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Prevalence, Treatment, Outcome, and Drug Susceptibility Pattern for Multi-Drug Resistant Tuberculosis Patients in the Southern Region of Khyber Pakhtunkhwa, Pakistan

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Abstract: *Tuberculosis is a 5000-year-old bacterial disease and the second leading cause of death. The MDR strain of Mycobacterium Tuberculosis has exacerbated TB's medication resistance in Pakistan. Our study aims to assess the prevalence, treatment outcome, and medication resistance pattern of MDR TB patients in Dere Ismail Khan Mufti Mehmood Hospital's PMDT Unit. From 2013 to March 2019, 298 patients were recorded on PMDT. Our investigation found 10% of MDR TB cases. Among 298 MDR TB patients, 62 (20.8%) are being treated, and all are drug-resistant. Our study had 133 (44.6%) successful treatments. 103 (34.5%) treatments fail. To control the high resistance rate, low treatment success rate, and primary transmission of MDR-TB in D.I.Khan Pakistan, we recommended that each MDR patient support socially, improve living standards, and medical security, and evaluate proper treatment, understand risk factors, and improving treatment outcome.*

Key Words: Multidrug Resistance, Tuberculosis, Prevalence, Drug Susceptibility

Introduction

The most significant global public health issue, surpassing HIV, is tuberculosis, which is particularly widespread in south Asia and Pakistan (Khan et al. 2019a). The WHO calculated that Pakistan had 231-376 cases per 10,000 persons in 2012. The WHO reported MDR retreatment cases in 2012, particularly in the 3,700 pulmonary TB cases that were documented. In Pakistan, there were 55/1602 retreatment cases with lab confirmation (Akhtar et al., 2016). According to the WHO, 480000 new cases of drug-resistant tuberculosis would be reported in 2014. MDR TB is defined as MTB-caused TB in people who are also resistant to second-line injectable drugs and at least fluoroquinolones. MDR TB is characterized as TB triggered by MTB and individuals who are impervious to both medications, with 8.7% of patients anticipated to create considerable medicine resistance. MDR tuberculosis is characterized as TB that is unresponsive to at least isoniazid and rifampicin treatments. INH and RIF, which together constitute the basis of first-line anti-TB therapy, are the most potent anti-TB drugs (Mitnick et al., 2016). MDR-TB patients and

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their families described the condition as the worst of the worst illnesses in a study recently done in Mumbai, and they also stated that the sickness treatment was worse than the illness itself (Ahmad et al., 2016). The WHO notes alarmingly that individuals with TB and MDR-TB are growing more and more resistant to at least isoniazid and rifampicin each year, which is the principal barrier to the elimination of the disease. According to a recent meta-analysis of data from 25 countries, MDR patients had a combined treatment success rate of just 61%, compared to drug-susceptible patients' rate of 82%. This is the main reason for the surge in MDR-TB cases. Khan and colleagues 2019a. 9 million people had TB worldwide in 2013, according to the WHO, and 1.5 million people died as a result. All existing anti-TB measures have resulted in a 45% decrease in the death rate for tuberculosis since 1945; however, the disease has been managed using programmatic, directly observed therapy short courses strategies. The MDR-TB is solely the product of human error, including wrong diagnosis, ineffective treatment, ignorance of the illness, neglect to adequately care for TB patients, extended waiting times, and noncompliance, especially concerning side effects of anti-TB medicine (Khan et al., 2015). Patients who failed first-line drug therapy fell behind in treatment and relapsed after it is more likely to develop MDR-TB, and those MDR-TB cases are more difficult due to the prolonged treatment period, which lasts roughly 18 to 24 months and includes second-line drugs (SLDs), such as fluoroquinolone. As we all know, inefficient MDR treatment can result in subpar patient outcomes and a rise in the risk of XDR-TB, making the diagnosis and treatment of MDR-TB patients critical. As a result, MDR may spread more quickly throughout the populace in the absence of effective care. Pakistan is ranked fourth out of the top 22 countries with MDR-TB, and according to the WHO, there are around 15000 MDR-TB cases there each year, based on 4.2% primary resistance and 19% resistance in patients receiving re-treatment (Khan et al., 2015). A study conducted in Pakistan in 2017 estimated that there were 27000 MDR-TB cases, of which 4.2% were newly infected patients and 16% involved those who had already had TB therapy. The first National Drug Resistance Survey of Pakistan, which was completed in September 2013, found that the prevalence of new cases of pulmonary tuberculosis was 3.7% and that of retreatment cases was 18.1%. This suggests that due to poor anti-TB treatment in the past, a lack of patient adherence, and poor/inadequate TB drug quality in Pakistan, retreatment patients are more common than non-retreatment cases. According to the WHO in Pakistan, rather than starting them on a Category II regimen, patients who experience treatment failure, such as those in category 1, should instead be evaluated for drug resistance (Atif et al., 2017). There are two types of drug resistance: primary and acquired. Patients who have acquired drug resistance had previously undergone anti-TB treatment, as opposed to those who have primary drug resistance, and who have never taken anti-TB medication. The prevalence of drug resistance is an essential epidemiological indicator for measuring the extent of the transmission of resistant diseases in the population because people with drug-resistant bacilli remain contagious for a protracted period and can infect others with the infection (Kumar et al., 2018).

The current goal of our study is to determine the prevalence, prognosis, and drug resistance profile of patients with MDR-TB at the KPK's Ismail Khan Mufti Mehmood Memorial Teaching Hospital.

Material and Methods

Study Design and Setting

Patients are treated using a program designed to control drug-resistant TB because the incidence of DR-TB in Pakistan is increasing (PMDT). Mufti Mehmood Memorial and Teaching Hospital is one of the healthcare facilities that utilize one of the several PMDT sites in the region. In 2014, the NTP suggested DIK's MMMTH as a potential PMDT site. Consequently, this study was conducted in the PMDT unit MMMTH D.I.KHAN. 500 confirmed patients with pulmonary MDR will receive treatment at the

study facility from 2018 through March 2020. The medical record, patient history, Electronically Nominal Recorded Reporting System data, and standard data collection forms were used to collect the patients' data. At the start of the patient's enrollment, once a month during the intensive phase of treatment, and once a month during the continuous phase, chest x-rays, Genexpert, AFB smears, and cultures were performed. For contact tracing and infection control at home, home visits are also available for individual patients and MDR-TB patients. According to WHO recommendations, a consistent methodology was used for reporting and treatment outcomes.

Specimen Processing

All patients who were sent to the study site underwent treatment and diagnosis following the NTP protocol. All of the patients who were suspected of having tuberculosis were referred, and the two sputum samples underwent an initial evaluation that included an Xpert MTB/RIF test to check for rifampicin resistance and mycobacterium tuberculosis as well as a direct smear examination using the auramine-rhodamine staining method. These two tests yielded negative results. Both of these tests came back positive for every patient who was thought to have tuberculosis. Patients who may have had DR-TB were admitted to the PMDT facility and sent there for an initial evaluation. Rifampicin resistance was quickly identified using the Xpert MTB/RIF assay, and the presence of acid-fast bacilli in two sputum sample spots and the AM of the following day was examined using direct smear microscopy with auramine dye. After a positive smear and RR were discovered using the fast drug susceptibility Xpert MTB/RIF assay, the sample is further indicated for culture. The complete sample was first decontaminated with N-acetyl-L-cystein (NALC) sodium hydroxide, and Mycobacterium tuberculosis was then isolated using Lowenstain-Jensen (LJ) medium at 37 C. Within 24 hours, a sample was sent to the provincial TB control program in Peshawar for drug susceptibility testing via courier service under the cold chain system. DST was conducted using the Middle-brook 7H10 medium and the BACTECTM Mycobacterium Growth Indicator Tube. 15 ml of the PENTA (polymyxin B, amphotericin B, nalidixic acid, trimethoprim, and azlocillin) was added to inoculate the MGIT vials with the supplement. The MGIT tube received 800 ul of the suspension, the PENTA received 500 ul, and the slide received 200 ul. At baseline visits, DST was completed and reiterated as essential, and AFB sputum smear and cultures were executed every month.

Drug Susceptibility Testing

During a drug sensitivity test, a subject's body is examined to determine which drugs the tuberculosis germs are susceptible to being treated with. DST is becoming more and more important with the expansion of anti-TB drug resistance surveillance, as well as for the effective treatment of MDR, whose incidence is steadily rising in many parts of the world. The susceptibility of the tubercle bacilli to anti-TB drugs serves three main functions: first, it can be used to direct chemotherapy for patients; second, it can be used to confirm that drug resistance has emerged when patients have not responded satisfactorily to treatment; and third, it can be used to track the emergence of new drug resistance.

According to the manufacturer's recommendations, drug susceptibility testing was conducted using MGIT^{tm} and an enriched middle-brook 7H9 medium. The middle-brook 7H9 medium and pyrazinamide were used to evaluate first-line medicines (FLD) such as rifampicin, isoniazid, streptomycin, and ethambutol as well as second-line drugs (SLD) like ofloxacin, amikacin, kanamycin, ethionamide, and capreomycin on MGIT^{tm}.

Treatment Protocol

Information Patients with MDR-TB are treated using a single PMDT unit, and information about their drug resistance pattern, total management, treatment results, and factors contributing to treatment failure or unsatisfactory treatment results is gathered from this unit. Expert advisers

and direct observers of the therapeutic facilities closely checked patient compliance and medication. Every patient was checked out, had their psychological health assessed, and had individualized therapy during the monthly follow-up session. A range of various therapy techniques was quickly used to monitor and treat a potentially hazardous occurrence like SLD. To lessen the chance of treatment suspension in the event of any negative drug reactions, patients who had been absent from follow-up for more than four or five weeks and did not show up to receive medications and the routine investigation was phone contacted and tracked through the treatment coordinator. A phone call was placed to patients who had been gone for more than four or five weeks and had missed appointments for medication and routine examinations. All patients with suspected MDR-TB received the first doses of AM, KM, CM, OFX, ETO, CS, PZA, and vitamin B6. Along with the aforementioned medications, patients who have a history of SLD (PRE XDR) also take para-aminosalicylic acid (PAS). Following the DST results for Amikacin, which is no longer prescribed, capreomycin and badaquenalone were utilized. If patients refused badaqaenalone because of its negative effects, amikacin should be continued. If no additional diseases are present, the medicine that demonstrates susceptibility in new patients will be continued on STR after the DST result is known. Patients who had a history of disease were given a protracted course of treatment. For even resistance, pyrazinamide is advised for FLD, the cause of pregnancy. The entire medication was given at the highest dosage advised based on body weight. Table No. 1 below lists the treatment protocol in place at the time of treatment start-up and the current treatment plan.

Table 1. Show Treatment Protocol of MDR-TB Patients

Treatment Regimen at the time of treatment initiation i.e. 8 Lfx, Am, Eto, Cs, Z, B6 / 12 Lfx, Eto, Cs, Z, B6	Current Treatment Regimen i.e. 8 Lfx, Am, Eto, Cs, Z, B6 / 12 Lfx, Eto, Cs, Z, B6
8 Lfx,Am,Eto,Cs,Z,PAS,B6/12 Lfx,Eto,Cs,Z,PAS,B6	8 Mfx,Am,Eto,Cs,Z,B6/12 Mfx,Eto,Cs,Z,B6
8 Lfx,Cm,Eto,Cs,Z,E,B6/12 Lfx,Eto,Cs,Z,E,B6	8Mfx,Am,Lzd,Clf,Eto,Cs,Z,B6/12Mfx,Eto,Lzd,Clf,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Mfx,Am,Eto,Cs,Z,Lzd,B6/12 Mfx,Eto,Cs,Z,Lzd,Cfz,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8Mfx,Am,Eto,Cs,Z,Lzd,Cfz,B6/12Mfx,Eto,Cs,Z,Lzd,Cfz,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Lzd,Z,B6/12 Lfx,Eto,Cs,Lzd,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Lzd,Cs,Z,B6/12 Lfx,Eto,Lzd,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	8 Lfx,Am,Cs,Z,Cfz,,B6/12 Lfx,Cs,Z,Cfz,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8Mfx,Am,Eto,Cs,Lzd,Cfz,Z,B6/12Mfx,Eto,Cs,Lzd,Cfz,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Mfx,Am,Eto,Cs,Lzd,Z,B6/12 Mfx,Eto,Cs,Lzd,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Mfx,Am,Eto,Cs,Lzd,Z,B6/12 Mfx,Eto,Cs,Lzd,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Mfx,Am,Eto,Cs,Lzd,Z,B6/12 Mfx,Eto,Cs,Lzd,Z,B6

Treatment Regimen at the time of treatment initiation i.e. 8 Lfx, Am, Eto, Cs, Z, B6 / 12 Lfx, Eto, Cs, Z, B6	Current Treatment Regimen i.e. 8 Lfx, Am, Eto, Cs, Z, B6 / 12 Lfx, Eto, Cs, Z, B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Lzd,Z,B6/12 Lfx,Eto,Lzd,Z,B6	8 Lfx,Am,Eto,Lzd,Z,B6/12 Lfx,Eto,Lzd,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Lzd,Eto,Z,B6/12 Lfx,Lzd,Eto,Z,B6	8 Lfx,Am,Eto,Lzd,Z,B6/12 Lfx,Eto,Lzd,Z,B6
8 Lfx,Am,Eto,Lzd,Z,B6/12 Lfx,Eto,Lzd,Z,B6	8 Lfx,Am,Eto,Lzd,Z,B6/12 Lfx,Eto,Lzd,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz	4 Mfx,Am,Eto,B6,Z,E,INH,Cfz/5,Z,E,INH,Mfx,Cfz
8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6	8 Lfx,Am,Eto,Cs,Z,B6/12 Lfx,Eto,Cs,Z,B6

Drug abbreviation: FLD): H=Isoniazis/R=Rifampacin/E=Etambutol/Z=Pyrazinamide/S=Streptomycin/T=Thiacetazone. SLD): KM=Kanamycin/AM=Amikacin/CM=Capreomycin/OFX=Ofloxacin/CFX=Ciprofloxacin/LFX=Levofloxacin/ MFX=Moxifloxacin/CS=Cycloserine/ETO=Ethionamide/PTO=Prothionamide/PAS=Para aminosalycilic acid.

Results

A total of 298 patients were registered for treatment at the PMDT unit MMMTH DIK during the trial, which lasted from 2013 until March 2020. All 298 patients who met the criteria for TB infection and MDR-TB conformity were confirmed to be infected with tuberculosis. There were a total of 298 patients who were diagnosed with MDR-TB; 133 of them (44.6% of patients) were cured, 59 of them (19.7% of patients) died while they were receiving treatment, 30 of them (10.0% of patients) could not be located for follow-up, 7 of them (2.3%) failed treatment, and 7 of

them (2.3%) were not evaluated. The remaining 236 MDR-TB patients were not included in the study because 62 of them, or 20.8% of the total, were receiving therapy at the time of the investigation.

Drug Resistance Patterns

Drug resistance was detected at an elevated level amongst the contributor's patients. In 62 MDR-TB patients 30 (48.3%) were resistant to Rifampicin and Isoniazid, 16(25.8.%) were resistant to pyrazinamide, 07(11.2%) were resistant to Ethambutol, 03(4.8%) to Ofloxacin while resistance to the 4 drugs Amikacin, Capreomycin, Levofloxacin, and Moxifloxacin only (1.6%), The following drugs showed no resistance to the MDR-TB patients. E.g.Streptomycin, kanamycin, Ethionamide, and Ciprofloxacin. As mentioned above the resistance pattern of first-line drugs was observed high as compared to the second-line drugs (Table 2).

Table 2. Drug Resistance Pattern of Different Antibiotics

S. No	Name of drugs	Number of Resistance	Percentage of Resistance
1.	Rifampicin,	30	48.3%
2.	Isoniazid	30	48.3%
3.	Ethambutol	7	11.2%
4.	Pyrazanamide	16	25.8 %
5.	Ofloxacin	03	4.8%
6.	Amikacin,	01	1.6%
7.	Capreomycin,	01	1.6%
8.	Levofloxacin	01	1.6%

Treatment Outcome

Only 62 of the 298 MDR-TB patients were included in the investigation's final report. The treatment success rate of our study is 133(44.6%). The unsuccessful treatment outcome is 103(34.5%), based on the result of our study we have not accomplished the medicine accomplishment rate set out in the goal of stop TB strategy (75%), End TB strategy (90%), and united Nation Sustainable Development Goals (80%) (Table 3).

Table 3. Patients Treatment Outcome Percentage

Treatment outcome	NO. (%)
Cured (successful)	133 (44.6%)
Died	59(19.7%)
Lost to fallow up	30(10.0%)
Failed	07(2.3%)
Not evaluated	07(2.3%)
Total unsuccessful	103(34.5%)

Discussion

Because tuberculosis (TB) is such a major threat to public health, it is critical that patients receive the appropriate treatment, that they receive an accurate diagnosis as soon as possible, and that they avoid passing the disease on to others. The frequency of tuberculosis and the development of treatment resistance because drug-resistant bacteria can remain infectious for an extended time and may pose a threat to other individuals, tuberculosis is one of the most important indicators that can be used to determine the prevalence of drug-resistant bacteria in a

community. Because of this, it is strongly recommended that MDR-TB patients undergo continuous monitoring. The World Health Organization (WHO) reports that the incidence rate of tuberculosis in 2012 was 231/10,000 and the prevalence rate was 376/10,000. (Khan et al., 2019b). A total of 614 individuals were included in the research that was carried out in Karachi in the year 2028, and among those patients, the prevalence of MDR TB patients was 5.0%. The fact that the majority of patients in Pakistan get their treatments and tests done in the private sector is the primary reason why Pakistan does not have accurate information or prevalence data regarding drug-resistant tuberculosis (Ejaz et al., 2010). According to the findings of a study carried out in Pakhtunkhwa Pakistan and presented in the BSL-III laboratory, the prevalence of multidrug-resistant tuberculosis patients is 10.4% among patients who have previously received anti-TB treatment (Ali et al., 2020). Our study's prevalence rate is 10.0%, which is lower than the other studies mentioned above. This is because the majority of patients in our region are still unaware of our tuberculosis control program; as a result, the majority of patients are not registered with the PMDT unit. This is one of the reasons why our study's prevalence rate is lower than other studies. According to the findings of our research, the majority of MDR-TB patients were resistant to the first four FLD (isoniazid, rifampicin, ethambutol, and pyrazinamide), but not a single patient was resistant to streptomycin. On the other hand, only slightly more than half of the patients (11.2%) were resistant to the second-line drugs. When compared to the other SLD, the percentage of resistant SLD strains to ofloxacin was the highest (4.8%). The resistance pattern of SLD was found to be lower in the current study than it was in other studies carried out in Pakistan. For example, in a study carried out in Baluchistan, a high degree of resistance to OFX was seen at a rate of 52.2%, whereas in our study, only 4.8% resistivity was seen against such a drug. This finding contrasts with the results of another study carried out in Sindh, which found that OFX (Khan et al., 2019a). According to the findings of other investigations conducted in Peshawar and Multan, the OFX resistivity is, respectively, 52.7% and 48.9%. (Khan et al., 2019a). The purpose of this study is to investigate and assess the treatment outcomes of MDR-TB patients who were treated at MMMTH D.I.KHAN. After our research project, there were a total of 298 MDR-TB patients were available. Of these patients, 62 (20.8%) were currently receiving therapy, and 133 (44.6%) were categorized as having a successful treatment outcome.

Our study had a lower overall success rate than the NTP trial did when compared to the treatment outcomes of previous studies that were undertaken as part of Pakistan's national TB control program. In terms of the unsuccessful category, 12 people (15%) passed away, and 9 people (11.3%), which is a lower number than our study found, were lost to follow-up (Atif et al., 2017). According to the findings of our research, it is abundantly obvious that the location of the study has not attained the percentage of successful treatment that was outlined in the goal of halting TB (75%) and ending TB (90%) plan. Khan et al(2019b)'s research on tuberculosis in Peshawar was effective in meeting a closed target of positive outcomes (74.3%), which is near to the aim set by "The Global Plan to eradicate TB 2011-2015," which was >75%. The success rate of treatment was found to be 42.6% in Karachi and 40.5% in Multan, while it was found to be 44.6% in the current study. This success rate is significantly higher than those previously reported in Karachi and Multan. Our research found that there was a mortality rate of 19.7%, which, when compared to the results of other studies carried out in Peshawar (19.3%) and Multan (25%), is quite close to the same. A disturbing discovery made by our research was that there was a positive correlation between SLD and the outcome of treatment being ineffective. The success rate is particularly low when dealing with MDR-TB when compared to drug-sensitive tuberculosis. Because of the difficulty in implementing DOTs and the low education level, rural areas are significantly related to the primary problem of a growing default rate, failed treatment results, and a rise in death rate. This is a problem that is strongly associated with

rural areas. Patient education, which is crucial for better treatment outcomes, is, therefore, the most critical component in improving the treatment outcome of MDR-TB patients in rural areas. There are many contributing factors and reasons for this, but from the perspective of Pakistan's healthcare system, there is a shortage of clinical hospitals and pharmacists who can develop dose modification protocols, particularly to adjust the amount of anti-TB medication taken. The high degree of loss to follow-up must be further investigated in our study as well as in other investigations. Although help was offered to the participant in the study, it is impossible to comprehend why this follow-up system has failed.

Conclusion

The prevalence, drug resistance pattern, and low treatment outcome in MDR-TB cases were alarming highly as MDR-TB has been a serious public health problem in Pakistan as well as worldwide and affects the TB control strategy. In conclusion, to reduce the resistance pattern, increase treatment outcome, and decrease the level of loss to follow-up and mortality rate, we should fully utilize the protocol of National TB guidelines to prevent the further emergence of the following factor and drug resistance. The goal of our study is to support and focus on the successful implementation of DOTS and the need to develop a role for those patients who have lost their follow and dropped out of their treatment protocol to prevent MDR-TB.

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