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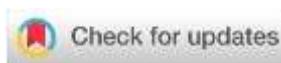
Evaluating the effectiveness of first-Line anti-tuberculosis in Al Dhafra Hospitals

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Abstract

Background: Tuberculosis (TB) continues to be a significant public health issue despite extensive efforts to control it. The standard treatment for TB involves the use of first-line anti-TB drugs administered at a standard dose. However, the effectiveness of this treatment can vary between individual patients, resulting in differing cure rates.

Methodology: The objective of this retrospective study was to assess the effectiveness and safety of first-line generic anti-TB medications administered at Liwa Hospital in the Al Dhafra Region. Data was collected from the electronic medical records of 140 TB patients admitted to Liwa Hospital from January to December 2022. The study included patients with positive acid-fast bacillus (AFB) or polymerase chain reaction (PCR) test results, indicating active TB infection. Patients resistant to first-line anti-TB medications or with lung cancer were excluded. Data collected included demographic information, length of stay conversion time, hospital admission, prescribed medications, treatment duration, and treatment outcomes.

Results: This study observed an average length of stay of 21 days for patients treated with first-line generic anti-TB medications at Liwa Hospital. Over 80% of the patients were discharged within 30 days of admission, indicating a positive response to the medications. Approximately 13% of the patients required a longer duration of treatment and were discharged between 30 and 60 days after admission. Only 5% of the patients had a prolonged stay of over 60 days, most of whom had co-morbidities or rifampicin resistance, but achieved AFB conversion within three months. The average conversion time for patients was 25 days, with over 92% achieving conversion within two months.

Conclusion: This study demonstrated the efficacy and safety of first-line generic anti-TB medications in treating TB patients at Liwa Hospital. The majority of patients responded well to the medications, leading to discharge within 30 days.

Keywords: Tuberculosis, Ethambutol, Pyrazinamide, Rifampicin, Isoniazid, First line drugs, Anti TB drugs

INTRODUCTION

Tuberculosis (TB) caused by Mycobacterium Tuberculosis remains a major global health issue [1]. It ranks among the top 10 causes of death worldwide and is the leading cause of death from infectious diseases [2]. According to the 2019 tuberculosis report by the World Health Organization (WHO), in 2018 TB was the cause of approximately 1.2 million deaths of HIV-negative individuals and 251,000 individuals with HIV[3]. The WHO's ambitious strategy, known as "END TB", aims to achieve a 90% reduction in TB incidence and a 95% reduction in mortality by 2035, compared to 2015[4]. Treatment for active pulmonary tuberculosis (TB) always involves a combination of multiple drugs[5]. The standard and recommended dosage regimen consist of an initial therapy phase lasting two months, during which four drugs (ethambutol, pyrazinamide, rifampicin, and isoniazid) are administered[6]. This is followed by a four-month phase where the treatment consists of isoniazid and rifampicin alone [7].

Recent attempts to shorten tuberculosis (TB) treatment to four months by incorporating "fluoroquinolones" as "first-line treatment" have proven unsuccessful[8]. The standard practice involves administering first-line anti-TB drugs at standard doses according to the patient's total body weight [9]. In clinical trial conditions, the four-drug treatment regimen for drug-susceptible tuberculosis (TB) can achieve cure rates as high as 95-98% based on protocol analysis. However, in resource-limited areas, the success rates of this treatment approach can decline to as little as 65%([10]. There are various reasons for treatment failure and the development of drug-resistance during standard six-month therapy with the four-drug regimen. One potential contributing factor is the presence of suboptimal drug concentrations, which can result from variations in the pharmacokinetics of these drugs between individuals [11]. Considering the inter-individual variability, optimizing drug concentrations and ensuring adequate exposure to the medications is crucial to improving treatment outcomes and minimizing the development of drug resistance [12]. Additionally, the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) present particularly challenging scenarios, necessitating prolonged treatment with "second-line" and "third-line anti-

TB drugs" [13]. These second-line and third-line alternative medications are more expensive, associated with greater adverse effects, and have relatively lower success rates. Some patients require treatment for over 20 months in such cases [14].

To address these issues, this retrospective study aims to assess the efficacy and safety of first-line generic anti-TB medications. Through this, it will provide valuable insights for optimizing treatment outcomes, minimizing drug resistance, and addressing challenges specific to this TB population.

METHODOLOGY

Study Design and Settings: This was a retrospective cohort study conducted at Liwa Hospital in the Al Dhafra Region. The study included 140 TB patients admitted to Liwa Hospital during the period from January to December 2022.

Objective and Aims

The primary objective of this study was to evaluate the efficacy and safety of the generic anti-TB medications used at Liwa Hospital in the Al Dhafra Region.

Additionally, the study aimed to identify areas of potential improvement and research opportunities related to the use of generic anti-TB medications.

Inclusion Criteria

The inclusion criteria required patients to have physical signs and symptoms suggestive of TB, positive acid-fast bacillus (AFB), or polymerase chain reaction (PCR) test, indicating active TB infection.

Exclusion Criteria

Patients meeting any of the following criteria were excluded from the study:

- Patients with negative AFB or PCR test results.
- Patients who are resistant to any of the first-line anti-TB medications.
- Patients suffering from tuberculous pleurisy.
- Pregnant women.
- Psychiatric patients or patients with a history of mental illness.
- Patients with extra-pulmonary tuberculosis.

Data Collection Procedure

Data for this study were extracted from the electronic medical records (EMRs) of the eligible patients admitted to Liwa Hospital. The collected data included relevant demographic information (age and gender), clinical characteristics (symptoms and comorbidities), laboratory test results (AFB/PCR test results), length of stay, hospital admission rates, prescribed generic anti-TB medications, and treatment duration and outcomes.

Anti-TB Medications

The first-line medications used to treat tuberculosis (TB) are Isoniazid, Rifampin, Ethambutol, and Pyrazinamide [15]. These drugs are highly effective in treating TB when taken as prescribed. Isoniazid and Rifampin are the most important drugs in the treatment of TB. They are effective against the active form of the TB bacteria and are able to penetrate the cells where the bacteria hide [16]. Ethambutol is also effective against the active form of TB bacteria and is used to prevent the development of drug resistance [17]. Pyrazinamide is used to kill both active and dormant TB bacteria (18). First-line anti-

TB medications are generally safe and well-tolerated. However, like any medication, they can have side effects. Common side effects include nausea, vomiting, loss of appetite, and changes in liver function tests [19]. Less common side effects can include skin rashes, fever, and visual changes [20]. Generic anti-TB medications are widely available and are an important part of global efforts to make TB treatment more accessible and affordable. The World Health Organization (WHO) recommends the use of generic anti-TB medications as a strategy to improve access to TB treatment.

In this retrospective research, data was collected from 140 patients who received identical generic anti-TB medication from the same batches throughout 2022. Analysis of the medical records confirm that all patients received appropriate doses based on weight (WT), kidney function tests (KFT), and liver function tests (LFT).

Data Analysis

The collected data was analyzed to assess the efficacy and safety of the first-line generic anti-TB medications. Statistical analysis was conducted using appropriate methods. Continuous variables were analyzed using the t-test or analysis of variance (ANOVA), depending on the number of independent variables and groups involved. The significance level was set at $p < 0.05$.

Ethical Considerations

This study followed all relevant ethical guidelines and regulations regarding patient privacy and data protection. Patient identifiers were anonymized during data collection and analysis to ensure confidentiality.

RESULTS

The study observed an average length of stay of 21 days for patients undergoing treatment with first-line generic anti-TB medications at Liwa Hospital (Fig 1). This indicates that, on average, patients required three weeks of hospitalization for their tuberculosis treatment. In addition, more than 80% of the patients involved in the study were discharged within 30 days of their admission (Fig 1). This suggests that the majority of patients responded well to the first-line generic anti-TB medications, enabling their timely discharge from the hospital.

As it is indicated in Graph 1, approximately 13% of the patients required a longer duration of treatment and were discharged between 30 and 60 days after their admission. A small percentage, accounting for 5% of the patients, were discharged after 60 days due to specific conditions. Among these patients, one had rifampicin resistance, while the others had various co-morbidities such as diabetes mellitus (DM), hypertension (HTN), anemia, hyperuricemia, urinary stones, and hematuria. Notably, all of these patients achieved AFB conversion within three months, indicating successful treatment outcomes despite the longer length of stay (Fig 1). The study also found that the average conversion time for patients undergoing treatment with first-line generic anti-TB medications at Liwa Hospital was 25 days. More than 92% of the patients included in the study achieved conversion within two months and approximately 6% of the patients had a conversion time ranging from two months to four months (Fig 2). These patients required a slightly longer duration of treatment.

Additionally, the study identified one patient who had a conversion time exceeding four months. This specific patient might have experienced challenges or complications during their treatment, resulting in an extended conversion time.

Figure 1: Average length of stay 21 days, >80% of the patients discharged within 30 days.

Figure 2 : AFB Conversion Time (Time to negative AFB X 3 samples)

DISCUSSION

The objective of this retrospective study was to assess the effectiveness and safety of first-line generic anti-TB medications in the Al Dhafra Region, with a specific focus on Liwa Hospital. The study observed an average length of stay of 21 days for patients undergoing treatment, indicating that patients required three weeks of hospitalization on average for their tuberculosis treatment. In a retrospective observational study focused on the efficacy of rifampicin (RIF) in tuberculosis (TB) patients, the administration of rifampicin was associated with a significant reduction in the length of hospital stay [21]. However, it is essential to acknowledge that this study solely focused on rifampicin as the major treatment drug, while our study looks at a combination of first-line anti-tuberculosis drugs. Therefore, the findings of this research may not fully represent the efficacy of the entire first-line treatment regimen. Further research considering the combined effects of all first-line anti-TB medications would provide a more comprehensive understanding of their efficacy and impact on hospitalization duration.

Our study also revealed that more than 80% of the patients involved in the study were discharged within 30 days of their admission, indicating a positive response to first-line generic anti-TB medications. This high percentage suggests that the majority of patients responded well to the treatment, enabling discharge from the hospital within a month. However, approximately 13% of the patients required a longer duration of treatment, leading to discharge between 30 and 60 days

after admission. This subset of patients may have had more complex cases or factors contributing to a slightly extended stay for effective treatment. These findings highlight the importance of individualized care and comprehensive management for patients with more challenging tuberculosis infections.

Furthermore, Requena-Méndez et al. conducted a study to examine the "effects of dosage", "comorbidities", and food on the pharmacokinetics of isoniazid (INH) in tuberculosis patients from Peru [22]. The results indicated that 34% of patients had lower INH concentrations during the intensive phase, while 33.3% experienced lower concentrations during the continuation phase. Notably, these patients achieved conversion within three months. This is in line with the study conducted by Burhan et al., which provided evidence that TB patients with comorbidities had a conversion time of three months [23].

While, according to our research, a small percentage of patients (5%) require prolonged stays exceeding 60 days, specific conditions such as rifampicin resistance or comorbidities like diabetes mellitus, hypertension, anemia, hyperuricemia, urinary stone, and hematuria were identified in these cases. In addition, all of these patients achieved AFB conversion within three months, indicating successful treatment outcomes despite the longer length of stay. This suggests that, even in complex cases, the first-line generic anti-TB medications at Liwa Hospital proved effective in eliminating tuberculosis bacteria.

Our study revealed that the average conversion time for patients undergoing treatment with first-line generic anti-TB medications at Liwa Hospital was 25 days, "conversion" being the point at which tuberculosis bacteria can no longer be detected in the patient's sputum. This contrasts with other studies in which longer conversion times were noted. For example, Pasipanodya et al. conducted a study comparing the treatment outcomes of patients based on their peak concentration of rifampicin (RMP), specifically examining concentrations above and below 6.6 mg/L [24]. The researchers evaluated culture conversion at two months and long-term outcomes at two years. Among patients with a peak concentration below 6.6 mg/L, 19% still tested culture-positive at two months, while only 1% of patients with a peak concentration above 6.6 mg/L had a positive culture at the same time point. A similar pattern was observed in long-term outcomes when patients were divided into groups with concentrations above and below 13 mg/L•h AUC. In the group with concentrations below 13 mg/L•h AUC, 33% had a poor outcome compared to only 12% in the group with concentrations above 13 mg/L•h AUC. Two recently-conducted controlled clinical trials provided evidence regarding the relationship between drug exposure and treatment outcomes [25, 26]. Both studies demonstrated that increasing the dose of rifampicin resulted in higher drug exposure. However, only one of the studies showed that the higher exposure group achieved faster culture conversion, indicating a positive treatment response.

Moreover, in our research, more than 92% of the patients achieved conversion within two months, while approximately 6% had a conversion time ranging from two to four months. This could be attributed to various factors, such as the extent of infection or individual responses to treatment. Past research has compared the treatment outcomes of patients based on their culture conversion at two months, with consideration of whether their isoniazid (INH) peak concentration is above or below 8.8 mg/L [27]. Among patients with an INH peak concentration below 8.8 mg/L, 13% still had positive cultures at the two-month mark, while none of the patients with an INH peak concentration above 8.8 mg/L had positive cultures. In terms of assessing the long-term treatment outcomes, the patient group with a below-the-curve (AUC) of INH above 52 mg/L•h had a poor treatment outcome rate of 20%, whereas the patient group with an AUC of INH below 52 mg/L•h had a higher rate of poor treatment outcomes, accounting for 70% . Furthermore, Sekaggya-Wiltshire et al. reported an association between low INH and rifampicin (RMP) concentrations and poor culture conversion [28]. However, in our research one patient had a conversion time exceeding four months, suggesting challenges or complications during their treatment.

There are several limitations to consider regarding this study. Firstly, its retrospective nature introduces inherent limitations as it relies on existing electronic medical records, which may be incomplete. Additionally, the reliance on data collected for clinical purposes can introduce potential biases. Furthermore, being a single-center study conducted at Liwa Hospital, the generalizability of the findings to other settings or populations may be limited.

However, the results of our study can provide valuable insights into the efficacy and safety of first-line generic anti-TB medications at Liwa Hospital in the Al Dhafra Region. The identified areas of improvement and potential research opportunities will guide future interventions and further research aimed at enhancing TB treatment outcomes and patient safety.

CONCLUSION

In conclusion, the findings provide valuable insight into the treatment outcomes and duration associated with generic first-line anti-TB medications. The results indicate that the majority of patients responded well to the first-line generic anti-TB medications, as evidenced by their timely discharge within 30 days of admission. The average length of hospital stay was 21 days, indicating a three-week duration for tuberculosis treatment on average. The study also identified a subset of patients with more complex cases or comorbidities requiring a longer treatment duration, yet achieving successful treatment outcomes. These findings highlight the efficacy and safety of generic anti-TB medications in the Al Dhafra Region and provide valuable information for further improving TB treatment strategies. Continued efforts are necessary to optimize treatment outcomes and address challenges faced by patients with prolonged conversion times, ultimately enhancing the effectiveness of TB treatment in the region.

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