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A 5-year experience characterizing the demographic and clinical profile and directly observed treatment short-course treatment outcome in National Tuberculosis Center of Duhok province, Iraqi Kurdistan

Muayad Aghali Merza

Abstract

Background: The objectives were to describe the demographic and clinical profile and treatment outcomes in the National Tuberculosis Program Center of Duhok governorate.

Methods: This was a descriptive retrospective study of all forms of drug-susceptible tuberculosis cases in the National Tuberculosis Program Center of Duhok. The Electronic Nominal Recording Reporting System data of tuberculosis cases were reviewed during 2014–2018. Information on the demographic, clinical, and laboratory characteristics of the patients were analyzed. Tuberculosis trends and treatment outcomes were determined.

Results: A total of 1063 tuberculosis patients visited the National Tuberculosis Program Center, of whom 905 were from Duhok. The estimated tuberculosis notification rate per 100,000 people in Duhok governorate was 14.06, 16.16, 10.43, 11.05, and 10.34 for the years 2014, 2015, 2016, 2017, and 2018, respectively. The most affected age group was 15–24 years. The male cases were predominant. Most patients (97.3%) were native Iraqi. There were 718 (67.5%) pulmonary tuberculosis cases and 345 (32.5%) extra-pulmonary tuberculosis cases; tuberculosis lymphadenitis was the most common presentation. The majority of extra-pulmonary tuberculosis patients were females aged 15–24 years ($p = 0.019$), and patients aged $\geqslant 65$ years were associated with pulmonary tuberculosis and extra-pulmonary tuberculosis in males ($p \leqslant 0.001$). The highest tuberculosis incidence occurred in winter (288 patients). The patient treatment outcomes were as follows: 90.7% successful treatment, 1.6% lost to follow-up, 6.7% death, 0.3 transferred out, and 0.8 treatment failure.

Conclusion: There was a high frequency of extra-pulmonary tuberculosis, which may reflect overestimation in its diagnosis. Therefore, meticulous evaluations should be provided. The treatment outcome was satisfactory in the center. Hence, we should maintain the favorable work to attain tuberculosis control objectives. Performing GeneXpert for all tuberculosis cases and introducing culture and drug susceptibility testing should be an urgent plan to strengthen the diagnosis of susceptible and drug-resistant tuberculosis cases.

Keywords

Tuberculosis, demographic and clinical profile, treatment outcome, Duhok

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Introduction

Tuberculosis (TB) is an abject infectious disease primarily affecting the lungs; however, any organ in the body can be involved. On a global scale, 1.7 billion people are currently infected with *Mycobacterium tuberculosis*, the causative agent of TB; 5%–10% develops the disease.[1]

The challenge in the TB epidemic is stated in the latest World Health Organization (WHO) report; as in 2017, 10 million people developed TB disease with males leading a higher proportion. The burden of TB varies depending on the geographic region. It is the highest in Southeastern Asia, Africa, and the Western Pacific region that accounts for 87% of the world's TB cases.[1] Despite high expectations regarding

Department of Internal Medicine, Azadi Teaching Hospital, College of Pharmacy, University of Duhok, Duhok, Iraq

Corresponding author:
Muayad Aghali Merza, Department of Internal Medicine, Azadi Teaching Hospital, College of Pharmacy, University of Duhok, Azadi Hospital Street, Duhok, Kurdistan Region 1006AJ, Iraq.
Email: muayad.merza@uod.ac

Table 1. Population density and notification rate statistics of Duhok Governorate over 2014–2018 (n = 1063).

District	Year					Total
	2014	2015	2016	2017	2018	
Crude population						
Duhok	363,172	374,606	386,210	397,966	409,497	
Zakho	267,279	275,694	284,234	292,886	302,062	
Akre	174,947	180,455	186,045	191,708	197,742	
Semel	181,390	187,102	192,897	198,769	203,967	
Amedy	112,095	115,624	119,206	122,834	126,119	
Shekhan	143,324	147,837	152,416	157,056	161,930	
Bardarash	137,470	141,798	146,190	150,640	155,703	
Total	1,379,677	1,423,116	1,467,198	1,511,859	1,557,020	
Number of tuberculosis cases						
Duhok	194	230	153	167	161	905 (85.1%)
Mosul	52	53	23	17	13	158 (14.9%)
Grand-total	246	283	176	184	174	1063
Notification rate[a]	14.06	16.16	10.43	11.05	10.34	

[a]Tuberculosis notification rate in Duhok governorate only.

the elimination of TB, there is evidence the disease's incidence is increasing in some parts of the world.[2] The escalating number of TB cases is considered to be a consequence of the AIDS pandemic, the resistance to anti-TB drugs, and increasing levels of immigration.[3] The emergence of multidrug resistance tuberculosis (MDR-TB), that is, TB strains resistant to isoniazid (INH) and rifampicin (RIF), is threatening the TB epidemiology. Hence, the best way to stop these strains is to detect and treat drug-susceptible, mono- or poly-drug resistant TB before it evolves into MDR-TB.[2,3] Additional factors such as poverty, unemployment, malnourishment, and war have perplexed the TB epidemiology.

Iraq with a population of 38 million people is one of the countries in the World Health Organization Eastern Mediterranean Region (WHO-EMR) with a TB incidence rate of 42 per 100,000 and a TB case detection rate of 54%.[1,4] It is considered one of the seven highest TB burden countries in the EMR, constituting 3% of the total TB patients.[5] The directly observed treatment short-course (DOTS) strategy has been adopted in Iraq since 1998, except for the three Kurdish provinces of Iraq (Erbil, Sulaimani, and Duhok), which had implemented the program in 2001.[6] The outcome of DOTS has been well documented to increase the treatment success rate and decrease the economic burden in pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB) patients, particularly in developing countries.[7,8] Overall, according to the WHO country profile, Iraq has a higher incidence rate of TB than all neighboring countries, that is, Syria, Jordan, Iran, Saudi Arabia, and Turkey,[4] but knowledge on demographic, clinical, and treatment outcome has not been studied extensively. Hence, this study aimed to describe the demographic and clinical profile, and treatment outcome in the National Tuberculosis Program Center (NTP) of Duhok governorate.

Patients and methods

Setting

The NTP, also called Tuberculosis Respiratory Diseases Consultation Center (TRDCC) is a specialized center in Duhok governorate for managing and following up all forms of drug-susceptible TB patients. It is provided with a laboratory, radiology unit (chest X-ray (CXR)), and pharmacy unit mainly for providing anti-TB drugs. The center is also in charge of managing some other respiratory diseases in Duhok district. There are six more tuberculosis management units (TBMUs) in Zakho, Akre, Semel, Amedy, Sheikhan, and Bardarash districts of Duhok Governorate. These TBMUs are under the direct supervision of TRDCC. Overall, the TRDCC and TBMUs have had been serving Duhok governorate residents with a population density shown in Table 1.[9] The DOTS program is the standard of care in all TB centers, which follows the five components of Stop TB Strategy: political commitment, case detection, standardized treatment with supervision, effective drug supply, and monitoring and evaluation.[10] Patients newly diagnosed with all forms of drug-susceptible TB were provided with 6 months anti-TB regimen containing 2 months INH, RIF, pyrazinamide (PZA), and ethambutol (EMB) and 4 months of INH and RIF according to WHO's recommendation. Meningeal and bone TB, which were an exception, demanded a longer duration of anti-TB drugs. The relapse TB cases were initially treated by the regimen of 3 months INH, RIF, PZA, EMB, and 2 months of streptomycin followed by 5 months of INH, RIF, and EMB.[1] The NTP is under the technical supervision of the National Reference Laboratory (NRL) of Baghdad, Iraq, for quality assurance. Laboratory experts from NRL Baghdad were trained at the Supra National Reference Laboratory (SNRL) in Egypt on External Quality Assurance (EQA). Several TB

cases from a few districts of Mosul were also consulting the NTP of Duhok governorate.

Study design and patients

It was a descriptive retrospective study of all forms of drug-susceptible TB cases in Duhok governorate and nearby districts from Mosul. The Electronic Nominal Recording Reporting System (ENRS) data of TB cases were reviewed during 2014–2018. Information on the demographic, clinical, and laboratory characteristics of the patients was analyzed. TB trends and treatment outcomes for the mentioned years were determined. The inclusion criteria were TB patients diagnosed based on laboratory or clinical criteria according to national TB management guidelines,[11] whereas the exclusion criteria were outcome diagnosis changed, and TB caused by non-tuberculous mycobacteria.

Diagnosis and measures

The demographic and clinical profile defines the TB notification rate, age, gender, seasonality, nationality, clinical presentation, and site of all forms of drug-susceptible TB patients. The diagnosis of TB patients was made according to the NTP of Iraq, that is, smear microscopy (Acid Fast Bacilli "AFB") and/or GeneXpert MTB/RIF or clinical criteria including radiological findings.[11] The diagnosis of MDR-TB patients was established based on GeneXpert results when resistance to RIF was detected. Specimens of these patients were transported to NRL of Baghdad for further evaluation. All TB cases underwent human immunodeficiency virus (HIV) testing by the enzyme-linked immunosorbent assay (ELISA) technique as a part of the routine evaluation of such patients. Anti-TB drugs were provided free of charge for TB patients.

Measurement principles

The TB case notification rate was the new cases per 100,000 population per year.[1] "Treatment success" is a summation of a cured and completed treatment. "Lost to follow-up (LTFU)" is a TB patient whose anti-TB drugs were interrupted for two consecutive months or more. Any patient who died during the treatment for any reason is defined as "death." "Transfer-out" is defined as a TB patient who was transferred to another TB center without an informed treatment outcome.

Patients whose treatment failed at the end of the most recent course of anti-TB drugs were considered as treatment failure. A patient who has been declared cured or completed anti-TB treatment, and afterward diagnosed with a recurrent TB episode was named relapse:[12][AQ Please check whether the list provided below the sentence 'A patient who has been . . .' is correct as set.]

Smear-positive PTB: positive direct smear microscopy on two or three early morning sputum and/or positive GeneXpert result with or without CXR abnormalities consistent with active TB.

Smear-negative PTB: negative direct smear microscopy on two to three occasions and/or negative GeneXpert, but clinical and radiological finding consistent with active TB.

EPTB: cases of TB involving organ(s) other than the lungs.

The seasons were defined as follows: summer, June–August; autumn, September–November; winter, December–February; spring, March–May.

MDR-TB was defined as simultaneous resistance to INH and RIF.[12]

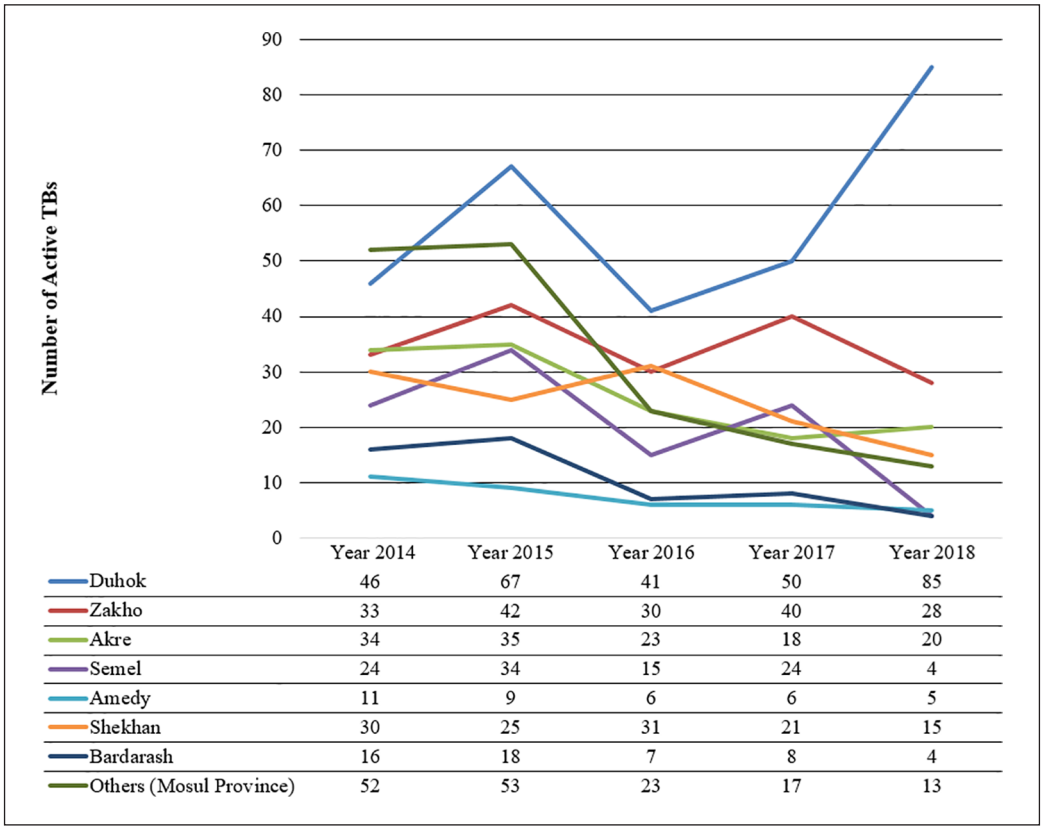
Statistical analysis

The raw information of the patients was entered into an excel spreadsheet for statistical analysis. The descriptive purposes of the study were determined in numbers and percentages, including TB rates for years 2014–2018, success rate, the prevalence of smear-positive and negative, and prevalence of clinical features of the patients. The trends of the TB notification and age groups for 2014–2018 were presented in a line graph. The difference in the prevalence of active TB between male and female patients, between different age groups, and among different seasons was examined in the Pearson's chi-square test. While Fisher's exact test was performed to examine the difference in the prevalence of TB cases between Iraqi and non-Iraqi patients. The odds ratio (OR) was measured in dividing odds in the treatment group by odds in the event in the control group. The OR was calculated for the odds if PTB and EPTB in patients had different characteristics. The comparison of PTB and EPTB patients was presented in ORs and was adjusted for gender. The p value of <0.05 was considered statistically significant. The statistical calculations were performed in Microsoft Excel 2013 and Statistical Package for Social Sciences version 25 (SPSS 25; IBM Corp., USA).

Results

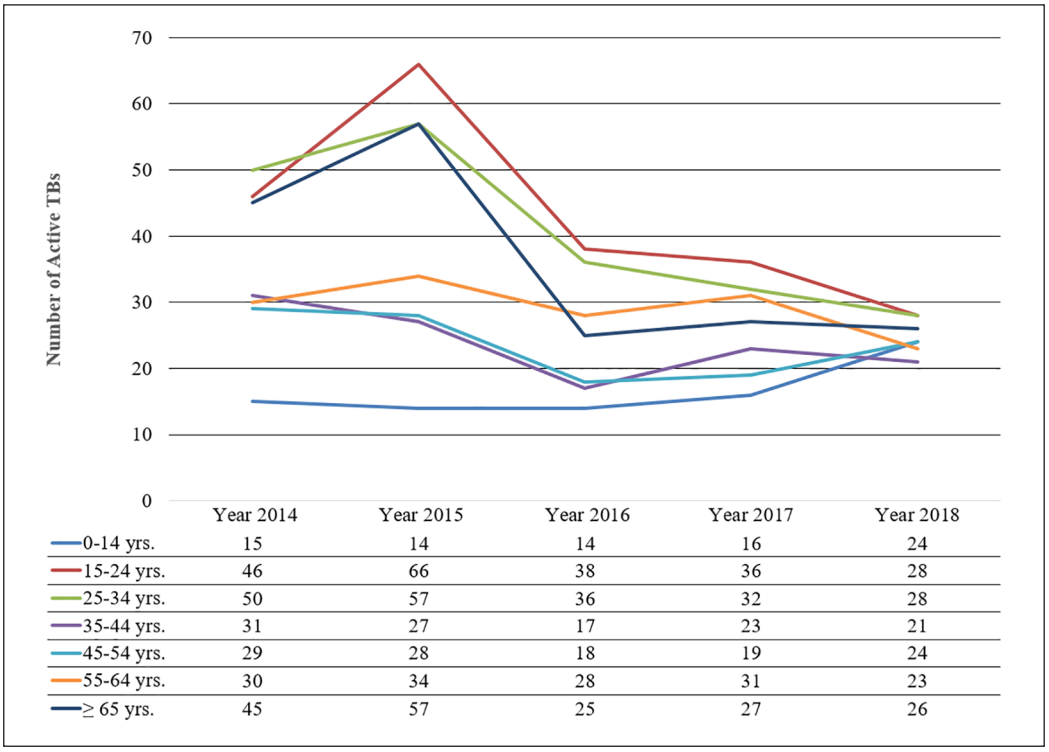
A total of 1063 patients were diagnosed with active TB at the NTP of Duhok. The study revealed that 905 of them were from Duhok itself. The estimated TB notification rate per 100,000 people in Duhok governorate alone was 14.06, 16.16, 10.43, 11.05, and 10.34 for the years 2014, 2015, 2016, 2017, and 2018, respectively. The average rate of the 5 years was 12.41 (Table 1). The majority of TB cases (43.5%) were reported from Duhok and Zakho districts. The slope of the TB cases was downward trend in all districts except for Duhok (Figure 1).

The trend of the number of active TBs in age groups over 2014–2018 was presented in Figure 2. The most common affected groups in order were aged 15–24 years, 25–34 years,



	Year 2014	Year 2015	Year 2016	Year 2017	Year 2018
Duhok	46	67	41	50	85
Zakho	33	42	30	40	28
Akre	34	35	23	18	20
Semel	24	34	15	24	4
Amedy	11	9	6	6	5
Shekhan	30	25	31	21	15
Bardarash	16	18	7	8	4
Others (Mosul Province)	52	53	23	17	13

Figure 1. Trend of the number of active TB patients of Duhok districts and Mosul province over 2014–2018 (n = 1063).



	Year 2014	Year 2015	Year 2016	Year 2017	Year 2018
0-14 yrs.	15	14	14	16	24
15-24 yrs.	46	66	38	36	28
25-34 yrs.	50	57	36	32	28
35-44 yrs.	31	27	17	23	21
45-54 yrs.	29	28	18	19	24
55-64 yrs.	30	34	28	31	23
≥ 65 yrs.	45	57	25	27	26

Figure 2. Trend of number of tuberculosis patients of age groups over 2014–2018 (n = 1063).

Table 2. Demographic characteristics of tuberculosis patients over 2014–2018 (n = 1063).

Sex and nationality	Year, n (%)					Total
	2014	2015	2016	2017	2018	
Sex						
Male	128 (52.0)	172 (60.8)	93 (52.8)	102 (55.4)	94 (54.0)	589 (55.4)
Female	118 (48.0)	111 (39.2)	83 (47.2)	82 (44.6)	80 (46.0)	474 (44.6)
Nationality						
Iraqi	243 (98.8)	280 (98.9)	175 (99.4)	179 (97.3)	171 (98.3)	1048 (98.6)
Syrian	2 (0.8)	3 (1.1)	1 (0.6)	5 (2.7)	2 (1.1)	13 (1.2)
Others	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (0.2)
Total	246	283	176	184	174	1063

Table 3. Trends of clinical presentations of active TB cases in Duhok governorate over 2014–2018.

Parameter	Year, n (%)					Total
	2014	2015	2016	2017	2018	
Pulmonary TB (PTB)	*188 (76.4)*	*194 (68.6)*	*116 (65.9)*	*108 (61.4)*	*112 (64.37)*	*718 (67.5)*
Smear positive	124 (66.0)	121 (62.4)	73 (62.9)	71 (65.7)	75 (67.0)	464 (64.6)
Smear negative	53 (28.2)	61 (31.4)	38 (32.8)	35 (32.4)	35 (31.3)	222 (30.9)
NA	11 (5.8)	12 (6.2)	5 (4.3)	2 (1.9)	2 (1.8)	32 (4.5)
Extra-pulmonary TB (ETB)	*58 (23.6)*	*89 (31.4)*	*60 (34.1)*	*76 (43.2)*	*62 (35.63)*	*345 (32.5)*
Lymph node	11 (19.0)	16 (18.0)	14 (23.3)	24 (31.6)	25 (40.3)	90 (26.1)
Pleural	20 (34.5)	24 (27.0)	7 (11.7)	17 (22.4)	11(17.7)	79 (22.9)
Osteo-articular	9 (15.5)	14 (15.7)	13 (21.7)	9 (11.8)	7 (11.3)	52 (15.1)
Central nervous system	7 (12.1)	5 (5.6)	6 (10.0)	7 (9.2)	5 (8.1)	30 (8.7)
Genito-urinary	0 (0.0)	8 (9.0)	3 (5.0)	2 (2.6)	1 (1.6)	14 (4.1)
Pericarditis	0 (0.0)	3 (3.4)	2 (3.3)	2 (2.6)	1 (1.6)	8 (2.3)
Others	4 (6.9)	12 (13.5)	10 (16.7)	10 (13.2)	6 (9.9)	42 (12.2)
Missing	7 (12.1)	7 (7.9)	5 (8.3)	5 (6.6)	6 (9.7)	30 (8.7)
Total PTB + EPTB	*246 (100.0)*	*283 (100.0)*	*176 (100.0)*	*184 (100.0)*	*174 (100.0)*	*1063 (100.0)*

TB: tuberculosis; NA: data were not available; TB: tuberculosis; Duhok governorate: Duhok is one of four governorates of Iraqi Kurdistan located in Northern part of Iraq.

followed by age >65 years. The slope seen in the graph showed that the trend of the TB cases was downward from 2014 to 2018 in all age groups (Figure 2).

Male cases were predominant during these 5 years. The M:F ratio for all forms of drug-susceptible TB was 1.08:1, 1.55:1, 1.12:1, 1.24:1, and 1.18:1 for years 2014, 2015, 2016, 2017, and 2018, respectively. The majority of patients (97.3%) were native Iraqi (Table 2). Overall, the M:F ratio for PTB cases during the 5 years was 1.49:1 (Table 4). All patients were negative for HIV infection.

There were 718 (67.5%) PTB cases and 345 (32.5%) EPTB cases. TB lymphadenitis and pleural TB were the most predominant EPTB during the study period (Table 3).

Figure 3 demonstrates the incidence of TB cases for each month. The highest incidence occurred in February and most cases were in the winter season (288 patients).

In comparison of TB sites between age groups, the 0–14 age group was considered the reference group. The study showed that the patients aged 15–24 and 25–34 years were more likely to be affected by TB sites, 0.52- and 0.64-fold, respectively, compared to 0–14 age group, while patients aged ⩾65 years were as 1.31-fold as likely to be affected by TBs compared to the reference age group ($p = 0.001$). The adjusted calculations showed that in patients aged 15–24 years, PTB and EPTB were common in males and females, respectively ($p = 0.019$), whereas no significant difference in the prevalence of PTB and EPTB between male and female patients of 25–34 years was found. Considering patients aged ⩾65 years, both PTB and EPTBs were significantly more common in male patients ($p < 0.001$). In addition, there was no significant difference in the notification rate of TB in patients with different nationalities ($p = 1.000$). Furthermore, there was no substantial difference in the notification rate of TB among different seasons (Table 4).

The study showed that most of the patients with active TB in Duhok governorate were treated successfully over 2014–2018 (90.7%), that is, 89.4%, 91.5%, 90.3%, 90.3%, and 91.4% in years 2014, 2015, 2016, 2017, and 2018,

Table 4. Comparison of PTB and EPTB patients of Duhok governorate over 2014–2018 (n = 1063).

Variable	TB site		OR (95% CI), p value	Gender				Gender-adjusted OR (95% CI), p value
				Male		Female		
	PTB	EPTB		PTB	EPTB	PTB	EPTB	
Sex								
Male	430 (59.89)	159 (46.09)	1.75 (1.35–2.26), <**0.001**					
Female	288 (40.11)	186 (53.91)						
Age groups (years)								
0–14	62 (74.70)	21 (25.30)		34 (75.56)	11 (24.44)	28 (73.68)	10 (26.32)	1.1 (0.41–2.98), 0.495
15–24	130 (60.70)	84 (39.30)	0.52 (0.3–0.92), **0.011**	78 (69.64	34 (30.36	50 (49.02	52 (50.98	2.39 (1.36–4.17), **0.019**
25–34	133 (65.50)	70 (34.50)	0.64 (0.36–1.14), **0.033**	70 (70.0)	30 (30.0)	64 (62.14	39 (37.86	1.42 (0.79–2.55), 0.361
35–44	79 (66.40)	40 (33.60)	0.67 (0.36–1.25), 0.075	42 (66.67)	21 (33.33)	38 (67.86)	18 (32.14)	0.95 (0.44–2.04), 0.669
45–54	72 (61.0)	46 (38.98)	0.53 (0.29–0.98), 0.056	44 (62.86)	26 (37.14)	28 (58.33)	20 (41.67)	1.21 (0.57–2.56), 0.292
55–64	99 (67.81)	47 (32.19)	0.71 (0.39–1.31), 0.101	54 (71.05)	22 (28.95)	45 (64.29)	25 (35.71)	1.36 (0.68–2.74), 0.866
⩾65	143 (79.44)	37 (20.56)	1.31 (0.71–2.42), **0.001**	98 (79.67)	25 (20.33)	45 (78.95)	12 (21.05)	1.05 (0.48–2.27), <**0.001**
Nationality								
Iraqi	708 (98.61)	340 (98.55)	1.04 (0.35–3.07), 1.000					
Non-Iraqi	10 (1.39)	5 (1.45)						
Season								
Summer	184 (25.63)	94 (27.25)	1.08 (0.74–1.56), 0.54					
Autumn	140 (19.50)	77 (22.32)	1.29 (0.89–1.88)					
Winter	202 (28.13)	86 (24.93)	1.2 (0.82–1.75)					
Spring	192 (26.74)	88 (25.51)						

TB: tuberculosis; OR: odds ratio "the OR was calculated with 95% confidence intervals (CIs)"; PTB: pulmonary tuberculosis; EPTB: extra-pulmonary tuberculosis; Duhok governorate: Duhok is one of four governorates of Iraqi Kurdistan located in Northern part of Iraq.
The autumn was considered the reference to calculate the ORs of seasons in this table. The 0–14 age group was considered the reference to calculate ORs and p values of age group difference. Crude odds ratios were calculated for the TB sites of the patients. The bold numbers show the significant difference.

respectively (Table 5). The TB relapse was noted in 5.8% of the 964 patients who were successfully treated. The relapse rates were 6.1%, 6.4%, 5.1%, 6.0%, and 5.2% for years 2014, 2015, 2016, 2017, and 2018, respectively.

Discussion

The WHO is struggling to control TB; however, it remains a major public health problem and a top leading killer infectious disease. To the best of our knowledge, no similar study has been performed to show demographic and clinical profile and treatment outcome in Duhok.

In this study, the number of TB cases registered did not show a significant decline in the trend. The high number of TB cases for the years 2014 and 2015 is due to the referral of TB patients from Mosul districts (Table 1; Figure 1). In addition, in these years, there was a peak of war by the Islamic State of Iraq and Syria (ISIS) forcing internally displaced people (IDP) to flee their home in Mosul and reside in Duhok, which markedly increased the number of TB patients within the governorate. TB cases were reported from all districts of Duhok; however, the highest counts (43.5%) were from Duhok and Zakho districts as these locations comprise the highest population density in comparison with other districts (Table 1). Over the 5-year study period, the number of TB cases had been slowly declining, which indicates the demand for improving TB control program in Duhok governorate. This slight drop is not in favor of the WHO goal that is trying to establish a decline at a rate of 4%–5% per year by 2020 to achieve TB elimination.[1] The notification rate of TB cases for each of the 5-year study period was not exceeding 17 cases per 100,000 people. The rate is lower in comparison with the WHO estimates from Iraq.[4] In comparison with neighboring countries, the current study showed an average notification rate higher than that of Saudi Arabia, and Jordan with an incidence rate of 10 and 6.8, respectively. On the contrary, the rate was lower than that reported from Iran (14/100,000), Turkey (17/100,000), and Kuwait (27/100,000).[4]

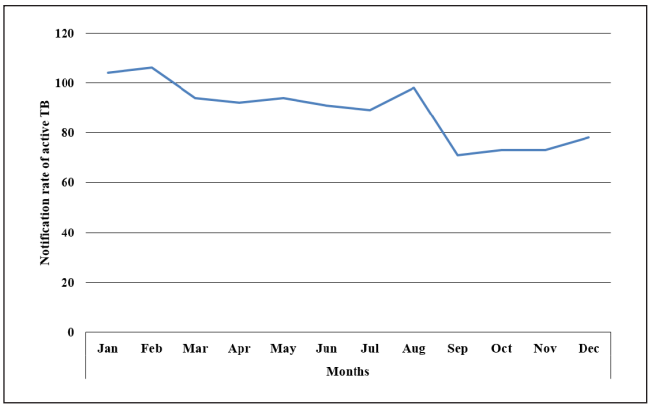


Figure 3. Trend of notification rate of TB cases of Duhok National Tuberculosis Program center over months for 2014–2018 periods (n = 1063).

The most commonly affected groups in this study were aged 15–24 and 25–34 years, which was consistent with the findings of most developing countries.[13,14] Similarly, Mokdad et al.[15] indicated that people aged 30–39 years were mostly affected in Arab countries. This was an expected finding as TB is a disease of the labor force population. Conversely, in developed countries, elder people account for a significant proportion of the cases, and the reason behind this is claimed to be multi-factorial, particularly the increase of latent tuberculosis infection (LTBI) in geriatric age group.[16] In this study, considering all forms of drug-susceptible TB cases, the predominance of male gender over females for all 5 years was found with a ratio not exceeding 1.6:1. For the PTB cases, the average M:F ratio was 1.49:1 during the 5 years. This finding was in accordance with several studies.[7,17] This is in parallel to the WHO global TB report in 2018,[1] which stated that the M:F ratio of TB cases is ranging from 1.3 in the WHO-EMR to 2.1 in the WHO-Western Pacific Region. In contrast to this study, few reports from the EMR such as Pakistan and Iran showed a higher incidence of TB cases among women in certain geographic locations; however, the exact cause for that finding was not conclusive.[13] The sex inequalities could be related to higher smoking rates among male patients in addition to other factors restricting the case detection rate among females such as access to health care facilities, socioeconomic, and cultural factors.[18–20] In the current study, although the majority of TB patients were native Iraqi patients, several cases were notified among

Table 5. Treatment outcome of tuberculosis patients of Duhok governorate over 2014–2018 (n = 1063).

Outcome	Year, n (%)					Total
	2014	2015	2016	2017	2018	
Successful treatment	220 (89.4)	259 (91.5)	159 (90.3)	167 (90.8)	159 (91.4)	964 (90.7)
Lost to follow-up	6 (2.4)	3 (1.1)	3 (1.7)	3 (1.6)	2 (1.1)	17 (1.6)
Death	16 (6.5)	20 (7.1)	12 (6.8)	12 (6.5)	11 (6.3)	71 (6.7)
Transferred out	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.6)	3 (0.3)
Treatment failure	3 (1.2)	1 (0.4)	2 (1.1)	1 (0.5)	1 (0.6)	8 (0.8)
Total	246	283	176	184	174	1063

Duhok governorate: Duhok is one of four governorate of Iraqi Kurdistan located in Northern part of Iraq.

Syrian patients. The reason for TB among refugees in this study is due to the Syrian conflict, which resulted in huge numbers of Syrians to escape into Iraqi Kurdistan, particularly Duhok province, which is in the direct border and considered the safe gate for Syrian refugees.

In the present study, the rate of EPTB was 32.5%, which is higher than the expected rate. Gonzalez et al.[21] conducted a population-based study in Houston, Texas, on 1371 HIV-negative TB patients and found 22% were EPTB. According to the recent WHO report,[1] EPTB represents 8% in the WHO-Western Pacific Region and 24% in the WHO-EMR. Although the frequency of EPTB in this study was high, there were no reported TB co-infected HIV cases during the 5 years; overall, Iraq is a very low HIV prevalence country.[1] Other studies reported a prevalence of 10%–34% and 50%–70% in EPTB without and with HIV infection, respectively.[22] Furthermore, the rate of EPTB in this study can be read higher as several cases of EPTB were diagnosed based on clinical ground. As a result, the diagnosis of EPTB should be keenly followed to reduce overestimation in its diagnosis.

The most common extra-thoracic manifestation in the current study was TB lymphadenitis followed by pleural TB. This finding was in keeping with other studies where the majority of EPTB were due to lymph node involvement.[16,20,21] TB lymphadenitis is more common among children and young aged women, whereas pleural TB is more common among adults, especially in HIV-positive patients.[23]

In this study, winter was the season of the highest TB incidence cases. This was in contrast to other studies, where the peak of TB incidence was in summer.[24] It has been suggested that low levels of vitamin D, frequent respiratory infections, and impaired immunity are factors contributing to the development of active TB in spring and early summer.[25] However, my finding was in line with studies from Spain[26] and South Africa[27] who found the peak of the disease in late winter. The majority of the aforementioned studies considered all forms of drug-susceptible TB rather than PTB alone, which could show a better correlation with seasonal patterns.

To address the association of certain variables with EPTB, female gender and age group of 15–24 years were independent risk factors for EPTB. This finding is in agreement with other studies.[21,28] The EPTB is associated with immune-compression and hence it is more common in children as their immune system is not completely developed.[29] Therefore, young adult females should be targeted properly whenever there is suspicion of EPTB, age $\geqslant$65 was identified as risk factor for PTB and EPTB in male gender. The association between old age and having PTB is consistent with the findings from previous studies.[16,30] Active TB in elderly people can occur as result of recent infection, reactivation of latent TB, and generally it can be exacerbated by underling comorbid diseases. Therefore, such vulnerable group should be paid special attention.

In this study, although the number of EPTB cases was higher in summer and spring seasons, the finding was not statistically significant. This finding was concordant with the finding of Korthals et al.[31] who studied the seasonality pattern and the site of TB disease in the Netherlands, where they found the peak of EPTB notification in June–July.

The treatment outcome among TB patients was as follows: 90.7% successful treatment, 1.6% LTFU, 6.7% death, 0.3 transferred out, and 0.8 treatment failure. At the global and national level, the End TB Strategy recommended 90% target treatment success before 2026,[1] which is on the corroborative side of this study that Duhok NTP achieved above their goal. In 2018, the WHO country profile reported a higher treatment success rate (93%) in Iraq compared with the rates of neighboring countries reportedly, 89%, 87%, 87%, 86%, 75% in Jordan, Turkey, Kuwait, Iran, and Saudi Arabia, respectively.[4] A recent 5-year retrospective study in a university medical center in Ethiopia reported a lower success rate by 88.2% and a higher rate of LTFU by 6.6%, death by 4.8%, and transfer out by 5.6% in comparison with the current study.[32] In general, the treatment outcome was satisfactory when compared with other studies.[8,20] The treatment success rate was optimal as health care providers of the center underwent different TB care training since they are working hard to follow the TB patients and their anti-TB regimen adherence. Furthermore, the non-HIV coinfection in this study improved the success rate as it is a well-known risk factor for unsatisfactory treatment success.

The overall treatment failure for 5 years in this realm was 0.8%, which is less than the WHO-EMR average failure rate of 1%.[5] On the other hand, a higher rate of 2.1% was reported by a study from Iraq.[33] The cases of treatment failure could represent MDR-TB cases for the study population. The WHO reported a 1.1% rate for MDR-TB cases in Iraq; however, the WHO suggests further monitoring of this rate as there was a high rate of mono-resistance to INH and RIF.[34] Therefore, the low rate of the failure in this study may indicate good compliance of the patients to the treatment and effectiveness of the DOTS strategy. Hence, short- and long-term measures to prevent and control TB such as prophylactic therapy for high-risk patients are mandatory to reduce TB incidence.

The main limitation of this study is that secondary data were used instead of population-based; hence, the data were more likely to represent TB notification cases rather than incidence rate. The case notification usually underestimates the true incidence because of the missing cases and under-reporting diagnosed cases. Several cases of EPTB were diagnosed on clinical bases, which may have overestimated their number in this study. In addition, there is a lack of TB culture in the NTP of Duhok and furthermore, the kits for GeneXpert are not available on a regular basis, which might be a source of missing TB cases in the center.

Conclusion

Prompt measures are required to address public health gaps, for example, people at high risk of progression to active TB to reduce incidence rate and to improve the TB control program.

There was a high frequency of EPTB, which necessities a keen follow-up to minimize overestimation in its diagnosis. The treatment outcome was satisfactory in the center. Hence, we should maintain the favorable work to attain TB control objectives. Performing GeneXpert for all TB cases and introducing culture and drug-susceptibility testing should be an urgent plan to strengthen the diagnosis of TB and furthermore, to detect drug resistance early, particularly MDR-TB cases.

Further larger scale studies, including all NTPs in Iraq, are needed to improve analyzing the demographic and clinical profile, and the treatment outcome of TB patients.

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Ethical approval

The study was approved by Ethical Research Committee of the College of Pharmacy, University of Duhok (Ref. No. 76; Date: 2 August 2018).

Informed consent

The study was retrospective and it was based on recorded data; hence, approval from administrative owners was taken.

ORCID iD

Muayad Aghali Merza https://orcid.org/0000-0003-1328-6469

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