



Faculty of Medical and Health Sciences, University of Poonch Rawalakot

# Journal of Pharma and Biomedics

ISSN: 3007-1984(online), 3007-1976 (Print)

<https://www.jpbsci.com/index.php/jpbs>


## High Prevalence of Pediatric Multidrug-Resistant Tuberculosis (MDR-TB) in Sindh, Pakistan: A Cross Sectional Study

Yasmeen Qureshi<sup>1\*</sup>, Abdullah Dayo<sup>1</sup>, Muhammad Ali Ghoto<sup>2</sup>, Rafi Siddique<sup>3</sup>, Jameela<sup>1</sup>, Geeta Kumari<sup>4</sup>, Sania Begum<sup>3</sup>, Razia Sultana<sup>5</sup>, Jabbar Abbas<sup>5</sup>, Tooba Khan<sup>1</sup>

<sup>1</sup> Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro, Pakistan.

<sup>2</sup> Department of Pharmacy Practice, Faculty of Pharmacy, University of Sindh, Jamshoro, Pakistan.

<sup>3</sup> Institute of Chest Diseases, Kotri, Pakistan.

<sup>4</sup> Department of Pharmacology, Faculty of Pharmacy, University of Sindh, Pakistan.

<sup>5</sup> Institute of Pharmaceutical Sciences, Peoples University of Medical and Health Sciences for Women, Nawabshah Shaheed Benazir Sindh, Pakistan.

*Received: August 30, 2025;*

*Revised: October 16, 2025;*

*Accepted: October 20, 2025*

### ABSTRACT

**Background:** Tuberculosis (TB) is a contagious disease caused by mycobacterium tuberculosis bacteria, mostly affecting lungs. It is one of the main causes of death worldwide and nearly 100% of transmission, by which 230,000 children died and 1million suffering, according to recent data of World Health Organization (WHO). Multidrug resistant (MDR) TB became a threat to health security specially in developing countries. The antibiotics used in pediatrics need to have medical audit to ensure rational use because children are at three times higher risk level to have medication error and it is crucial for medical practioners and researchers to pay attention on growing rates of antibiotic resistance. **Method:** Purposive observational cross-sectional study. **Date and place:** 01-04-2016 to 29-04-2019, Hyderabad and Jamshoro. Children of <16 years of age were reviewed prospectively after their clinical examination (including growth valuation), routine blood tests, chest X-ray (CXR), and two sputum samples sent for Mycobacterial tuberculosis culture and drug-susceptibility testing (DST). **Result:** Of 649 patients, 183 patients were male (28%) and 466 were females (72%). Age group, most prone to TB was adolescent with 87% and least affected age was neonates and infants with 0%. Majority of patients belonged to rural areas with 67%. Most prescribed combination of antibiotic was pyrazinamide+ kanamycin+ levofloxacin+ ethionamide+ cycloserine + para-aminsalicylic acid with percentage of 41.6 but many antibiotics were changed during regimen. Line of therapy was followed in 639 patients (98.5%). Most common replacement therapy was pyrazinamide+ ethambutol+ amikacin+ levofloxacin+ ethionamide+ cycloserine with 25.4% out of total replacements with p-value <0.01. All prescribed antibiotics were with correct dose according to guidelines. **Conclusion:** Ratio of MDR-TB in pediatrics is very high and preventative medicines are extremely crucial but implementation of prophylactic measures for these cases is quite low.

**Keywords:** Tuberculosis, MDR-TB, pediatrics, Jamshoro.

**Corresponding Authors:** Yasmeen Qureshi

Email: [yasmeen.qureshi@usindh.edu.pk](mailto:yasmeen.qureshi@usindh.edu.pk)

© 2025 Faculty of Medical and Health Sciences, UPR. All rights reserved.

### INTRODUCTION

One of the most common infectious diseases, Tuberculosis (TB) is caused by Mycobacterium tuberculosis bacteria

which mostly affect lungs. This disease is air-born but curable. People with pulmonary TB spread germs of TB in air by coughing, sneezing or spitting. And it takes only few

of these germs to be inhaled to get infected (WHO, 2019). Multidrug resistant TB (MDR-TB) is caused by the TB bacteria which have developed resistance from at least rifampin and isoniazid (Ormerod, 2005). The condition becomes complicated when this resistance is beyond these two anti-TB antibiotics. There is need of studies highlighting the efficacy, tolerance and safety of antibiotics in complicated MDR-TB (Sotgiu et al., 2009).

MDR-TB is the matter of concern from treatment point of view, which can be understood by the fact that resistance from both rifampin and isoniazid has chief effect on treatment outcome. Various controlled trials have revealed that regimen of 6 months of isoniazid (INH) and rifampin (RMP) with supplement of streptomycin and pyrazinamide (Z) or first 2 months of ethambutol, will deliver >95% cure in patients who have taken these medications properly. And this regimen will lead infectious patient to non-infectious within 2 weeks. If mono-resistance develops from isoniazid and rifampin with ethambutol is used for treatment, then this regimen will take 9-12 months along with 2 months of pyrazinamide initially. Similarly, mono-resistance of rifampin will render treatment with isoniazid and ethambutol for period of 18 months along with 2 months treatment with pyrazinamide initially. It means that resistance from two main antibiotics that is rifampin and isoniazid will prolong the treatment duration for several months for at least 12-24 months or may lead to second line agents, which are more toxic and less effective (Ormerod, 2005).

In 2008, the total cases of TB were 9.4 million estimated by WHO, from which 440,000 (3.6%) were of MDR-TB. Concerning point is, 10-15% from total burden of TB was of pediatric TB but information about MDR-TB burden in children is very little. Most likely, MDR-TB in children develops by close contact with adult having resistant strains. But children must be empirically treated after drug susceptibility testing of expected source. Although the treatment of children is done by same protocol of second line agents as that of adult along with monitoring of adverse drug reactions (Schaaf & Marais, 2011).

## **MATERIALS AND METHODS**

### **Study population and design**

We prospectively reviewed all the children <16 years of age, admitted to Institute of Chest Diseases Kotri. It is one of the two public TB specialist hospitals, treating MDR tuberculosis in Sindh, province of Pakistan, receiving patients of TB from all around Sindh province. It was an observational study, conducted from 01-04-2016 to 29-04-2019, using the hospital patient's record files. Purposive

sampling technique was used, and 2000 patients were included in the study from which 649 were suffering from TB. Sample size was calculated with the help of Raosoft website, in which population size was estimated 20,000 with 95% confidence level, 2.1% margin of error and 50% response distribution.

### **Study method**

Upon arrival of the patient at the hospital, all children underwent a careful history (including history of TB contacts and symptoms consistent with TB) and clinical examination (including growth valuation), routine blood tests, chest X-ray (CXR), and two sputum samples sent for Mycobacterial tuberculosis culture and drug-susceptibility testing (DST) using Gene Xpert MTB/Rif test, which is a cartridge based fully nucleic acid amplification test (NAAT) for simultaneous rapid tuberculosis diagnosis and rapid antibiotic sensitivity test. Once DST was confirmed then children were started with individualized treatment regimens according to WHO guidelines. Children diagnosed with MDR-TB, started with regimen consist of at least four drugs and were selected from following drugs such as amikacin [Am], kanamycin [Km], or capreomycin [CPM], cycloserine (Cs), ethionamide (Eto), levofloxacin (Lfx), moxifloxacin (Mfx), or para-amino-salicylic acid (PAS), based on DST result. The drug dosing was determined by body weight and treatment of adverse drug effects was immediate and adequate in order to minimize the risk of treatment interruption. Drugs were altered if resistance was developed. Injectables were used for minimum of eight months with at least four months of negative culture. Missing or contaminated results were not counted. Minimum length of treatment was 20 months.

### **Eligibility criteria**

Children were eligible for study inclusion if they had a confirmed diagnosis of pulmonary TB and were initiated on treatment. Consent was taken and data from medical records was keenly assessed and analyzed. Follow-up care, results and outcomes were also documented.

### **Statistical analysis**

The data obtained was coded and analyzed using SPSS 24. Descriptive, both qualitative and quantitative, variables were summarized with proportions, medians and interquartile ranges (IQR); they were compared using the Chi-squared test.

## **RESULTS**

### **Characteristics of the Patients**

Out of 649 patients, 183 patients were male with percentage

of 28% and 466 were females with 72%. Age group which was most prone to TB among pediatrics was adolescent with 87% and least affected age was neonates and infants with 0%. Majority of patients belonged to rural areas with 67% as mentioned in table 1.

### Medications Prescribed

In the treatment of tuberculosis, combination of antibiotics must be prescribed according to the recognized protocol, based on sensitivity test of each patient, which was done prior starting of the regimen. Different combinations of antibiotics prescribed, and most prescribed combination of antibiotic was pyrazinamide+ kanamycin+ levofloxacin+

ethionamide+ cycloserine + para-aminsalicylic acid with percentage of 41.6 as shown in table 2 and figure 1. Most common replacement therapy was pyrazinamide+ ethambutol+ amikacin+ levofloxacin+ ethionamide+ cycloserine with 25.4% out of total replacements as showed in table 4 figure 2. Line of therapy was followed in 639 patients which is 98.5% as mentioned in table 8. All prescribed antibiotics with correct dose according to guidelines and after sputum test. Statistical analysis of mode and range in mentioned in table 3 and 5 whereas statistical comparison by Chi-square test is showed in table 6 and 7 along with their bar charts in figure 3 and 4.

Table 1: Characteristics of the study patients.

| Characteristics         | No. (and %) of respondents |
|-------------------------|----------------------------|
| Variables               | No (and %)                 |
| Sex                     | n = 649                    |
| Male                    | 183 (28.2)                 |
| Female                  | 466 (71.8)                 |
| Age Group               |                            |
| Children (2-12years)    | 83 (12.8)                  |
| Adolescent (12-16years) | 566 (87.2)                 |
| Locality                |                            |
| Urban                   | 269 (41.4)                 |
| Rural                   | 380 (58.6)                 |
| District                |                            |
| Hyderabad               | 160 (24.7)                 |
| Jamshoro                | 159 (24.5)                 |
| Dadu                    | 67 (10.3)                  |
| Matari                  | 87 (13.4)                  |
| Thatta                  | 30 (4.6)                   |
| Others                  | 146 (22.5)                 |

Table 2: Antibiotics prescribed in tuberculosis in study patients.

| Medication Prescribed          | Frequency | Percent |
|--------------------------------|-----------|---------|
| Z+Km+Lfx+Eto+Cs                | 36        | 5.5     |
| Z+Km+Lfx+Eto+Cs+PAS            | 37        | 5.7     |
| Z+Am+Lfx+Eto+Cs+Clr+PAS+AmxClv | 12        | 1.8     |
| Z+Cm+Mfx+Eto+Cs+PAS+AmxClv     | 62        | 9.6     |
| Z+Am+Lfx+Eto+Cs                | 190       | 29.3    |
| Z+Am+Lfx+Eto+Cs+PAS            | 270       | 41.6    |
| Z+Am+Lfx+Eto+Cs+Mfx+PAS        | 10        | 1.5     |
| Z+Cm+Lfx+Eto+Cs                | 10        | 1.5     |
| Z+Km+Eto+Cs+PAS                | 12        | 1.8     |
| Total                          | 639       | 98.5    |
| Single medication              | 10        | 1.5     |
| Total                          | 649       | 100.0   |

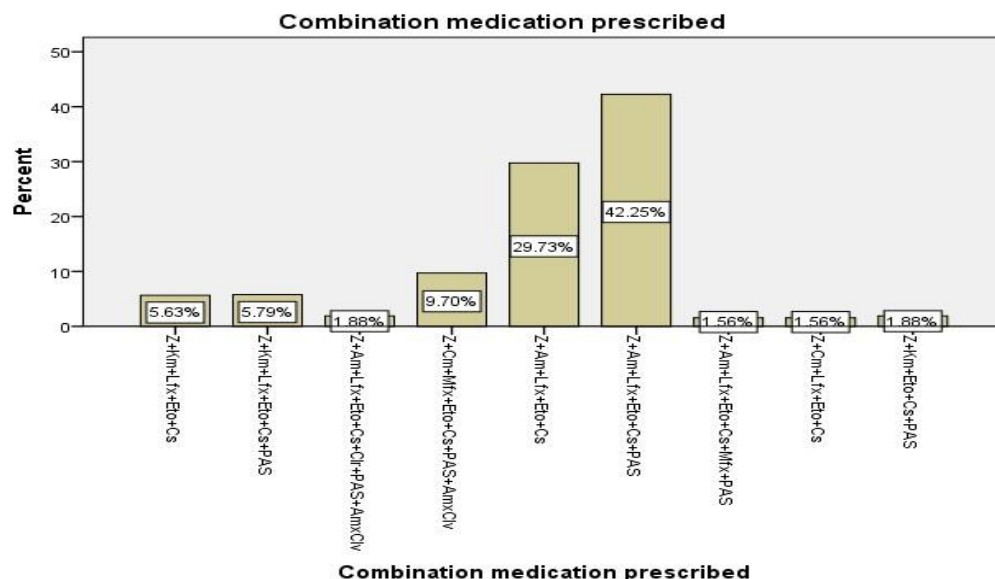


Figure 1: Bar chart showing combination medication prescribed in tuberculosis.

Table 3: Statistical analysis of combination medication prescribed in tuberculosis.

|       |       |
|-------|-------|
| Valid | 639   |
| Mode  | 15.00 |
| Range | 15.00 |

Value 15 was assigned to Z+Am+Lfx+Eto+Cs+PAS combination, mentioned in above table.

Table 4: Antibiotics which were prescribed as a replacement in tuberculosis.

| Medication Prescribed       | Frequency | Percent |
|-----------------------------|-----------|---------|
| Z+Mfx+Eto+Cs+PAS+AmxClv     | 62        | 10.4    |
| Z+Am+Mfx+Eto+Cs+PAS         | 50        | 8.4     |
| Z+Lfx+Eto+Cs                | 108       | 18.2    |
| Z+Am+Eto+Cs                 | 65        | 10.9    |
| Z+E+Am+Lfx+Eto+Cs           | 151       | 25.4    |
| Z+E+Am+Eto+Cs+Mfx+PAS       | 57        | 9.6     |
| Z+E+Am+Eto+Cs+PAS           | 10        | 1.7     |
| Z+E+Am+Lfx+Eto+Cs+PAS       | 11        | 1.9     |
| Z+Am+Lfx+Eto+Cs             | 11        | 1.9     |
| Z+E+Am+Mfx+Eto+Cs+PAS       | 10        | 1.7     |
| CRO+R                       | 10        | 1.7     |
| Z+Am+Lfx+Eto+Cs+PAS         | 37        | 6.2     |
| Z+Lfx+Eto+Cs+Clr+PAS+AmxClv | 12        | 2.0     |
| Total                       | 594       | 100.0   |

Table 5: Statistical analysis of medication changed into other antibiotics in tuberculosis.

|       |       |
|-------|-------|
|       | 594   |
| Mode  | 17.00 |
| Range | 13.00 |

Value 13 was assigned to Z+Mfx+Eto+Cs+PAS+AmxClv combination and 17 to Z+E+Am+Lfx+Eto+Cs combination.

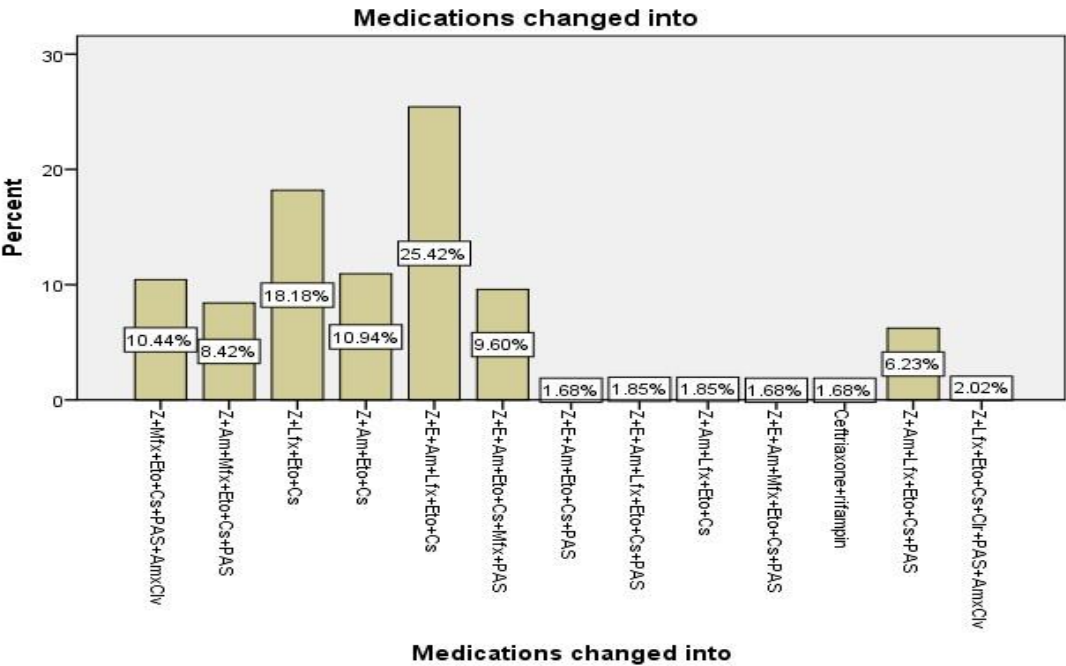


Figure 2: Bar chart showing medication changed into other antibiotics in tuberculosis.

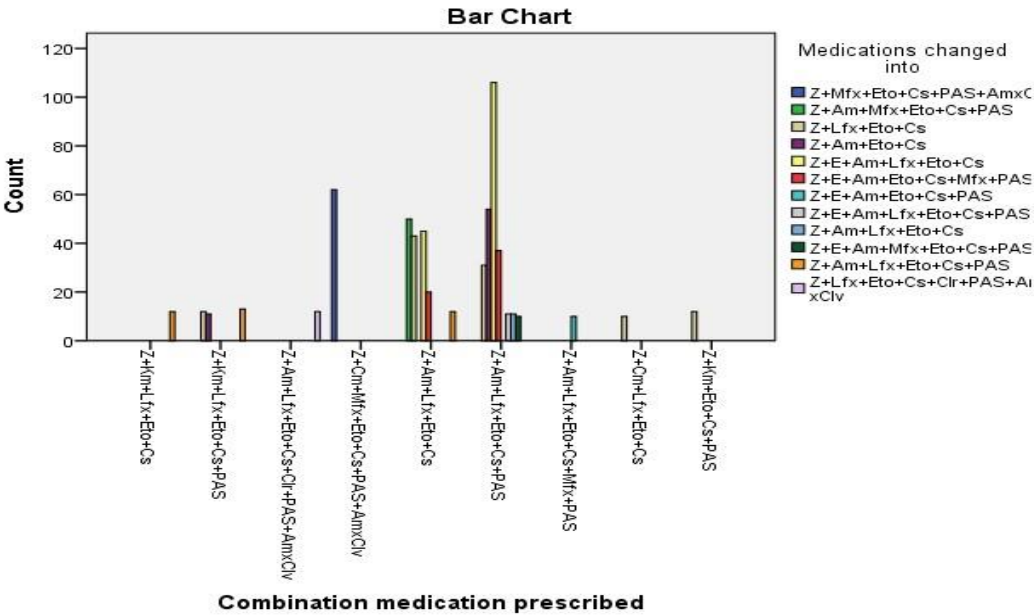


Figure 3: Bar chart showing comparison of combination prescribed and medications changed into other antibiotics.

Table 6: Statistical analysis by chi-square of medication changed in tuberculosis.

|                    |                       |
|--------------------|-----------------------|
| Statistical test   | Asymp. Sig. (2-sided) |
| Pearson Chi-Square | .000                  |

Value is less than 0.05, which is statistically significant.

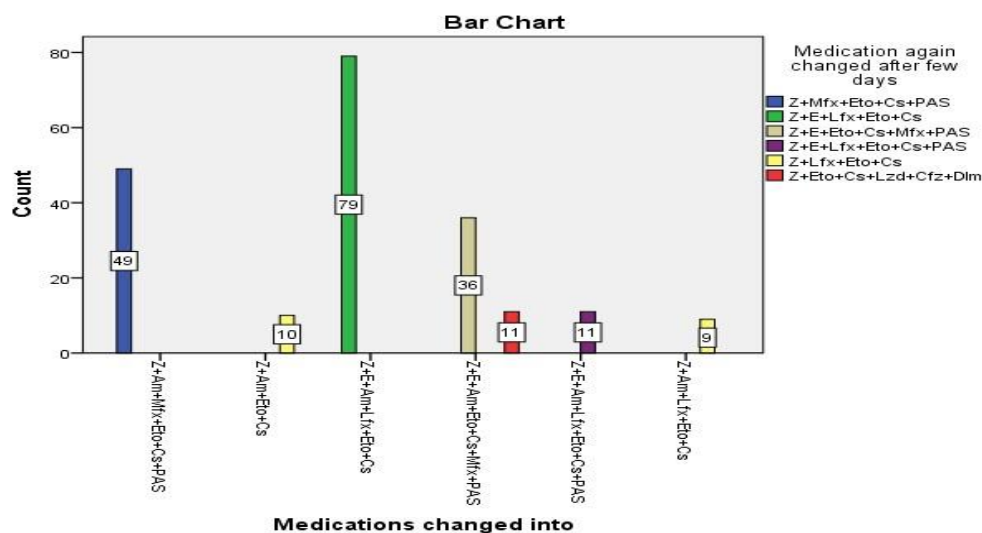


Figure 4: Bar chart showing comparison of replaced medication and combination changed again into in TB.

Table 7: Statistical analysis of chi-square of medication replaced and then changed again in TB.

|                    |                       |
|--------------------|-----------------------|
| Statistical Test   | Asymp. Sig. (2-sided) |
| Pearson Chi-Square | .000                  |

P-value is less than 0.05, which is statistically significant.

Table 8: Number of cases in which line of therapy was not followed in Tuberculosis.

| Line of Therapy Followed | Frequency | Percent |
|--------------------------|-----------|---------|
| No                       | 10        | 1.5     |
| Yes                      | 639       | 98.5    |
| Total                    | 649       | 100.0   |

## DISCUSSION

Unsuccessful trials to detect, diagnose, treat, and eradicate TB results in increase in the emergence of MDR-TB (Ahmad et al., 2012). Countries like Pakistan are already facing crises such as humanitarian catastrophes and pay little consideration to this rising health concern (R., 2007). Our study reported an MDR-TB incidence in pediatric patients. Similarly, another study was done in nearby area of present study that is Jamshoro, Pakistan, by Khan, Shaikh, & Bulaadi, 2019, conducted in the Civil Hospital Department of Pulmonology on MDR-TB patients from January 1, 2017, to December 31, 2017 with the similar study design of prospective observational study. But it was done on patient aged 18 years or older, unlike the present study, which was restricted on pediatrics of less than 16 years of age. In their study, among the cases of MDR-TB, there were 53% male and 47% female, which was not consistent with present study in which male were 28% and

females were 72%.

Evaluating the prescribed antibiotics in one of the Lower respiratory tract infection (LRTI) that was TB, showed that 639 (98.5%) children out of total 649 were resistant to isoniazid and rifampicin and were prescribed combination of second and first line of agents. This result was not consistent with the study done in South Africa by Fairlie, Beylis, Reubenson, Moore, & Madhi, 2011, on children under 14years of age, which is almost same age group as present study (0-16years). In their study only 14.2% were of isoniazid resistant and 10.1% were of rifampin resistant. They did retrospective analysis from January 2008-December 2008 (1year) whereas this study was prospective and compiled data for almost 4years. Similarly, Schaaf & Marais, 2011, presented results of three surveys on pediatric TB which showed that resistance to isoniazid or rifampin was 6.9%, 12.9% and 15.1%. Multidrug resistance was 2.3%, 5.6% and 6.7%. On the contrary, from total TB

patient collected in present study 98.5% were of MDR-TB. Furthermore, some of the results of present study were similar to Am et al., 2010 study, which was observational prospective and carried out in Shree Krishna Hospital, India and it was carried out in January – February 2009. 100 different outpatients were selected and information was gathered by interrogated at their exit from tertiary care hospital, which was quiet less than present study in which 2000 were selected and also done in similar setting and the findings were almost similar despite the fact that their study was done in India and this study was done in Pakistan. Another comparison to point out was that they selected outpatient randomly, but present study was only focused on pediatrics suffering from RTI. In their study, all the gathered data was examined for following parameters such as magnitude of services of pharmacy utilized by patients and doctors, extent of non-utilization of services, pattern of prescriptions, number of prescribed drugs from hospital formulary, prescribed drugs with brand or generic names, drugs prescribed.

As a result, it was found that 94.86% were prescribed from formulary of hospital which was also part WHO list of essential drugs but during this study no hospital formulary was established by authorities. Though it was observed that WHO guidelines were followed to considerable extent in present study setting. In their study, 53% cases were rational, 30% were partly rational and 17% were not rational whereas in this study, 348 number of improper doses prescribed were 17.4%, which was irrational practice. Line of therapy was not followed in 51.5% cases but followed in 48.5% of the cases showing rational use and in 24.2% antibiotics were prescribed without need. Both study type was similar but unlike their study, we selected 2000 patients for analysis.

## CONCLUSION

Ratio of MDR-TB in pediatrics is very high and preventative medicines are extremely crucial but implementation of prophylactic measures for these cases is quite low. WHO implemented program is extremely helpful in fighting the spread of MDR-TB.

## REFERENCES

- Ahmad, A. M., Akhtar, S., Hasan, R., Khan, J. A., Hussain, S. F., & Rizvi, N. (2012). Risk factors for multidrug-resistant tuberculosis in urban Pakistan: A multicenter case-control study. *International Journal of Mycobacteriology*, 1(3), 137–142. <https://doi.org/10.1016/j.ijmyco.2012.07.007>
- Am, S., Jv, D., Rb, S., Agrawal, A., Bm, G., Swami, P., ... Gujarat, K. (2010). Evaluation of prescription pattern in terms of essentiality and rationality and assessment of Hospital pharmacy services utilization in tertiary care teaching rural hospital . *Ijopp*, 3(2), 11–15.
- Fairlie, L., Beylis, N. C., Reubenson, G., Moore, D. P., & Madhi, S. A. (2011). High prevalence of childhood multi-drug resistant tuberculosis in Johannesburg, South Africa: A cross sectional study. *BMC Infectious Diseases*, 11, 3–11. <https://doi.org/10.1186/1471-2334-11-28>
- Khan, R. A., Shaikh, A. A., & Bulaadi, G. Q. (2019). Incidence of Multidrug-resistant Tuberculosis in Sindh, Pakistan. *Cureus*. <https://doi.org/10.7759/cureus.4571>
- Ormerod, L. P. (2005). Multidrug-resistant tuberculosis (MDR-TB): Epidemiology, prevention and treatment. *British Medical Bulletin*, 73–74, 17–24. <https://doi.org/10.1093/bmb/ldh047>
- R., C. (2007). Tuberculosis in complex emergencies. *Bulletin of the World Health Organization*, 85(8), 637–640. <https://doi.org/10.2471/BLT>.
- Schaaf, H. S., & Marais, B. J. (2011, March 1). Management of multidrug-resistant tuberculosis in children: A survival guide for paediatricians. *Paediatric Respiratory Reviews*. W.B. Saunders. <https://doi.org/10.1016/j.prrv.2010.09.010>
- Sotgiu, G., Centis, R., Ambrosio, L. D., Alffenaar, J. C., Anger, H. A., Caminero, J. A., ... Skrahina, A. (2009). Safety, tolerability and efficacy of linezolid in the treatment of MDR and XDR- TB. A TBNET survey, (November 2016). <https://doi.org/10.1055/s-0029-1214065>
- WHO. (2019). Tuberculosis. Retrieved March 6, 2020, from <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>.