Evaluating the Effects of Decentralized District-Based Treatment of Drug-Resistant Tuberculosis in Pakistan: An Alternative Model of Care

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LINK MEDICAL INTERFACE

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Disclaimers

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ABSTRACT

Background: Pakistan faces a high burden of drug-resistant tuberculosis (DR-TB), with traditional centralized care resulting in delays and poor treatment outcomes. Decentralizing care to district-level hospitals offers a potentially more effective alternative.

Objective: This study aimed to evaluate the impact of decentralized DR-TB care on treatment initiation time, patient follow-up, and treatment outcomes.

Methods: A descriptive post-intervention study was conducted at a decentralized DR-TB clinic in Sheikhupura, Punjab, between June 2021 and December 2022. Data from 100 patients were retrospectively collected from hospital records and diagnostic labs, including demographic information, treatment compliance, smear and culture conversion rates, and adverse drug reactions. SPSS 25 was used for statistical analysis, including descriptive statistics.

Results: The average time from diagnosis to treatment initiation was 14.9 days. Smear conversion by the sixth month was 99%, while culture conversion was 98%. The treatment success rate was 70%, with a 7% loss to follow-up, 2% treatment failure, and 15% mortality.

Conclusion: Decentralized DR-TB care significantly reduced delays in treatment initiation and improved patient outcomes. This model is feasible for national implementation with potential to enhance DR-TB management in Pakistan.

INTRODUCTION

Tuberculosis (TB) remains one of the most significant public health threats globally, ranking among the leading causes of mortality due to infectious diseases. In 2020, approximately 150,000 people worldwide were reported to have started treatment for multidrug-resistant tuberculosis (MDR-TB) or rifampicin-resistant TB (RR-TB). However, the number of patients receiving treatment for drug-resistant TB decreased by 15%, from 177,100 in 2019 to 150,359 in 2020, according to the Global Tuberculosis Report 2021 (1). The emergence of drug-resistant strains of TB poses a major challenge to global TB control efforts, which have been hampered by poor real-time surveillance, inadequate screening practices, and inefficient patient referral mechanisms, all of which hinder the timely identification, management, and treatment of affected individuals (2). In Pakistan, the situation is especially dire. The country ranks fifth globally in TB incidence, with an incidence rate of 259 per 100,000 population, placing it among the nations most burdened by the disease. A national survey conducted in 2011-2012 found that 4.2% of newly diagnosed pulmonary TB patients developed RR-TB, and 16% of those undergoing retreatment developed MDR-TB (3).

To combat this growing threat, Pakistan initiated a DR-TB control program in 2010, expanding its care infrastructure with the support of the Global Fund to more than 33 tertiary and specialized hospitals. These Programmatic Management of Drug-Resistant Tuberculosis (PMDT) sites performed GeneXpert testing, Line Probe Assays (LPA), culture-based drug susceptibility testing (DST), and second-line drug regimens for DR-TB patients, alongside social support services (4). However, this centralized approach to DR-TB care posed significant challenges, particularly for patients from rural or peri-urban areas, who were required to travel long distances to receive treatment at tertiary hospitals. This often led to delays in treatment, poor patient compliance, and unfavorable outcomes, exacerbating the spread of drug-resistant TB within communities. Analysis of treatment outcomes revealed a decline in the treatment success rate for DR-TB patients in Pakistan, from 70% for the 2011 cohort to 64% for the 2017 cohort, underscoring the inadequacies of the centralized care model (5).

The limitations of centralized care prompted the Joint Program Review Mission (JPRM) in 2019 to recommend the decentralization of DR-TB treatment to district hospitals. This shift aimed to bring treatment closer to patients' homes, reducing delays in diagnosis and enrollment in care. Consequently, a DR-TB clinic was established in February 2021 at the District Headquarters (DHQ) Hospital in Sheikhupura, as part of a pilot effort to decentralize DR-TB care (6). This initiative was designed to address the logistical and socio-economic barriers faced by patients and improve the timeliness and quality of care. Decentralization not only

brought diagnosis and treatment services to district hospitals but also integrated these services with the existing Directly Observed Therapy, Short-Course (DOTS) clinics at these facilities, providing a more accessible, community-based model of care. In accordance with national and international guidelines, the National Tuberculosis Program (NTP) developed standard operating procedures (SOPs) for decentralized DR-TB care, which included detailed protocols for planning, implementation, and supervision (7).

The decentralized DR-TB care model involved multidisciplinary teams at district-level hospitals, consisting of pharmacists, TB coordinators, pulmonologists, medical officers, and laboratory staff, all trained in national DR-TB guidelines and programmatic management protocols (8). These teams were responsible for patient management, follow-up, and ensuring patient compliance with treatment regimens. In addition to clinical care, the decentralized model incorporated patient-centered approaches, including home-based DOTS, contact investigation, nutritional support, and psychological counseling, which were designed to improve patient adherence and morale. Provincial TB control programs provided ongoing monitoring and supervision to ensure the quality and consistency of care across decentralized sites (9).

This study aims to assess the impact of decentralizing DR-TB care services on diagnosis, enrollment, and treatment outcomes, and to contribute to the broader effort to strengthen TB control programs in Pakistan. By examining patient outcomes at a decentralized DR-TB clinic in Sheikhupura, this research seeks to evaluate whether district-based care models can effectively reduce delays in treatment initiation, improve patient adherence, and achieve higher rates of treatment success compared to the centralized approach. The findings of this study have the potential to inform future policy decisions regarding the expansion of decentralized DR-TB care across Pakistan and provide a blueprint for other countries facing similar challenges in TB control.

MATERIAL AND METHODS

The study was conducted as a descriptive, post-intervention analysis of patients diagnosed with drug-resistant tuberculosis (DR-TB) and receiving treatment at a decentralized clinic in District Sheikhupura, Punjab, Pakistan. The study included patients diagnosed with rifampicin-resistant tuberculosis (RR-TB) and treated between June 2021 and December 2022. The inclusion criteria required that all patients be either diagnosed with RR-TB through phenotypic or molecular methods. Patients who were transferred to other facilities for treatment and had a stay exceeding one month were excluded from the analysis.

Data were collected retrospectively from hospital records, patient cards, and diagnostic laboratories. The study recorded demographic, clinical, and laboratory information from an electronic database, including patients' age, gender, smoking status, history of TB and DR-TB, diabetes status, previous history of second-line drug use, and diagnostic information such as smear microscopy, Xpert MTB/RIF, and culture-based drug susceptibility testing (DST). Patients' outcomes were also assessed, including treatment initiation time, smear and culture conversion, adverse drug reactions, and final treatment outcomes.

The ethical approval for this study was obtained from the institutional review board of the Common Management Unit (CMU) with IRB number F. NO. IRB-CMU-2023-02. The study adhered to the principles outlined in the Declaration of Helsinki, ensuring that patient confidentiality was maintained. Since the study relied on retrospective data collection from patient records, no informed consent was required from the patients. However, all identifying information was anonymized, and access to the data was restricted to the principal investigator and authorized personnel for the purpose of analysis.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 25. Descriptive statistics were used to summarize the characteristics of the study population, including frequencies, proportions, and medians. Continuous variables such as age and time to treatment initiation were presented as means with standard deviations. Categorical variables were summarized using frequencies and percentages. Although this was a pilot study with a limited sample size, results were interpreted descriptively without the application of inferential statistics due to the nature of the analysis. Data were further analyzed to assess the compliance of patients with follow-up, smear and culture conversion rates, and adverse drug reactions.

RESULTS

The study included a total of 100 drug-resistant tuberculosis (DR-TB) patients treated at the decentralized clinic in Sheikhupura, Punjab. The patients ranged in age from 15 to 84 years, with the majority (63%) being male. Most patients (69%) resided in rural areas, and 27% were smokers. Diabetes mellitus was present in 26% of the patients, while none were HIV positive. Only 3% had a previous history of second-line drug use. The socio-demographic and clinical characteristics of the patients are summarized in Table 1.

Table 1: Socio-demographic and clinical characteristics of DR-TB patients enrolled at a district-level decentralized clinic

Characteristic	n (%)
Gender	
Male	63 (63%)
Female	37 (37%)
Age (years)	
15-34	41 (41%)

Characteristic	n (%)
35-54	26 (26%)
>54	33 (33%)
Residence	
Urban	41 (41%)
Rural	69 (69%)
Smokers	27 (27%)
Diabetes	26 (26%)
HIV Positive	0 (0%)
Previous Second-Line Drug History	3 (3%)

The average time from diagnosis to treatment initiation was 14.9 days, demonstrating the effectiveness of the decentralized care model in reducing treatment delays. As shown in Figure 1, the transition from diagnosis to treatment initiation in the decentralized model was significantly faster compared to the previous centralized system, where delays often exceeded 30 days.

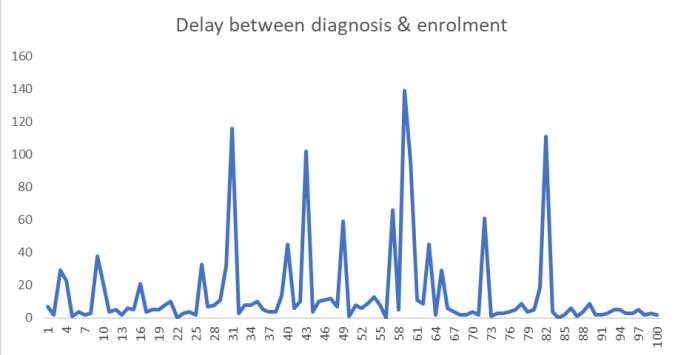

Figure 1: Average delay between diagnosis and treatment initiation (days)

At the beginning of treatment, patients were placed on various regimens according to the availability of second-line drugs. As shown in Figure 2, 44% of patients were placed on LTR-1, 33% on modified STR, and the remainder on LTR-2 or LTR-3 regimens. The sputum smear AFB results conducted at the beginning of treatment indicated that 65% of patients were MTB positive, while 30% were negative. Five patients did not undergo sputum smear testing at the start of treatment (Figure 3).

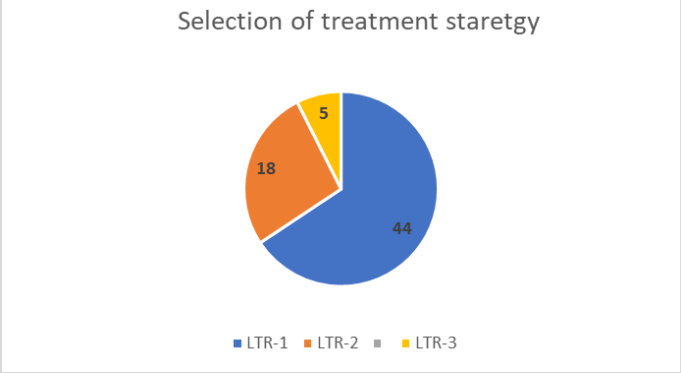

Figure 2: Treatment strategies among DR-TB patients

Adverse drug reactions (ADRs) were reported by many patients during treatment, with arthralgia (40%) being the most common, followed by gastrointestinal irritation (34%) and allergic reactions (10%). Detailed adverse reaction data are presented in Table 2.

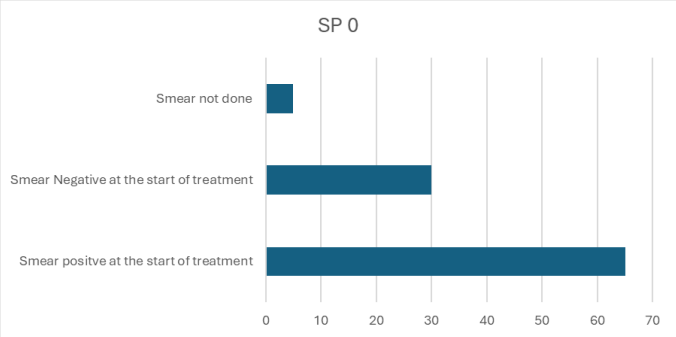

Figure 3: Sputum smear results at the beginning of treatment

By month six, nearly all patients had converted, with a smear conversion rate of 99% and a culture conversion rate of 98%. By the sixth month of treatment, interim smear and culture conversion showed a high success rate. As depicted in Figure 4, 40 patients achieved smear conversion by month one, and 60 patients achieved culture conversion.

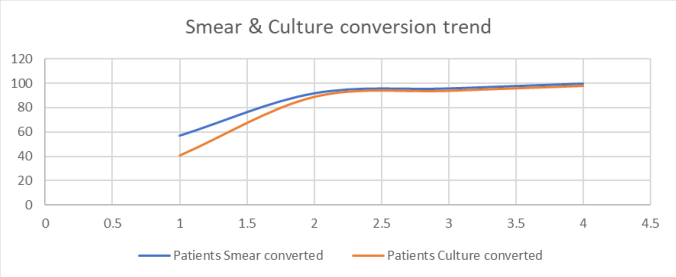

Figure 4: Interim smear and culture conversion (6th month)

Most adverse drug reactions were mild to moderate, with only a small percentage requiring dose adjustments. Table 3 outlines the severity of ADRs, actions taken, and patient outcomes. There were three deaths associated with severe ADRs during the treatment period. At the time of data collection, treatment outcomes were available for all 100 patients.

Of these, 71 patients (71%) were cured, and 15 patients (15%) died during the course of treatment. Seven patients (7%) were lost to follow-up, and two patients (2%) experienced treatment failure (Table 4). In summary, the decentralized model showed significant improvements in treatment initiation, patient follow-up, and clinical outcomes. The study demonstrated a high rate of smear and culture conversion, reduced time to treatment initiation, and favorable treatment outcomes for a majority of the patients. However, the presence of adverse drug reactions highlights the importance of ongoing patient monitoring and care

Table 2: Adverse drug reactions (ADRs) among DR-TB patients

Adverse Reaction	n (%)
Arthralgia	40 (40%)
Gastrointestinal Irritation	34 (34%)
Allergic Reaction	10 (10%)
Hepatotoxicity	7 (7%)
QT Prolongation	4 (4%)
Palpitations	12 (12%)
Myelosuppression	12 (12%)
Peripheral Neuropathy	26 (26%)
Renal Injury	4 (4%)
Depression	21 (21%)
Anxiety	17 (17%)
Psychosis	1 (1%)
Retinopathy	0 (0%)

Table 3: Severity, actions taken, and outcomes of adverse drug reactions

Parameter	n (%)
Severity	
Mild	4 (5%)
Mild-Moderate	25 (31.3%)
Moderate	2 (2.5%)
Moderate-Severe	15 (18.8%)
Severe	6 (7.5%)
Action Taken	
Dose Interrupted	17 (21.3%)
Ancillary Drugs Added	35 (43.8%)
Dose Not Changed	28 (35%)
Outcome	
Recovering	12 (15%)
Recovered	37 (46.3%)
Died	3 (3.8%)

Table 4: Treatment outcomes of DR-TB patients at decentralized clinic

Outcome	n (%)
Cured	71 (71%)
Lost to Follow-up	7 (7%)
Died	15 (15%)
Treatment Failure	2 (2%)

DISCUSSION

The decentralization of drug-resistant tuberculosis (DR-TB) care to district-level hospitals in Pakistan has shown promising results in terms of reducing treatment delays, improving patient compliance, and achieving favorable treatment outcomes. The findings of this study demonstrate that the shift to decentralized care significantly minimized the average time between diagnosis and treatment initiation, with a mean of 14.9 days compared to the delays of over 30 days reported in earlier studies conducted under centralized care models (1). This reduction in delays is crucial for DR-TB management as earlier initiation of treatment is associated with better patient outcomes and reduced transmission within communities. Similar improvements in reducing treatment delays have been reported in studies from South Africa, where decentralized care models for DR-TB have also shown to enhance access to care and accelerate treatment initiation (2).

The high rates of smear and culture conversion observed in this study further underscore the benefits of decentralized care. By the sixth month of treatment, 99% of the patients had achieved negative smear conversion and 98% had negative culture conversion. These findings are consistent with previous studies conducted in Ethiopia and other countries that have implemented decentralized DR-TB care models, which have also reported high rates of microbiological conversion within the first six months of treatment (3). The success of decentralized care in achieving early conversion can be attributed to better patient follow-up, timely interventions, and the provision of community-based care, which minimized the need for patients to travel long distances to tertiary hospitals, thus improving compliance with treatment regimens (4). In contrast, previous studies on centralized care models in Pakistan have reported lower conversion rates due to logistical barriers and patient non-adherence (5).

The overall treatment success rate of 70% observed in this study is comparable to the success rates reported in

decentralized DR-TB programs in other countries, such as India, where a success rate of 72% was documented (6). However, the study's relatively low loss to follow-up rate (7%) and treatment failure rate (2%) suggest that decentralized care may be more effective in addressing the challenges associated with patient retention and treatment adherence, which have been significant issues in centralized care models (7). In previous centralized models in Pakistan, higher loss to follow-up rates and treatment failures were attributed to the distance patients had to travel for care, economic challenges, and the lack of comprehensive patient support systems (8). The decentralized model's emphasis on home-based Directly Observed Therapy (DOT), nutritional support, and psychosocial counseling likely played a role in improving patient adherence and reducing the loss to follow-up.

Despite the positive outcomes, this study identified several adverse drug reactions (ADRs) among patients, with arthralgia (40%) and gastrointestinal irritation (34%) being the most reported. While most ADRs were mild to moderate in nature and did not lead to treatment interruptions, the occurrence of severe ADRs in a small number of patients resulted in three deaths. These findings highlight the importance of continuous monitoring of patients for ADRs and the need for appropriate management protocols to mitigate the impact of these adverse events. Similar challenges with ADRs have been reported in other decentralized DR-TB programs, emphasizing the necessity for comprehensive pharmacovigilance systems to ensure patient safety (9).

The strengths of this study lie in its real-world evaluation of a decentralized care model in a district hospital setting, providing evidence that district-based DR-TB care can be both feasible and effective. The study also benefits from the inclusion of a diverse patient population from both urban and rural areas, making the findings more generalizable to the broader population of DR-TB patients in Pakistan. However, there were limitations, including the lack of a control group to directly compare the outcomes of decentralized versus centralized care. Additionally, the study relied on retrospective data collection, which may have introduced biases related to missing or incomplete data. Future studies should include a prospective design and control groups to better assess the comparative effectiveness of decentralized care models.

To sustain and further improve the decentralized DR-TB care model in Pakistan, several recommendations should be considered. Continued investment in the training and capacity building of healthcare workers at district hospitals is essential to ensure they can competently manage DR-TB patients and handle ADRs effectively. Moreover, the provision of adequate financial support for both DOT providers and patients, along with the expansion of community-based diagnostic facilities such as GeneXpert, will be critical for maintaining early diagnosis and timely treatment. Strengthening data management systems and conducting periodic program evaluations will also help identify areas for improvement and ensure the long-term success of the decentralized care model. Lastly, stakeholder involvement at all levels, including local government, healthcare providers, and international donors, will be key in securing the necessary resources and support for scaling up the decentralized care model across Pakistan.

CONCLUSION

In conclusion, the decentralization of DR-TB care to district hospitals in Pakistan has shown to be an effective approach in improving access to care, reducing treatment delays, and achieving high rates of treatment success. However, ongoing support, monitoring, and refinement of the model will be necessary to address the challenges of ADRs and ensure that the model remains sustainable and effective in the long term. Further research and continued advocacy will be critical in solidifying the role of decentralized care in the management of DR-TB both in Pakistan and globally.

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