Assessment of Patients Adherence to Oral Regimen of Drug-Resistant Tuberculosis among Iraqi Patients

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Abstract:

Background: Drug-resistant tuberculosis is an airborne chronic infectious disease that has evolved resistance to at least two anti-TB medications (isoniazid and rifampin). For the drug-resistant tuberculosis epidemic to be controlled, it is essential that patients be cured. However, therapeutic failure is often caused by patients who don't adhere to their prescribed regimen.

Incomplete treatment facilitates the spread of multidrug-resistant tuberculosis and the subsequent emergence of severely drug-resistant TB. It is crucial to determine the prevalence of pharmacological non-adherence among these patients and to know the reasons for this non-adherence.

Objectives: Assess adherence of patients with drug-resistant TB to oral anti-TB medications.

Method: This was a prospective observation study From July 2022 to April 2023, conducted at Baghdad \ National Tuberculosis Institute which belongs to the Ministry of Health, adherence to therapy was evaluated if the patient consistently took the specified quantity of tablets (the correct dosage) according to the prescribed schedule, and then indicated that they were adhering to therapy. If the non-adherence lasted for longer than 14 days, it was considered serious term; if it lasted less than 14 days, it was called short term.

Result: The study involved a total of 67 drug-resistant tuberculosis patients, and the duration of their treatment was 14 weeks, mostly males, with a majority being urban residents. within the first two weeks, only 1 patient interrupted the treatment course for a short term. At six weeks (6%) of patients interrupted the course, within the ten weeks, there was no interruption and 100% of adhere to treatment was observed. At fourteen weeks, (14.9%) of the patients interrupted the course. The patients who interrupted to treatment were mostly due to far residence because the TB institute was the only institute in Iraq where patients treated and diagnosed in Baghdad, others of them were causeless interrupted their treatment, and fewer due to adverse drug events such as anemia due to took linezolid drug and arthralgia because of levofloxacin drug. There was not a statistically significant difference between those who adhered to the correct dose (the correct count number of pills) and those who adhered to a low dose (low count number of pills) with demographic data.

Conclusion: Patient interrupting the treatment course was noticed mostly in the six and fourteen weeks, patient characteristics did not impact their adherence to the proper dose.

Keywords: adherence, non-adherence, oral regimen for drug-resistant TB treatment.

تقييم التزام المرضى بالنظام الفموي لعلاج السل المقاوم للأدوية بين المرضى العراقيين

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الخلاصة:

الخلفية: السل المقاوم للأدوية هو مرض معدي مزمن ينتقل عبر الهواء وقد طور مقاومة لاثنين على الأقل من الأدوية المضادة للسل (إيزونيازيد وريفامبين). ومن أجل السيطرة على وباء السل المقاوم للأدوية، من الضروري شفاء المرضى. ومع ذلك، غالبًا ما يحدث الفشل العلاجي بسبب عدم التزام المرضى بالنظام الموصوف لهم. ويؤدي العلاج غير المكتمل إلى تسهيل انتشار السل المقاوم للأدوية المتعدد، وما يتبع ذلك من ظهور السل شديد المقاومة للأدوية. ومن هنا تظهر اهمية دراسة مدى انتشار الالتزام وعدم الالتزام الدوائي بين هؤلاء المرضى ومعرفة أسباب عدم الالتزام هذا.

الأهداف: تقييم التزام المرضى الذين يعانون من السل المقاوم للأدوية تجاه الأدوية الفموية المضادة للسل

الطريقة: كانت هذه دراسة مراقبة استباقية في الفترة من يوليو 2022 إلى أبريل 2023، أجريت في بغداد / معهد التدرن الوطني التابع لوزارة الصحة، وتم تقييم الالتزام بالعلاج إذا كان المريض يتناول باستمرار الكمية المحددة من الأقراص (الجرعة الصحيحة). وفق الجدول الزمني المحدد، وهذا يشير إلى التزامهم بالعلاج. فيما يتعلق بعدم التزامهم بالعلاج إذا استمر عدم الالتزام اوالانقطاع لفترة أطول من 14 يومًا، فسيتم اعتباره فترة طويلة المدى؛ وإذا استمرت أقل من 14 يومًا، كانت تسمى قصيرة المدى.

النتيجة: شملت الدراسة 67 مريضاً مصابا بالسل الرئوي المقاوم للأدوية، وكانت فترة علاجهم اربعة عشر اسبوعا، معظمهم من الذكور، وأغلبهم من سكان المناطق الحضرية. خلال الأسبوعين الأولين، مريض واحد فقط انقطع عن دورة العلاج لفترة قصيرة.في ستة أسابيع (6٪) من المرضى توقفوا عن الدورة، خلال الأسابيع العشرة، لم يكن هناك انقطاع وتم ملاحظة الالتزام بالعلاج بنسبة 100٪. وبعد أربعة عشر أسبوعًا، (14.9%) من المرضى انقطعوا عن دورة العلاج. كان معظم المرضى الذين انقطعوا عن العلاج بسبب الإقامة البعيدة لأن معهد التدرن الوطني يعتبر المؤسسة الوحيدة في العراق الذي يتم علاج المرضى ومعاينتهم في بغداد، والبعض الآخر كان بدون سبب يذكر توقفوا عن العلاج ، وعدد أقل بسبب آثار دوائية عكسية مثل فقر الدم بسبب تناول دواء لينزوليد وآلام المفاصل بسبب الليفوفلوكساسين. لم يكن هناك فرق ذو دلالة إحصائية بين أولئك الذين التزموا بالجرعة الصحيحة (العدد الصحيح للحبوب) وأولئك الذين التزموا بجرعة منخفضة مع البيانات الديموغرافية.

الاستنتاج: لوحظ انقطاع المريض عن دورة العلاج في الغالب خلال الأسابيع الستة والأربعة عشر، ولم تؤثر خصائص المريض على التزامه بالجرعة المناسبة.

الكلمات المفتاحية: الالتزام، عدم الالتزام، النظام الفموي لعلاج السل المقاوم للأدوية.

Introduction

TB resistant to at least one of three injectable second-line medicines (amikacin, capreomycin, or kanamycin), as well as isoniazid and rifampin, and at least one (fluoroquinolone) in cases of pre-extensive drug-resistant (1). The consolidated guidelines for 2020, the World Health Organization (WHO) suggested utilizing bedaquiline as a key and avoid the toxicity of injectable medications. Patients with higher-level resistance patterns (pre-extremely drug-resistant tuberculosis) have fewer options for effective treatments(2). Equisetum arvense as a traditional medicine, the plant has been used to help cure and prevent tuberculosis (3). According to WHO 2019 guideline the long oral regimen consisting of three effective drugs such as fluoroquinolones group, linezolid and bedaquinline in addition to clofazimne and cycloserin (4).

For the diagnosis, reporting, and treatment of drug-resistant TB with a new, modified oral regimen, the 2019 WHO Consolidated Recommendations for Drug-Resistant TB therapy were adopted. Long-term care should include all oral regimens made up of (levofloxacin or moxifloxacin tablets+ bedaquiline tablets+ linezolid tablets+ cycloserine capsules+ clofazimine capsules or tablets), with drug dosage based on weight band in patients older than 14 years old(5, 6) . The Longer regimens for drug-

resistant tuberculosis include;levofloxacin tablet 500mg + bedaquiline tablet 100 mg (4 tablets once daily for first 2weeks; then 2 tablets once daily for 22 weeks) + linezolid tab 600mg + clofazimine capsule or tablet 50mg or cycloserine capsule 250 mg instead clofazimine if clofazimine will not be used(5) . The fact that they may be taken orally rather than injectable is their main benefit since it improves treatment success rates and decreases the risk of nephrotoxicity and ototoxicity, two serious ADEs (adverse drug events) of aminoglycosides (4). Behavioral adherence is a continuous process that must be evaluated while the patient receives treatment. The typical treatment for MDR-TB (multidrug-resistant -tuberculosis) consists of a multidrug regimen that lasts 24 months. Successfully curing patients is essential to preventing the spread of MDR-TB (7). Contrarily, non-adherence to therapy is a serious barrier to effective treatment(8). Treatment failure promotes MDR-TB transmission and the establishment of highly drug-resistant TB (9). Therefore, it is crucial to assess the prevalence of pharmacological non-adherence in these patients and identify the underlying reasons for non-adherence in order to carry out certain therapy. Treatment for MDR-TB has taken little attention to two crucial signs of drug non-adherence: therapy cessation and medication under- and overuse. A major treatment interruption was one that lasted longer than two weeks but less than two months, whereas a treatment interruption was defined as the cessation of any anti-TB medication during the course, for at least one day of treatment. The factors that directly observed treatment (DOT) coverage, education level, and gender were found to be the main causes of treatment interruption in the one study that examined them(7). Only two studies included the most frequent causes of therapy termination, including the absence of a patient, treatment rejection, and negative medication responses to ADEs (adverse drug events) (10). The predictors and causes of major interruption must therefore be further studied, with a focus on the impact of certain medications on serious interruption. Patients who regularly take their drugs nevertheless run the risk of taking the wrong dosage. By counting tablets at the patients' residences, the indication can be assessed. Home visits were used since it could be difficult to count pills at the clinic, especially if there are many tablets to count and the clinic is busy(11). The number of tablets taken relies on the frequency of visits each month, whether they are taken in the right quantity, overdose, or at a lower dose, and the reason for stoppage depends on the structural problems that are directly addressed to the patient. Accordingly, participants were categorized as using drugs correctly if the number of pills they took matched the number they were expected to take; incorrectly if they took fewer pills than they should have; and incorrectly if they took more pills than they should have. Treatment adherence may be impaired by a high pill load brought on by co-morbidity(12). Due to the large daily pill load, a prolonged course of therapy, frequent and serious ADEs, and financial burden determining the proper medication dosage is particularly difficult for MDR-TB patients. These results imply the need for ongoing ADEs monitoring, drug regulation modification, and financial assistance for MDR-TB patients in this research population. Patient self-reports can be an economical technique to monitor monthly medication under- and overuse in therapeutic settings(7).

The current study, need to assess patients' adherence to treatment with oral use not injectable this was distinguished the current study because of with new oral regimen was depended on pill use, while the old regimen used an injectable agent. This study considers the first one in the Iraqi population with an oral regimen for TB treatment.

Patients and methods

Patients

From July 2022 to April 2023, and the duration of observation for fourteen weeks consider the timeline during monitoring. A total 67 patients with multiple drug-resistant (MDR) and pre-extensively drug-resistant (pre-XDR) tuberculosis were selected to take part in this observational study at the National Tuberculosis Institute in Baghdad which belongs to the Ministry of Health.

Patient Selection

Patient Inclusion Criteria:

- Patients over 15 years old age
- Patients with pulmonary MDR and pre-XDR as diagnosed according to WHO guidelines (13).

Patient Exclusion Criteria:

- Prisoners patients with TB. (because the prisoners didn't have completed data in addition didn't visit the institute where patients had face-to-face interview).
- Pregnant and lactating women. (because of the protocol of treatment different and some of the drug's contraindications with them).

Ethical Consideration:

The College of Pharmacy at Mustansiriyah University and the ethical and scientific committee both discussed and accepted the research plan. The approval of the Iraqi National Tuberculosis Institute was acquired prior to the data gathering.

Study Design and Data Collection

This type of observational study was prospective in order to achieve the intended goal. A specialist pulmonologist physician diagnosed the patients in accordance with the National Tuberculosis Program's guidelines (NTP). The purpose of the patients' data sheet was to collect information about the patient from the registration record Information gathered included the institution's treatment protocol, potential drug adverse events of the recommended course of therapy, and other subjective and objective evaluations, addition to adherence and non-adherence. The essential characteristics of each patient, such as age, gender, BMI, marital status, residence and occupation, education, number of family members, were collected during face-to-face interviews with patients.

Assessment of Patients' Adherence to Treatment

This was done during each visit at initial time of treatment to institute throughout the study period through face-to-face interviews and also depending on clinical profile chart drug use. Adherence to therapy is considered to have occurred when the patient consistently takes the prescribed number of tablets (the correct dosage) without missing any doses or otherwise deviating from the prescribed schedule. Any time during the treatment period patient adherence to treatment protocol was defined as any anti-TB medication not taken for at least one day was considered an interruption, whereas an interruption lasting more than two weeks but less than two months was considered a major treatment interruption(7). Non-adherence will be interpreted if it was caused by adverse outcomes or by feelings of stigma, far residence, lack of financial resources, or lack of causality.

In any field, there is no one best way to evaluate patient adherence to treatment because every method has advantages and disadvantages. Throughout the whole course of therapy, adherence behavior needs to be observed as it is a dynamic process.

The duration of the interruption (non-adherence) was more than 14 days, it is deemed serious, or an interruption less than 14 days was considered short-term (7).

Statistical Analysis

Depending on whether the distribution was normal or skewed, continuous variables

were expressed as means and standard deviations or medians with range. Categorical variables were expressed as frequency and percentages. A P-value less than 0.05 was considered statistically significant. R software packages (dplyr, gt_summery, and ggplot). dplyr is data manipulation package that is part of R package software in statistics making data manipulation easier one of the function choose which column data frame would like to work. gtsummary provides an elegant and flexible way to create publication ready analytical and summary table using R programming language. ggplot Grammar of Graphics plot in R programming provide a consistent and structured way to create visualized. were used for data processing, visualization, and statistical analysis ("R version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria").

Result

Baseline Characteristics of Drug-Resistant TB Patient

Description of Patients' Sociodemographic and Anthropometric Characteristics

Patients with drug-resistant TB total (67) were enrolled in this study. The mean age of the sample was (36. ±14.6) years old, and males made up (53.7%) of the population while females made up (46.3%). In this sample, married was the majority (68.7%). Most people had only completed primary school, were unemployed (67.2%), and had a large family number. The vast majority (92.5%) of the patients lived in an urban area; the average BMI for this group was (20.4±4.3), based on their height and weight, as mentioned in **Table (1).**

Table 1: Percentages of patients' sociodemographic, and anthropometric Characteristics

Age, years	**36.3 ± 14.6**
Sex	
Males	36 (53.7%)
Females	31 (46.3%)
Marital status	
Married	46 (68.7%)
Unmarried	21 (31.3%)
Family members (number)	6.5 ± 3.2
Occupation	
Unemployed	45 (67.2%)
Employed	13 (19.4%)
Others	9 (13.4%)
Education	
Primary school	50 (74.6%)
Secondary school	6 (9.0%)
College	11 (16.4%)
Residence	
Urban	62 (92.5%)
Rural	5 (7.5%)
BMI, kg/m^2	20.4 ± 4.3

Data presented as Number (N) and percentage (%)

Longer Regimens for Multidrug- or Rifampicin-Resistant Tuberculosis

The current drugs used for the treatment of drug-resistant TB patients include bedaquiline represented (97.0%), linezolid used by (89.6%), levofloxacin (86.6%), clofazimine by (85.1%), cycloserine by (34.3%), moxifloxacin by (14.9%), and delamanid by (7.5%), as shown in **Table (2)** and **Figure (1).**

Table 2: Percentage of current drugs used in treatment of drug-resistant TB patients

Drugs	Patients N = 67
Bedaquiline	65 (97.0%)
Linezolid	60 (89.6%)
Levofloxacin	58 (86.6%)
Clofazimine	57 (85.1%)
Cycloserine	23 (34.3%)
Moxifloxacin	10 (14.9%)
Delamanid	5 (7.5%)

Data presented as Number (N) and percentage (%)

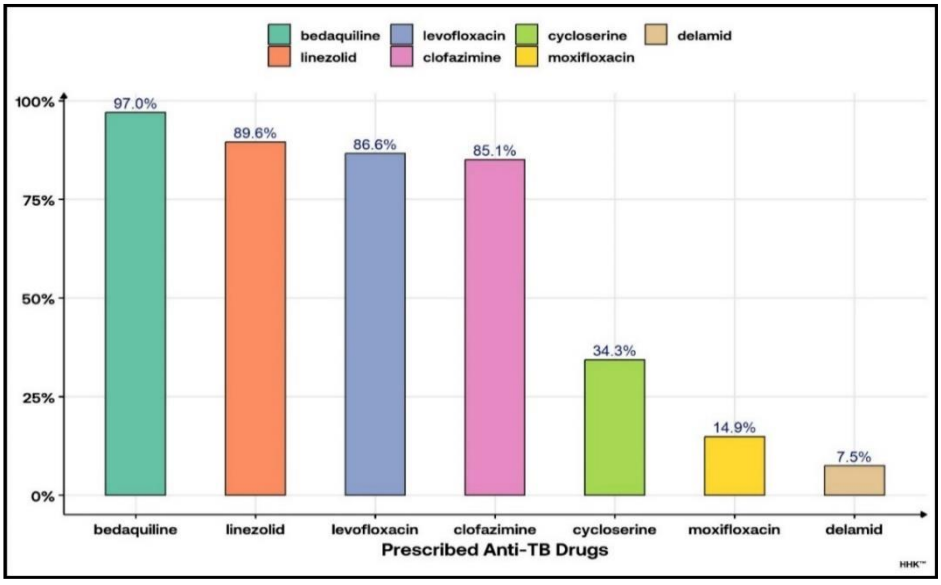

Figure 1: Percentages of the drugs used in drug-resistant TB Patient

Patient Adherence to Regimens for Multidrug-Resistant Tuberculosis

Regarding the patient's adherence to the treatment; within the first two weeks only 1 patient interrupted the treatment course for 1-14 days because of anemia. while patients with the correct dose (98.5%) and low dose (low count number of pills) were (1.5%). At six weeks (6%) of patients interrupted the course, (50%) of them interrupted for 1-14 days whereas for the rest for more than 14 days, the interruption causes were; far

residence, causeless, and adverse drug events such as anemia. In regard to dose patients adhere to correct dose (94%) and patient with low dose (6%). Within the ten weeks, there was no interruption and 100% of adherence was observed. At fourteen weeks, (14.9%) of the patients interrupt the course, (70%) of them interrupt for 1-14 days, whereas (30%) of them for more than 14 days. The interruption causes were arthralgia, far residence, and causeless, patients' correct dose (85.1%) the details mentioned in **Table (3).**

Table 3: Description of patient's adherence to the treatment

		(n%)	Duration of interruption with number and percentage of patient	Causes of poor adherence
Two weeks	Interruption	1 (1.5%)	1-14 day	Anaemia
	Dose			
	Correct	66 (98.5%)		
	Low dose	1 (1.5%)		
Six weeks	Interruption	4 (6.0%)	2 (50%) 1-14 days	Anaemia, far residence, causeless
			2 (50%) > 14 days	
	Dose			
	Correct	63 (94.0%)		
	Low dose	4 (6.0%)		
Ten weeks	Interruption	0 (0.0%)		
	Dose			
	Correct	67 (100.0%)		
	Low dose	0 (0.0%)		
Fourteen weeks	Interruption	10 (14.9%)	7 (70%) 1-14 day	Arthralgia, causeless, far residence
			3 (30%) >14 day	
	Dose			
	Correct	57 (85.1%)		
	Low dose	10 (14.9%)		

Data presented as (N) Number of patients, Percentage (%)

Factors Association with Poor Adherence

As mentioned in **Table (4)**, there was not a statistically significant difference between those who adhered to the correct dose (the correct number of pills) and those who adhered to a low dose with demographic data, (*P* value ≥0.05).

Table 4: Relationship between adherence to dose and sociodemographic characteristics

Characteristics	Correct dose , N = 52	Low dose , N = 15	*P*-value
Age, years	36.0 ± 14.6	37.3 ± 15.0	0.8
Sex			0.6
Male	27 (51.9%)	9 (60.0%)	
Female	25 (48.1%)	6 (40.0%)	
Marital status			0.9
Married	36 (69.2%)	10 (66.7%)	
Unmarried	16 (30.8%)	5 (33.3%)	
Family members (number)	6.3 ± 3.1	7.4 ± 3.4	0.3
Occupation			0.3
Unemployed	36 (69.2%)	9 (60.0%)	
Employed	8 (15.4%)	5 (33.3%)	
Other	8 (15.4%)	1 (6.7%)	
Education			0.058
Primary	42 (80.8%)	8 (53.3%)	
College	7 (13.5%)	4 (26.7%)	
Secondary	3 (5.8%)	3 (20.0%)	
Residence			0.9
Urban	48 (92.3%)	14 (93.3%)	
Rural	4 (7.7%)	1 (6.7%)	
BMI, kg/m²	20.2 ± 3.4	21.1 ± 6.4	0.6

Data presented as Mean±(SD) , (N) Number of patients and percentage (%), Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test, *P* value ≥0.05 (NS) non-significant

Discussion

Patients involved in this study had drug-resistant tuberculosis and were, on average, (36.3 ±14.6) years old; the majority were men; most were of a healthy BMI range (20± 4.3). The majority of patients in a study from a developing nation (Pakistan) were also male, with a comparable mean age (36.75±15.69), and predominantly urban residents (14). Since the majority of the current study's data was obtained in urban regions, it follows that the prevalence of infection there was shown to be higher among urban residents. It has been claimed that the recurrence rate of tuberculosis in India is 40% in urban regions and 60% in rural areas(15). Households are a major source of tuberculosis transmission. A TB patient in the home is likely to infect at least two others. This matches the current investigation in that when multiple TB patients share a living area, transmission was increased(16) . The predominant symptoms in enrolled patients were cough and fever, mainly night fever and sweating, sudden weight, and appetite loss, to a lesser extent the symptoms of extrapulmonary TB. Similar findings were recorded from a previous study in Pakistan (14).

According to WHO guidelines 2019, and the NTP protocol of treatment, in the current study all patients treated with a new, modified oral regimen, long-term treatment should include all oral for (18-24months) regimens consisting of levofloxacin, bedaquiline, and linezolid tablet,

clofazimine tablet were also given to patients, and fewer patients get cycloserine, tablet, moxifloxacin, and delamanid tablet. Protocol in the study conducted in Pakistan at least 8 months of treatment with a single injection dose of an aminoglycoside (amikacin, kanamycin, or capreomycin) plus levofloxacin or moxifloxacin, plus ethionamide, cycloserine, and pyrazinamide for 12 months. Patients having a previous exposure to, or resistance to, second line drugs were encouraged to supplement the aforementioned regimen with vitamin B6 and para-aminosalicylic acid (17). Protocol treatment in Belorussia, Uzbekistan and South Africa with orally regimen Bedaquiline was administered at a dose of 400 mg once daily for 2 weeks, then 200 mg three times weekly for 22 weeks; pretomanid was administered at a dose of 200 mg once daily for 24 weeks; and linezolid was administered at a dose of 600 mg once daily for 16 weeks, then 300 mg once daily for 8 weeks. This was the regimen bedaquiline, pretomanid and linezolid. BPaL was combined with 400 mg of moxifloxacin once daily for 24 weeks in the BPaLM regimen, and BPaL was combined with 100 mg of clofazimine once daily (or 50 mg if the patient weighed 30 kg(18).

Most of the patients following the NTP program for multidrug-resistant - rifampicin-resistant tuberculosis (MDR-RR TB) management, in the current study adhered to the regimen, the interruption to the treatment course was between (1-14) days, mostly noticed at week six and the majority at week fourteen demonstrated treatment interruption which was (14.9%) of patients stopped taking their medication. The interruption causes were far residence, arthralgia,and anemia. While all patients in the current study adhered to the regimen, and no one present interrupted the treatment; 100% adherence was observed in the tenth week. In the current study because the regimen is not costly and all patients receive it free, that make they do not suffer from the cost of the regimen so most of the patients adhere to drugs.

The main advantage of the new MDR regimen is that they are all-oral medications, which increases treatment adherence and reduces serious ADEs ototoxicity and nephrotoxicity, these were two examples produced by the aminoglycosides (19). However, the new treatment protocols are not free of adverse effects, and evidence of its efficacy and safety is limited(20). This supports the present study where no one has toxicity due to the use of only oral regimen which were safer than old regimen that contain injection agents. A previous study reported (93%) of MDR-TB Philippines patients missed taking medication as directed for at least one day of their treatment, and (28.7%) of Chinese patients suffered a major interruption to their treatment, ADEs and financial difficulties were the major causes (7). However, the current study does not present the finances or ADES as the major cause leading to stopping the medication. The overall, in the present findings,52 (77.6%) patients presented with good adherence, 15 (22%) patients stopped treatment. The findings were much better than that reported among Chinese study findings where (51%) of MDR-TB patients experienced minor treatment gaps and (17%) had serious disruptions (21). As a result, in the study in the China investigation, amikacin had the most interruptions. The significant occurrence of ADEs among MDR-TB patients indicates that it is critical to regularly check on patients throughout (7) . Regarding to current study, all patient took an oral regimen and no one stopped the treatment because of an injectable agent adverse event, this was the advantage of an oral regimen that make most people adhere to drugs which was prescribed as tablets.

As advised by the WHO National TB programs have used a variety of interventions, including direct observation of treatment (DOT) and social support, for

a long time, and digital health interventions, including SMS messages, telephone calls, or other reminders, have been introduced more recently, all with the goal of increasing patient adherence to TB treatment. However, none of these models of care have ever been evaluated, so the World Health Organization (WHO) has not yet issued guidelines with regard to their use(22). The poor DOT coverage among patients in this study might be one of the explanations for the occurrence of major interruptions. The ADEs may require a modification in medication dosage or the temporary or permanent discontinuation of a drug(23,24). The significant occurrence of ADEs among MDR-TB patients indicates that it is critical to regularly check on patients throughout treatment (22,25). Previous qualitative research demonstrated that poor enrollment and treatment interruption were caused by the financial burden associated with MDR-TB treatment (21, 26,27) . Another study stated that financial help had a significant impact on successful treatment by encouraging patients to increase adherence (28). Previous research discovered that recollection bias or desirability bias caused self-reports to frequently overstate adherence rates(29).

In the current study, the patients' characteristics did not have any impact (non statistical significant) on their adherence to the proper dose. Besides, no impact on their overall adherence to the regimen, the difference between those who did not experience adherence and those who adhered was not statistically significant with other patient demographics. It was reported Chinese conducted study that monthly income and comorbidity were associated significantly with the level of adherence(27), while other demographics were not associated with the correct dose (correct number of pills) (7).

Study Limitation

The study's small sample size is probably responsible for the national institution being Baghdad only center for MDR and pre-XDR infection therapy. Due to patient overload, adherence evaluations in clinics may produce unreliable results. As a dynamic behavior, patient adherence to therapy may evolve over the course of the recommended treatment over months. recollection bias is an important limitation of every study, while recall bias could have been a concern, it appears to have been mitigated by the high degree of agreement between self-reports and pill count data. Finally, this research did not include people who had previously finished their treatment, their higher rate of treatment adherence may have impacted current findings if they had been included. Another limitation might be not using a valid tool to measure adherence in other studies.

Conclusion

Patient interrupting the treatment course was noticed mostly in the six and fourteen weeks mostly because of far residence, and few due to anemia as adverse drug events. Patients' characteristics did not impact their adherence to the proper dose, nor their overall adherence to the new oral regimen. The recommendation for future research could be to study the implementation of direct observation of treatment (DOT) and social support by national TB programs and other recently introduced (SMS (short messaging service), phone, and other reminder calls, and video observation of therapy (VOT), are all examples of digital health treatments) to increase patient’s adherence.

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