, consecutive sampling technique was used. The data was analyzed with descriptive statistics

using SPSS Version 26. Mean and standard deviation were calculated for numerical variables and frequency and percentages calculated for categorical variables. The results were presented in tables and figures.

RESULTS

274 samples were included in the study. 121 (44.16%) were from females and 153 (55.84%) from males (Table 1). The mean age was 9.77 ± 3.92 years having a range of 1-15 years (Table 2). 205 had pulmonary disease while 69 patients had extra pulmonary disease (Table 3). Among those with pulmonary disease 97 were females and 105 were males. Among extra pulmonary cases 24 were females and 45 were males. The samples used for analysis are shown in Table 4. In the cases in whom tuberculosis was detected by Genexpert 30 (24 females 6 males) had pulmonary disease while 7 patients (6 females 1 male) had extra pulmonary disease. Smear microscopy was positive in 14 cases and negative in 260 cases. MGIT culture was positive in 16 cases and negative in 258 cases. Genexpert was positive in 37 cases negative in 237 cases (Figure 10). Drug resistance was detected in one case (Figure 2). It showed resistance to Rifampicin, Isoniazid, Pyrazinamide and Ofloxacin and sensitivity to Ethambutol, Moxifloxacin, Amikacin, Kanamycin and Capreomycin.

DISCUSSION

In this cohort of 274 samples, smear microscopy detected 14 (5.10%), and culture detected 16 (5.90%) while GeneXpert detected MTBC in 38 (13.86%) of cases showing two and a half fold higher rate of positivity. One study reported a cohort of 245 samples in which smear microscopy detected 85 (34.7%) and culture detected 102 (41.6%) while GeneXpert detected MTBC in 111 (45.3%).⁷ This study also shows a trend similar to that in our study. In our study in 244 smear negative samples MGIT culture came positive in 7 (2.86%) cases while Xpert MTB detected 24 (9.83%) cases. Another study showed MGIT detected 12.1% and Xpert detected 48.6% smear negative cases.⁸ This finding is similar to our findings. Other studies have also found Genexpert to be more sensitive than acid-fast bacilli smear and culture in detecting both pulmonary and extrapulmonary tuberculosis in children.^{9,10}

In our study 69 (25.18%) samples were from patients with suspected extrapulmonary tuberculosis. This type of disease can occur with or without pulmonary disease and is quite common in pediatric age group.¹¹ Santiago-Garcia B and colleagues reported extrapulmonary tuberculosis in 17.7% of their study cohort.¹² Smear microscopy was negative in all samples, MGIT culture was positive in 4 (5.79%) while Xpert MTB/RIF in 7 (10.14%) in our study. Raizada N and colleagues have reported positivity rates for microscopy, culture and GeneXpert as 12.88%, 15.82% and 20.59% re-

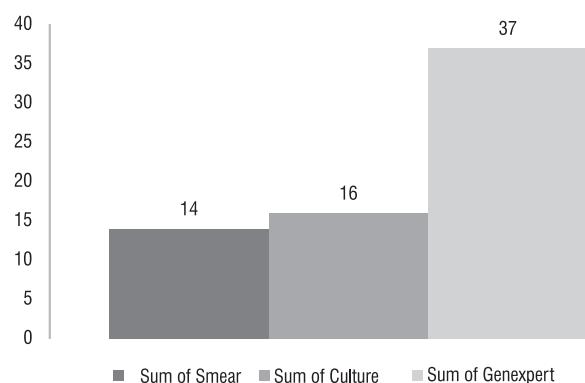


Figure 1. Microscopy, Culture and Genexpert Result

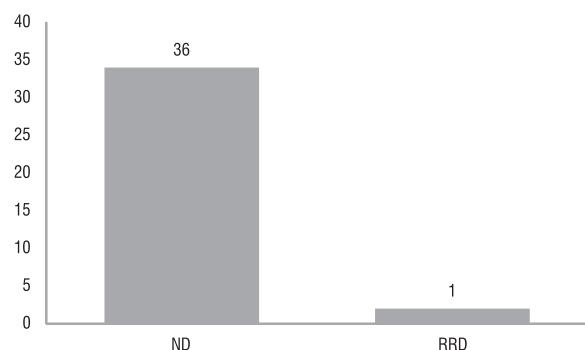


Figure 2. RRDR Result

Table 1. Distribution by Gender

Gender	Frequency	Percentage
Male	153	55.84%
Female	121	44.16%
Total	274	100%

Table 2. Distribution by Age

Age in years	Frequency	Percentage
1	2	0.7%
2	9	3.2%
3	8	2.9%
4	13	4.7%
5	17	6.2%
6	17	6.2%
7	19	6.9%
8	23	8.4%
9	11	4.0%
10	26	9.5%
11	16	5.8%
12	21	7.7%
13	29	10.6%
14	31	11.3%
15	32	11.7%
Total	274	100%

Table 3. Disease Type.

Disease Type	Frequency	Percentage
Pulmonary Tuberculosis	205	74.81%
Extra pulmonary Tuberculosis	69	25.19%
Total	274	100%

Table 4. Type of Samples Used

Sample	Frequency	Percentage
Sputum	142	51.82%
Gastric Aspirate	29	10.58%
Pus	22	8.02%
CSF	19	6.93%
Tissue Biopsy	19	6.93%
Peural Fluid	16	5.83%
Ascitic Fluid	6	2.18%
Broncho Alveolar Lavage	6	2.18%
Gastric Lavage	6	2.18%
Urine	3	1.08%
Bronchial Aspirate	2	0.72%
Lymph Node	1	0.36%
Bone	1	0.36%
Synovial Fluid	1	0.36%
Pericardial Fluid	1	0.36%
Total	274	100.00%

spectively.¹³ These studies provide evidence for better performance of GeneXpert MTB/RIF in extrapulmonary disease in pediatric patients.

In this study GeneXpert MTB/RIF detected one extensive drug resistant case of pulmonary tuberculosis which was resistant to Rifampicin, Isoniazid, Pyrazinamide and Ofloxacin but sensitive to Moxifloxacin, Amikacin, Kanamycin, Capreomycin and Ethambutol. The usefulness of GeneXpert MTB/RIF in detecting drug resistant tuberculosis in children has been documented by many studies.^{13,14,15,16}

CONCLUSION

Our study shows the fact that genexpert has higher positivity rate and better performance in diagnosing both pulmonary and extrapulmonary tuberculosis and in detecting drug resistant cases in children.

REFERENCES

- Global tuberculosis report 2019. Geneva: World Health Organization; 2019;1.
- Dodd PJ, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modeling study. *Lancet Glob Health.* 2014;2(8):e453–9
- Dodd PJ, Yuen CM, Sismanidis C, Seddon JA, Jenkins HE. The global burden of tuberculosis mortality in children: a mathematical modeling study. *Lancet Glob Health.* 2017;5(9):e898–906
- Mogahid ME, Miskelyemen AE, Ahmed LO, Mohamed EH. Challenges in diagnosing tuberculosis in children: a comparative study from Sudan. *Int J Inf Dis.* 2016;43:25–29
- Singh S, Dey B, Sachdeva KS, Kabra SK, Chopra KK, Shaudhary VK, Sharma P, Katoch VM. Challenges in tuberculosis diagnosis and management: recommendations of the expert panel. *J Lab Physicians.* 2015; 79(1):1-3
- Ullah I, Javaid A, Masud H, Ali M, Basit A, Ahmad W, Younis F, Yasmin R, Khan A, Jabbar A, Masroor Husain M, Butt ZA. Rapid detection of Mycobacterium tuberculosis and rifampicin resistance in extrapulmonary tuberculosis and sputum smear-negative pulmonary suspects using Xpert MTB/RIF. *J Med Micro* 2017; 66(4): 412-418
- Iram S, Zeenat A, Hussain S, Yusuf NW, Aslam M. Rapid diagnosis of tuberculosis using Xpert MTB/RIF assay - Report from a developing country. *Pak J Med Sci.* 2015;31(1):105-10
- Pang Y, Wang Y, Zhao S, Liu J, Zhao Y, Li H. Evaluation of the Xpert MTB/RIF assay in gastric lavage aspirates for diagnosis of smear-negative childhood pulmonary tuberculosis. *Pediatr Infect Dis J.* 2014; 33(10):1047-51
- Qureshi S, Sohaila A, Hannan S, Amir Sheikh MD, Qamar FN. Comparison of Xpert MTB/RIF with AFB smear and AFB culture in suspected cases of paediatric tuberculosis in a tertiary care hospital, Karachi. *J Pak Med Assoc.* 2019;69(9):1273-1278.
- Rachow A, Clowes P, Saathoff E, Mtafy A, Michael E, Ntinginya EN, Kowour D, Rojas PG, Kroidl A, Maboko L, Heinrich N, Reither K, Hoelscher M. Increased and Expedited Case Detection by Xpert MTB/RIF Assay in Childhood Tuberculosis: A Prospective Cohort Study. *Clinical Infectious Diseases,* 2012;54(10):1388-1396
- Kaba Ö, Kara M, Odacilar CA, Kamer İ, Sütçü M, Demir SÖ, Çalışkan E, Törün SH, Salman N, Somer A. Evaluation of cases of pediatric extrapulmonary tuberculosis: a single center experience. *Turk Pediatri Ars.* 2019;54(2) 86-92.
- Santiago-García B, Blázquez-Gamero D, Baquero-Artigao F, Ruiz-Contreras J, Bellón JM, Muñoz-Fernández MA, Mellado-Peña MJ. Pediatric Extrapulmonary Tuberculosis: Clinical Spectrum, Risk Factors and Diagnostic Challenges in a Low Prevalence Region. *Pediatr Infect Dis J.* 2016;35(11):1175-1181
- Raizada N, Sachdeva KS, Nair SA, Kulsange S, Gupta RS, Thakur R, Parmar M, Gray C, Ramach-

- andran R, Vadera B, Ekka S, Dhawan S, Babre A, Ghedia M, Alavadi U, Dewan P, Khetrapal M, Khanna A, Boehme C, Paramsivan CN. Enhancing TB case detection: experience in offering upfront Xpert MTB/RIF testing to pediatric presumptive TB and DR TB cases for early rapid diagnosis of drug sensitive and drug resistant TB. *PLoS One*. 2014;20;9(8):e105346
14. Mechal Y, Benaissa E, El Mrimar N, Benlahlou Y, Bssaibis F, Zegmout A, Chadli M, Malik YS, Touil N, Abid A, Maleb A, Elouennass M. Evaluation of GeneXpert MTB/RIF system performances in the diagnosis of extrapulmonary tuberculosis. *BMC Infect Dis*. 2019;19;19(1):1069
15. Saeed M, Ahmed A, Akbar M, Aslam M. GeneXpert: A new tool for the rapid detection of rifampicin resistance in mycobacterium tuberculosis. *J Pak Med Assoc* Feb 2017;67(2):270-4.
16. Amanullah F, Malik AA. Unmasking childhood tuberculosis in Pakistan: efforts to improve detection and management. *Int J Tubec Lun Dis* 2015;19(12):S47-S49.

ONLINE SUBMISSION OF MANUSCRIPT

It is mandatory to submit the manuscripts at the following website of KJMS. It is quick, convenient, cheap, requirement of HEC and Paperless.

Website: www.kjms.com.pk

The intending writers are expected to first register themselves on the website and follow the instructions on the website. Author agreement can be easily downloaded from our website. A duly signed author agreement must accompany initial submission of the manuscript.