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Prevalence and Drug Resistance Pattern of *Mycobacterium tuberculosis* Isolated from Tuberculosis Patients in Basra, Iraq

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A b s t r a c t

Drug-resistant *Mycobacterium tuberculosis* (DR-MTB) is a major health threat to human beings. This study aimed to evaluate the prevalence and drug resistance profile of MTB. Data were collected from 2,296 newly diagnosed, and 246 retreated tuberculosis (TB) patients who attended the Advisory Clinic for Chest Diseases and Respiratory in Basra province from January 2016 to December 2020. Both new diagnostic and retreated TB cases showed that DR-MTB cases were significantly higher at age 15–34 years, pulmonary TB, and urban residents but with no significant difference regarding gender. The drugs resistance was significantly higher among the retreated cases compared with the new diagnostic patients (20.3% vs. 2.4%, $p < 0.0001$), with the percentage of the resistance to first-line drugs in primary and secondary cases including isoniazid (1% and 17.1%), rifampicin (0.78% and 15.8%), ethambutol (0.56% and 8.5%), streptomycin (1.3% and 9.75%). Notice that the most common drug resistance was against streptomycin with 1.3% in new patients and against isoniazid (17.1%) in retreated patients. The rate of total drug-resistant TB, multi-drug resistant TB, mono-drug resistant TB, and rifampicin-resistant TB among new tuberculosis cases increased in this period from 2.2 to 6.7%, 0.17 to 1.6%, 0.85 to 4%, and 0.17 to 4%, with a percentage change of 204.54, 841.17, 370.58, 22.5%, respectively. The rates of poly-

Trends for first-line drug resustance among DR-TB cases
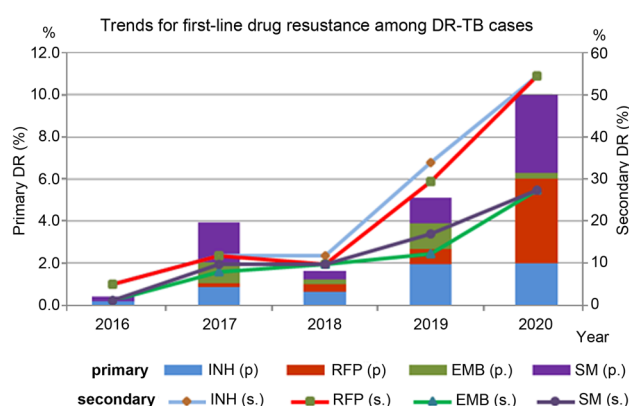
drug-resistant TB and ethambutol-resistant-TB dropped in this period by 15.96%, and 0.7%, with a decrease from 1.19 to 1% and from 1 to 0.3%, respectively. Similarly, the increase of drug-resistant TB among secondary cases has also occurred. In conclusion, the temporal trend showed an increase in the rate of drug resistance of *M. tuberculosis* since 2016, with a predominant multi-drug-resistant TB and isoniazid-resistant TB.

K e y w o r d s: *Mycobacterium tuberculosis*, drug resistance, MDR-TB, retreated TB, Basra

Introduction

Tuberculosis (TB) is considered to be a highly contagious disease, causing thousands of deaths globally (Sousa et al. 2020). It is caused mainly by *Mycobacterium tuberculosis* (MTB), responsible for 1.5 million deaths occurring each year in current times (WHO 2020). Since the twentieth century, after the invention of the BCG vaccine (Bacillus Calmette-Guérin, 1921) and the use of anti-TB agents (isoniazid (INH), rifampicin (RIF), ethambutol (EMB), pyrazinamide (PZA)), the occurrence of TB dropped rapidly (Godreuil et al. 2007). However, the rate of TB amplified in the 1980s due to the emergence of the strains resistant to anti-tuberculosis drugs. The increase of drug-resistant tuberculosis (DR-MTB) has become a significant public health concern that represents a risk to world TB control programs (WHO 2018). About 25% of TB cases recorded globally demonstrate resistance to one of the first-line drugs used to treat this disease. Approximately

5% of first-line DR-MTB cases progress to multi-drug resistant tuberculosis, which can progress to extreme drug-resistant tuberculosis (XDR-TB) (Madrazo-Moya et al. 2019).

The main two types of drug resistance in *M. tuberculosis* are primary (transmitted) resistance and secondary (acquired) resistance. Primary resistance is defined as drug resistance in people who have never taken anti-tuberculosis medicines or have only had them for less than a month. These individuals are thought to have an initial infection with drug-resistant bacteria (new cases). Resistance to anti-tuberculosis medicines that develops during treatment or in a person who has been on therapy for at least one month is referred to as an acquired resistance (retreated cases) (WHO 2003).

Resistance to anti-tuberculosis drugs is mainly associated with the infective TB control programs. Consequently, this has affected control efforts made by countries with a lack of accessibility to second-line anti-TB drugs. The reasons were insufficient therapy, low patient compliance, reduced drug supply, and unsuitable treatment routines (Urassa et al. 2008).

According to the data released in 2018 by World Health Organization, approximately 10 million people developed TB in 2017. Three and half percent of newly diagnosed and 18% of retreated TB cases were identified as multi-drug resistant (MDR) TB (WHO 2018).

Iraq is one of the countries in the World Health Organization Eastern Mediterranean Region (WHO-EMR), which has a population of approximately 38 million with a TB incidence rate of 42 per 100,000 (WHO 2018). It places Iraq in the top seven countries within the WHO-EMR for TB incidence, i.e., 3% of total TB cases (WHO 2009).

The present study aimed to investigate the prevalence of TB to understand the problem of DR-MTB and the issues related to its spread. It would help determine the high-risk population for drug-resistant TB, develop procedures to stop the spread, and provide effective management for future TB control.

Experimental

Materials and Methods

The study was based on the TB patient's data collected from the Advisory Clinic for Chest Diseases and Respiratory (ACCDR) in the Basra province (Fig. 1) from January 2016 to December 2020. A total of 2,296 newly diagnosed and 246 retreated TB patients, including 1,199 females and 1,343 males aged 4–87 years, were recruited in this study. Patients were from urban areas (city centers and surrounding areas with a high population density) and rural areas (coun-

tryside with a low population density). The study was approved by the Research and Development and Ethic Committee/Health Authority and the Advisory Clinic for Chest Diseases and Respiratory in the Basra province. Because of the retrospective nature of this study, which started several years ago, there was difficulty obtaining informed consent. In such circumstances, informed consent was not obtained, and all patients' records were deidentified before analysis.

The patients were clinically diagnosed with CCDR, and sputum samples were examined microscopically for acid-fast bacilli (AFB), cultured on Lowenstein-Jensen solid medium, and subjected to conventional drug susceptibility tests (Mankhi et al. 2009). For the rifampicin resistance test, the samples were processed with the GeneXpert MTB/RIF assay, following the manufacturer's instructions (Cepheid, USA).

The patients were classified into different categories and subjected to epidemiological analysis. The clinical and demographic features of enrolled patients based on age, sex, smoking, chest X-ray appearance, regions, and type of TB were gathered.

Statistical analysis. A package for Social Sciences (SPSS) Version 22 software was used for statistical analysis. The variables of the categorized groups, including age, sex, smoking, cavity, patients' type, and region for new and retreated TB cases, were calculated as total and proportions, respectively. Also, odds ratios (OD) and 95% CIs were calculated to compare newly diagnosed and retreated susceptible and DR-MTB cases. Drug susceptibility profiles of primary DR-MTB and acquired DR-MTB isolates were investigated using a Pearson chi-

Fig. 1. Districts of Basra Governorate.

square test, and a *p*-value < 0.05 was considered statistically significant. In addition, the changes and temporal trends in total and proportions of the different resistance patterns among total DR-MTB cases in the period from 2016 to 2020 were assessed (Nistal-Nuño 2018).

Results

Study population and data collection. During the study period (2016–2020), *M. tuberculosis* was detected in 2,542 patients, of which 2,296 TB patients were newly diagnosed, and 246 were the retreated MTB cases. The patients were classified into different categories and subjected to epidemiological analysis.

Table I clarifies the clinical and demographic characteristics of the study enrolled patients. Out of 2,296 newly diagnosed patients, 54 (2.4%) were drug-resistant TB, whereas among retreated cases, 50 (20.3%) patients represented drug-resistant TB. Among the newly diagnosed drug-resistant TB cases, there were more females (53.7%) than males (46.3%), more non-smokers (75.9%) than smokers (24.1%), and more pulmonary TB (98.1%) than extrapulmonary (1.9%). Additionally, most newly diagnosed drug-resistant TB – 52 cases (96.3%) were from three age groups: 15–34 years – 21 (38.9%), 35–54 years – 12 (22.2%), and more than 55 years – 19 patients (35.2%). The distribution of age, sex, smoking, etc., among treated drug-resistant TB cases was similar to the newly diagnosed cases (Table I).

When comparing new drug-susceptible TB cases to newly diagnosed drug-resistant TB cases, it might be observed that more patients were at the age of 15–34 years old (OR: 0.788, 95% CI: 0.420–1.479), and more numerous were females (OR: 1.324, 95% CI: 0.771–2.275). Also, newly diagnosed drug-resistant TB were more likely to be pulmonary TB (OR: 52.062, 95% CI: 7.187–377.129, *p* > 0.05), and more patients came from urban areas (OR: 1.939, 95% CI: 1.12–3.358, *p* < 0.05). Among retreated TB cases, secondary drug-resistant cases were more likely to be at the age of 15–34 years old (OR: 1.622, 95% CI: 0.758–3.470), presented pulmonary TB (OR: 18.634, 95% CI: 2.51–138.31, *p* > 0.05), and were from urban areas (OR: 2.661, 95% CI: 1.412–5.015, *p* > 0.05). There was no significant difference between males and females (OR = 1, *p* = 1) in this group of patients.

New TB cases were more likely to be diagnosed within patients at the age of 15–34 years (OR: 1.613, 95% CI: 1.166–2.233, *p* > 0.05), younger than 14 years (OR: 7.748, 95% CI: 3.109–19.308, *p* > 0.05), and aged 35–54 years old (OR: 0.851, 95% CI: 0.753–0.962). New TB was diagnosed less likely in patients aged more than 55 years (OR: 1.309, 95% CI: 0.945–1.813), compared with retreated TB cases (Table I).

The cavitary disease was associated with retreated cases more often than in patients with new TB cases (OR: 0.372, 95% CI: 0.256–0.541 *p* > 0.05). The cavity has a higher risk and more probability in patients of acquired resistance (OR: 0.391, 95% CI: 0.161–0.948, *p* > 0.05) (Table I).

In new TB cases, pulmonary drug-resistant TB occurred with a higher probability and risk than extrapulmonary drug-resistant TB (OR: 52.062, 95% CI: 7.187–377.129, *p* > 0.05). Also, in retreated cases, resistance developed more often in pulmonary TB that in extra-pulmonary TB (OR: 18.634, 95% CI: 2.51–138.31, *p* > 0.05). Furthermore, patients with pulmonary TB showed a higher risk of being retreated cases than those with extra-pulmonary TB (OR: 0.307, 95% CI: 0.225–0.418, *p* > 0.05).

The new patients from urban areas had a higher risk and more probability of developing resistance (OR: 1.939, 95% CI: 1.12–3.358, *p* > 0.05) than in retreated cases (OR: 2.661, 95% CI: 1.412–5.015, *p* > 0.05) when compared to patients from rural regions. New patients living in urban areas were more likely to be diagnosed (OR: 1.393, 95% CI: 1.059–1.832, *p* > 0.05) than retreated cases when compared to patients from rural regions. A higher frequency of retreated cases (64.6%) than new cases (56.7%) occurred in rural regions (Table I).

Resistance patterns. As demonstrated in Table II, among 2,296 newly diagnosed and 246 retreated MTB clinical isolates, drug resistance is significantly higher among the isolates from retreated patients than those from newly diagnosed cases (20.3% vs. 2.4%, *p* > 0.05). The frequency and percentage of the resistance to first-line drugs, involving INH, RIF, EMB, SM among the newly diagnosed and retreaded patients were as follows: 23 (1%) vs. 42 (17.1%), 18 (0.78%) vs. 39 (15.8%), 13 (0.56%) vs. 21 (8.5%), and 30 (1.3%) vs. 24 (9.75%), respectively. MTB's most common drug resistance was against streptomycin with a rate of 1.3% in new TB patients and isoniazid (17.1%) in retreated TB patients. When compared to retreated TB cases, new cases have lower rate of MDR-TB (0.34% vs. 14.2%, *p* < 0.05), PDR-TB (0.78% vs. 4.1%, *p* = 0.257), but the occurrence of MR-TB was virtually similar in this group (1.22% vs. 2%, *p* = 0.564). Out of 28 newly diagnosed MR-TB cases, the highest rate of MTB resistance was against SM (13, 0.56%), followed by RIF (7, 0.3%), INH (4, 0.17%), and EMB (4, 0.17%). The results showed the prevalence of four different types of newly diagnosed MDR-TB, for example, MDR1 (INH + RIF), MDR2 (INH + RIF + EMB), MDR3 (INH + RIF + EMB + SM), and MDR4 (INH + RIF + SM). Likewise, newly diagnosed PDR-TB mostly consist of two (0.08%) PDR1 (INH + EMB), seven (0.3%) PDR2 (INH + SM), three (0.13%) PDR4 (RIF + SM), two (0.08%) PDR5

Table I
Demographic and clinical characteristics of new and retreated tuberculosis patients, Basra, Iraq, 2016–2020.

Characteristics	New cases					Retreated cases					New cases vs. Retreated cases		Primary DR-TB vs. Acquired DR	
	Total n=2296	DR-TB n=54 (2.4)	Susceptible TB n=2242 (97.6)	OR (95% CI)	p-value	Total n=246	DR-TB n=50 (20.3)	Susceptible TB n=196 (79.7)	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age														
≤14	254 (11)	2 (3.7)	252 (11.23)	0.233 (0.054–1.008)	0.051	5 (2)	0	5 (2.6)	0.431 (0.023–8.207)	0.576	7.748 (3.109–19.308)	<0.0001	3.974 (0.178–89.003)	0.384
15–34	804 (35)	21 (38.9)	783 (34.9)	0.788 (0.420–1.479)	0.458	76 (30.8)	19 (38)	57 (29.1)	1.622 (0.758–3.470)	0.212	1.613 (1.166–2.233)	0.004	0.873 (0.348–2.186)	0.771
35–54	661 (28.7)	12 (22.2)	649 (28.9)	0.543 (0.261–1.129)	0.102	77 (31.3)	16 (32)	61 (31.12)	1.277 (0.584–2.791)	0.541	1.309 (0.945–1.813)	0.105	0.592 (0.216–1.624)	0.308
≥55	577 (25.1)	19 (35.2)	558 (24.9)	Ref.	Ref.	88 (35.7)	15 (30)	73 (37.2)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Sex														
Female	1076 (46.8)	29 (53.7)	1047 (46.7)	1.324 (0.771–2.275)	0.310	123 (50)	25 (50)	98 (50)	1.000 (0.537–1.861)	1.000	0.882 (0.678–1.147)	0.349	1.16 (0.537–2.506)	0.706
Male	1220 (53.1)	25 (46.3)	1195 (53.3)	Ref.	Ref.	123 (50)	25 (50)	98 (50).	Ref.	Ref.	Ref.	Ref.	Ref	Ref
Smoking														
Yes	580 (25.3)	13 (24.1)	567 (25.3)	0.937 (0.498–1.761)	0.839	70 (28.4)	15 (30)	55 (28.1)	1.099 (0.556–2.170)	0.786	0.850 (0.634–1.139)	0.276	0.740 (0.310–1.764)	0.497
No	1716 (74.7)	41 (75.9)	1675 (74.7)	Ref.	Ref.	176 (71.5)	35 (70)	141 (71.9)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Cavity														
Yes	710 (30.9)	32 (59.6)	678 (30.6)	1.018 (0.580–1.788)	0.950	153 (62.1)	39 (78)	114 (58.2)	0.958 (0.428–2.150)	0.917	0.372 (0.256–0.541)	<0.0001	0.391 (0.161–0.948)	0.038
No	474 (20.6)	21 (38.9)	453 (20.2)	Ref.	Ref.	38 (15.4)	1 (20)	28 (14.3)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Infiltration														
Yes	308 (13.4)	13 (24.1)	295 (13.2)	0.921 (0.486–1.746)	0.801	50 (20.3)	13 (26)	37 (18.9)	1.025 (0.490–2.140)	0.948	0.992 (0.700–1.404)	0.962	0.9 (0.369–2.194)	0.817
No	876 (38.1)	4 (74.1)	836 (37.3)	Ref.	Ref.	141 (57.3)	36 (72)	105 (53.6)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

Table I. Continued
Demographic and clinical characteristics of new and retreated tuberculosis patients, Basra, Iraq, 2016–2020.

Characteristics	New cases					Retreated cases					New cases vs. Retreated cases		Primary DR-TB vs. Acquired DR	
	Total n=2296	DR-TB n=54 (2.4)	Susceptible TB n=2242 (97.6)	OR (95% CI)	p-value	Total n=246	DR-TB n=50 (20.3)	Susceptible TB n=196 (79.7)	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Other abnormalities														
Yes	142 (6.1)	6 (11.1)	136 (6.04)	0.934 (0.392–2.226)	0.878	23 (9.3)	6 (12)	17 (8.7)	1.026 (0.380–2.770)	0.960	0.995 (0.622–1.592)	0.985	0.915 (0.274–3.052)	0.885
No	1042 (45.3)	47 (87)	995 (44.4)	Ref.	Ref.	168 (68.2)	43 (86)	125 (63.8)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Clear														
Yes	4 (0.17)	1 (1.9)	3 (0.13)	7.23 (0.739–70.71)	0.089	0	0	0	2.879 (0.056–147.03)	0.598	1.46 (0.078–27.227)	0.800	2.829 (0.113–71.087)	0.527
No	118 (51.3)	52 (96.3)	1128 (50.3)	Ref.	Ref.	191 (77.6)	49 (98)	142 (72.4)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Type														
Extra pulmonary TB	1112 (48.4)	1 (1.9)	1111 (49.6)	Ref.	Ref.	55 (22.3)	1 (2)	54 (27.6)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pulmonary TB	118 (51.5)	53 (98.1)	1131 (50.4)	52.062 (7.19–377.13)	0.0001	191 (77.6)	49 (98)	142 (72.4)	18.634 (2.51–138.31)	0.004	0.307 (0.225–0.418)	<0.0001	1.082 (0.066–17.768)	0.956
Region														
Urban	993 (43.2)	32 (59.3)	961 (42.9)	1.939 (1.12–3.358)	0.018	87 (35.3)	27 (54)	60 (30.6)	2.661 (1.412–5.015)	0.003	1.393 (1.059–1.832)	0.018	1.239 (0.570–2.965)	0.589
Rural	1303 (56.7)	2 (40.7)	1281 (57.1)	Ref.	Ref.	159 (64.6)	23 (46)	136 (69.4)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

OR – Odds Ratio, TB – Tuberculosis, DR-TB – Drug-Resistant Tuberculosis, CI – Confidence Intervals

Table II
Primary and acquired drug resistance profiles of *Mycobacterium tuberculosis* strains,
Basra, Iraq 2016–2020.

Drug resistance	New cases n = 2296 (%)	Retreated cases n = 246 (%)	*p*-value
DR-TB	54 (2.4)	50 (20.3)	0.0001
Any resistance to first-line drugs			
INH	23 (1)	42(17.1)	0.0001
RIF	18 (0.78)	39 (15.8)	0.0001
EMB	13 (0.56)	21 (8.5)	0.011
SM	30 (1.3)	24 (9.75)	0.007
MR-TB (Total)	28 (1.22)	5 (2)	0.564
INH	4 (0.17)	0	0.102
RIF	7 (0.3)	3 (1.2)	0.206
EMB	4 (0.17)	1 (0.4)	0.180
SM	13 (0.56)	1 (0.4)	0.001
MDR-TB (Total)	8 (0.34)	35 (14.2)	0.0001
MDR1: INH + RIF	7 (0.3)	20 (8.1)	0.011
MDR2: INH + RIF +EMB	0	2 (0.81)	0.317
MDR3: INH + RIF + EMB + SM	1 (0.04)	12 (4.8)	0.002
MDR4: INH + RIF + SM	0	1 (0.4)	0.564
PDR-TB (Total)	18 (0.78)	10 (4.1)	0.257
PDR1: INH + EMB	2 (0.08)	0	1.000
PDR2: INH + SM	7 (0.3)	3 (1.2)	0.564
PDR3: RIF + EMB	0	0	–
PDR4: RIF + SM	3 (0.13)	1 (0.4)	1.000
PDR5: INH + EMB + SM	2 (0.08)	4 (1.6)	0.317
Others (SM + EMB)	4 (0.17)	2 (0.81)	0.564

RIF – Rifampin, INH – Isoniazid, EMB – Ethambutol, SM – Streptomycin, TB – Tuberculosis,
DR-TB – Drug-Resistant Tuberculosis, MR-TB – Mono-Drug Resistant Tuberculosis,
MDR-TB – Multi-Drug Resistant Tuberculosis, PDR-TB – Poly-Drug Resistant Tuberculosis

(INH + EMB + SM), and four other isolates (0.17%) (SM + EMB). There were no PDR3 (RIF + EMB) isolates. The most common type of drug resistance in retreated cases is MDR (14.2%), with the highest resistance rate (8.1%) against INH and RIF, followed by PDR (4.1%) with the highest resistance rate (1.6%) for INH, EMB, and SM, and MR-TB (2%) with the highest resistance rate for RIF (1.2%) (Table II).

Overall and yearly new diagnosed drug resistance rate. Table III shows the total and annual newly diagnosed drug resistance rate of many TB subcategories from 2016 to 2020. Throughout the study period, the rate of newly diagnosed drug resistance among females, the 15–34-year-old TB subcategories increased by 365 and 274%. It varied from 1.75 to 8.13% and from 1.9 to 7.1%, respectively. The increased TB occurrence was observed in males and the other age groups as illustrated in Table III. Moreover, the rate of total DR-TB, MDR-TB, MR-TB, and RFP-resistant TB among new tuberculosis cases increased from 2.2 to 6.7%, 0.17 to 1.6%, 0.85 to 4%, and 0.17 to 4%, with a percentage

change of 205, 841, 371, and 23%, respectively. On the other hand, PDR-TB and EMB-resistant TB rates dropped by 15.9 and 0.7%, decreasing from 1.19 to 1% and from 1 to 0.3%, respectively.

Total and annual secondary drug resistance rates. Table IV shows the overall and annual secondary drug resistance rate of TB subcategories from 2016 to 2020. Through the study period, the secondary drug resistance rate amongst females, males, and patients of all ages increased, as illustrated in Table IV. Additionally, the rate of total DR-TB, MDR-TB, PDR-TB, and MR-TB also increased. Moreover, the first-line drug resistance INH, RIF, EMB, and SM-resistant TB was also elevated during this period.

Discussion

Our study enrolled 2542 cases of newly and retreated TB patients in Basra from 2016 to 2020 to decipher the epidemiology and prevalence of drug resistance

Table III
The time-based change trend of primary drug resistance rate amongst newly diagnosed
TB patients in Basra, Iraq, 2016–2020.

Characteristics	Primary drug resistance rate					Change
	*2016 n = 512	2017 n = 584	2018 n = 490	2019 n = 410	2020 n = 300	204.54
DR-TB (Total)	1 (0.1)	13 (2.2)	5 (1)	15 (3)	20 (6.7)	
Type						
MR-TB	0	5 (0.85)	2 (0.4)	9 (2)	12 (4)	370.58
MDR-TB	0	1 (0.17)	1 (0.2)	1 (0.2)	5 (1.6)	841.17
PDR-TB	1 (0.1)	7 (1.19)	2 (0.4)	5 (1.2)	3 (1)	−15.96
Age (years)						
≤ 14	0	1 (1.6)	0	0	1 (3.1)	93.75
15–34	1 (0.6)	4 (1.9)	2 (1.08)	6 (4.1)	8 (7.1)	273.68
35–54	0	4 (2.58)	2 (1.45)	2 (1.63)	6 (7.14)	176.74
≥ 55	0	4 (2.54)	1 (0.85)	7 (7.2)	5 (7.04)	177.16
Sex						
Female	1 (0.46)	5 (1.75)	3 (1.2)	10 (4.9)	10 (8.13)	364.57
Male	0	8 (2.67)	2 (0.8)	5 (2.4)	10 (5.64)	111.23
First-line drugs						
INH	1 (0.19)	5 (0.85)	3 (0.61)	8 (1.95)	6 (2)	1.35
RIF	0	1 (0.17)	2 (0.4)	3 (0.73)	12 (4)	22.5
EMB	0	6 (1)	1 (0.2)	5 (1.21)	1 (0.3)	−0.7
SM	1 (0.19)	11 (1.9)	2 (0.4)	5 (1.21)	11 (3.7)	18.47

$$\text{Primary drug resistance rate (\%)} = \left(\frac{\text{the number of each DR} - \text{TB subcategories}}{\text{the total of corresponding primary TB cases in the same year}} \right) \times 100\%$$

$$\text{The \% changes} = \frac{\text{incidence in 2020} - \text{incidence in 2017}}{\text{incidence in 2017}}$$

* – the column (2016) is not included in the calculation
DR-TB – Drug-Resistant Tuberculosis, MR-TB – Mono-Drug Resistant Tuberculosis,
MDR-TB – Multi-Drug Resistant Tuberculosis, PDR-TB – Poly-Drug Resistant Tuberculosis,
EMB – Ethambutol, INH – Isoniazid, RFP – Rifampin, SM – Streptomycin

in *M. tuberculosis* isolated from clinical samples in the Basra province.

The present results show that during the study period (five years), *M. tuberculosis* was detected in 2,542 samples at an average of 508.4 per year. WHO stated tuberculosis case detection for the last five years at a rate of about 43/100,000 population in Iraq (WHO 2019).

The total population in Basra is estimated to be 2,985,073 as of 2019 (Central Statistical Organization 2019), then the predictable tuberculosis cases would be about 1,284 patients per year. There were 508 identified patients in this study, as the average of the last five years, less than a half of the WHO predicted number. It could be attributed to an inadequate screening procedure or the overestimated case finding the target.

Relationship of TB with age. The study revealed that patients from the 15–34 years old group comprise the most affected group, and this observation is similar to most developing countries (Dogar et al. 2012). It was followed by the patients of 35–54 years old. These findings might be attributed to many young people in Iraq. At this age, individuals are more active and have a higher level of social activities, interactions with specific environmental factors, or lifestyle characteristics. These results agree with national and regional studies carried out by Al-Rubayai (2011), Mokdad et al. (2014), Khdban (2018), and Merza et al. (2020) but in contrast with Jappar and Low (2015), and Karadakhy et al. (2016) who reported that the most affected age groups are the older people.

Relationship of TB with sex. The present study illustrated that the TB rate was higher in males than in females, which may be related to the social behavior of males in our society, who have more social activities, travel, and more work outside the home than females. Our results are similar to those obtained by Al-Khafaji (2014) and Bedewi (2011) in Baghdad, Iraq. WHO also reported that men are more affected than women in Iraq (WHO 2017).

Table IV
The time-based change trend of secondary drug resistance rate amongst retreated
diagnosed TB cases in Basra, Iraq, 2016–2020.

Characteristics	Secondary drug resistance rate					Change
	2016 n = 81	2017 n = 51	2018 n = 51	2019 n = 41	2020 n = 22	856.23
DR-TB (Total)	5 (6.17)	8 (15.6)	10 (19.6)	14 (34.1)	13 (59)	
Type						
MR-TB	1 (1.2)	1 (1.9)	2 (3.9)	0	1 (4.5)	275
MDR-TB	3 (3.7)	6 (11.7)	3 (5.8)	12 (29.2)	11 (50)	1 251.35
PDR-TB	1 (1.2)	1 (1.9)	5 (9.8)	2 (4.8)	1 (4.5)	275
Age (years)						
≤ 14	0	0	0	0	0	0
15–34	2 (8.6)	3 (30)	4 (21)	6 (40)	4 (44.4)	416.27
35–54	1 (4)	2 (12.5)	4 (26.6)	4 (30.7)	7 (87.5)	2 087.5
≥ 55	2 (6.6)	3 (13)	2 (11.7)	4 (30.7)	2 (40)	506.06
Sex						
Female	2 (4.7)	3 (15.7)	4 (13.3)	11 (45.8)	5 (62.5)	1129.78
Male	3 (7.6)	5 (15.6)	6 (28.5)	3 (17.6)	8 (57.1)	651.31
First-line drugs						
INH	4 (4.9)	6 (11.8)	6 (11.8)	14 (34)	12 (54.5)	10.12
RIF	4 (4.9)	6 (11.8)	5 (9.8)	12 (29.3)	12 (54.5)	10.12
EMB	1 (1.2)	4 (7.8)	5 (9.8)	5 (12.2)	6 (27.3)	21.75
SM	1 (1.2)	5 (9.8)	5 (9.8)	7 (17)	6 (27.3)	21.75

$$\text{Secondary drug resistance rate (\%)} = \left(\frac{\text{the number of each DR} - \text{TB subcategories}}{\text{the total of corresponding primary TB cases in the same year}} \right) \times 100\%$$

$$\text{The \% changes} = \frac{\text{incidence in 2020} - \text{incidence in 2016}}{\text{incidence in 2016}}$$

DR-TB – Drug-Resistant Tuberculosis, MR-TB – Mono-Drug Resistant Tuberculosis,
MDR-TB – Multi-Drug Resistant Tuberculosis, PDR-TB – Poly-Drug Resistant Tuberculosis,
EMB – Ethambutol, INH – Isoniazid, RFP – Rifampin, SM – Streptomycin.

On the other hand, MTB isolates from females presented primary drug resistance with a higher frequency rate than males. There were no such differences in retreated cases. It could be due to cultural reasons when women provide care to in-home patients with DR-TB. It puts women at increased risk for exposure and subsequent DR-TB development. Our results agree with the studies in former Soviet Union countries (Faustini et al. 2006) and Republic of Georgia (Lomtadze et al. 2009), which showed that women are more likely to have MDR-TB than men in new cases of TB. Our findings, however, did not match with the results of the Iranian study, which presented females as more resistant to MDR-TB than males (Jimma et al. 2017).

Relationship of TB with pulmonary cavity. In the case of pulmonary TB, the cavity was more associated with retreated cases than new cases, which may cause the prolonged time to sputum culture conversion (Hernandez-Romieu et al. 2019). The presence of initial pulmonary cavitation can be considered a predictor for retreated TB because of containing a high bacillary load,

so it may associate with the progress of drug resistance throughout the time of treatment (Kempker et al. 2012).

Relationship of TB with type of infection. Our study showed that total pulmonary TB (PTB) (54%) is higher than total extra-pulmonary TB (EPTB) (45.9%). The present results are similar to those obtained by Ahmed (2018) but different from other studies carried out in Baghdad by Durib and Blinova (2020), who reported that PTB occurred in 47.64% and EPTB in 52.36% cases, respectively. The low rate of EPTB could be because of the absence or very low rate of HIV infection since it has been reported that the increase in EPTB rate is more than 50% if associated with HIV (Golden and Vikram 2005).

The present results showed a high frequency of drug resistance among PTB agreed with the study in Papua New Guinea (Diefenbach-Elstob et al. 2018).

Relationship of TB with urban vs. rural regions. The present study showed that TB in rural settings is higher than in urban areas. The reason may be that rural patients seek health care from traditional healers

which causes the delay in TB diagnosis, resulting in continuous transmission of the disease. Our results were similar to those obtained in China, which showed that approximately 80% of TB patients live in rural areas (Liu et al. 2005), but different from that what was found in Baghdad by Durib and Blinova (2020), who reported that the frequency of TB in urban populations was much higher than in rural ones. However, the global problem of TB infection is estimated to be higher in urban than in rural areas (Kapata et al. 2016).

Furthermore, we found that the total MTB drug resistance in urban regions was higher than in rural regions, similar to what was found in India (Almeida et al. 2003). There may be several reasons for these findings, such as those patients in rural settings have fewer admissions to different doctors, and rural areas are less crowded, so there is less transmission of drug resistance TB. The present results revealed that drug resistance was more likely found in retreated cases than in new TB patients. It was almost similar to the results reported in Tanzania (20.6% in retreated vs. 8.3% new cases) (Chonde et al. 2010) and lower than what was found in Sudan (62.8% retreated vs. 30.7% in new TB cases) (Hajissa et al. 2021), India (58.4% retreated vs. 24.9% in new TB cases) (Lohiya et al. 2020), and China (retreated 43.9% vs. 22% in new TB cases) (Yang et al. 2014). Our results also showed that retreated TB patients were significantly more likely to have MDR-TB than patients with primary TB, which may be due to inadequate use of treatment, incomplete treatments, or due lung cavities. These results were almost similar to a study carried out in Ethiopia, which showed the frequency of MDR-TB was 2% in primary cases and 15% in retreated cases (Eshetie et al. 2017), and lower than those obtained by Lomtadze et al. (2009), who found 6.8% vs. 27.4% of MDR-TB in new cases and retreated cases, respectively.

The frequency of MR-TB in the present study was higher in retreated cases than in new cases, which was consistent with another study in the north of Iraq (Merza et al. 2011), but in contrast with the situation in Sudan, where MR-TB was more prevalent in new cases than in retreated ones (Hajissa et al. 2021).

Globally, the occurrence of INH resistance in TB is poorly understood; however, in our study, the frequency of INH resistance was 17.1% in retreated cases and 1% in new cases. It is much less than the global prevalence of INH (27.2%) in retreated, and new cases (10.7%), and less than the Eastern Mediterranean retreated (23.5%) and new cases (10.7%), but almost similar to African retreated cases 13.5% (Dean et al. 2020). The wide variation in the prevalence of INH-resistant TB between different countries could be due to the absence of appropriate diagnostic tools for screening INH resistance, genetic diversity of MTB isolates, or the association of INH resistance with

other diseases HIV. However, it requires further studies to be confirmed.

Annual disparity of primary and secondary TB. There was an increase in total drug resistance in Basra during the five years from 2016 to 2020. This phenomenon is considered a public world health problem due to the rapid spread of MTB resistance worldwide. The annual trend of primary drug resistance revealed that the rate of MR-TB and MDR-TB sharply increased while PDR-TB decreased by 15.96%. The significant increase in MDR may be due to increased testing in recent years and the efficient spread of MDR strains. It alarms us about the challenge of eliminating the antimycobacterial drug resistance.

Furthermore, secondary resistance to the three types of MR-TB, MDR-TB, and PDR-TB, was markedly increased in the last five years, especially MDR, which showed a high percentage change (1,251%). The increase in secondary DR-TB was higher than in primary DR-TB, similar to studies carried out in China by Song et al. (2019) and He et al. (2016). It indicates that patients with prior TB infections are more likely to develop resistance.

Regarding the number of primary DR-TB, this parameter increased through the five years (2016–2020) in all age groups. This phenomenon was significantly visible in people 15–34 years old, for whom the percentage change was 274%. The number of secondary DR-TB was also elevated in all age groups, with the most significant increase in patients in age 35–54 years old with a distinct percentage change (2,079%). It is, therefore, also essential to concentrate on patients who are categorized as young and middle-aged. A similar finding was recorded in China (Song et al. 2019).

The number of infected females increased over the years studied more than infected males in primary and secondary DR-TB. According to the first-line drug in primary DR-TB, there was a decrease in EMB over the years by 0.7%, and an increase in INH, RIF, and SM, and RIF had the highest percentage change (22.5%). In secondary DR-TB, resistance to the four drugs has increased over time, so we need more focus on the drug regimen. It was the opposite of what was found in China, as there was a decline in drug resistance to these four drugs (Lan et al. 2019) but similar to those reported by Shamaei et al. (2009), in Iran, who stated that the resistance to the first-line drugs significantly increased.

Conclusion

The present study had defined the time-based trend of DR-TB in Basra province in Iraq from 2016 to 2020. The results showed that the prevalence of TB in Basra from 2016 to 2020 was at an average of 508.4.

The most affected age group was young people, a high frequency of TB infection was detected in males, and rural regions. The pulmonary cavity was more associated with retreated cases than new cases. The prevalence of drug resistance in retreated cases was higher than in new TB cases. The highest percentage of resistance was observed against isoniazid among first-line drugs. The temporal trend showed an increasing rate of drug resistance since 2016, especially in the number of MDR-TB patients, and with dominance in female patients. Concerning the primary resistance, the resistance against ethambutol is decreasing. The same trend follows the number of PDR-TB cases. These findings would enhance public responsiveness to TB prevention and control. It is fair to say that they can be deemed necessary in the aim of TB elimination and reduction in Iraq. However, the sample size and geographical sources of clinical samples may not be sufficient to generalize the conclusions to the whole country. More studies are required to investigate a larger sample size from different geographical locations to generalize the outcome information for the entire country.

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