Prevalence of multidrug resistant tuberculosis among TB patients in Malaysia.

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Abstract

Background: Currently multidrug-resistant tuberculosis (MDR-TB) poses a significant public health concern in Malaysia.

Objective: This study is aimed to evaluate the prevalence of MDR-TB in Malaysian tuberculosis patients. Method. A retrospective analysis was performed, and data was obtained from the Malaysian National TB Information System (TBIS) between 2009 and 2019. A record of 989 MDR-TB cases were identified and associated risk characteristics such as marital status, gender, ethnicity, employment status, alcohol consumption, diabetic status and smoking status were determined. The statistical analysis was performed using the SPSS software version 20.

Results: Overall, the occurrence of MDR-TB among patients with TB infections in Malaysia was 0.34% based on data collected from TBIS. The findings revealed major variations in the incidence of MDR-TB between male and female patients (0.44%, 0.20%, $p < 0.001$), single and married patients (1.63% vs 0.24%, $p < 0.001$), ethnicity ($p < 0.001$), working and non-working patients (0.48% vs 0.32%, $p < 0.001$), alcoholic and non-alcoholic patients (0.44% vs 0.32%, $p < 0.001$), diabetic patients and non-diabetic patients (0.39% vs 0.27%, $p < 0.001$), followed by smoking and non-smoking patients (0.13% vs 0.27%, $p < 0.001$).

Conclusion: This study provides a substantial assessment of MDR-TB prevalence and associated risk factors that could be useful for the implementation of new strategies in Malaysia's national TB policy.

1. Introduction

In 2019 about 600 000 MDR-TB cases reported worldwide with an estimated 250 million annual deaths [1]. Global TB report has stated that incidents of MDR-TB continue to rise, potentially threatening to undermine advances in TB control [2]. A variation of socio-economic and health risk account for the high incidence of MDR-TB worldwide. Multidrug-resistant TB is basically an infectious disease caused by inadequate drug-sensitive treatment of tuberculosis [3]. In 2018 almost 480,000 new MDR-TB incidents with 100,000 rifampicin-resistant (RR) incidents were reported worldwide [4]. An approximate 500,000 new isoniazid-resistant (IR) cases have been reported in 2018, of which 78% were MDR-TB cases [5]. Despite this increase, however, the majority of patients diagnosed in 2017 and 2018 were only one in three (32%) of about 500,000 patients who developed (MDR-TB) [6].

MDR-TB is distinguished by high medication costs, longer time of therapy, poor effectiveness compared to vulnerable medicinal products [7]. The MDR-TB epidemic is exacerbated by inadequate health education for TB patients, an increasing number of respiratory infections and some other possible health factors related to this disease [8]. The frequency of MDR-TB cases is projected to increase in 2021 due to lack of knowledge among TB patients and poor awareness of its contributing factors [9]. In developing a comprehensive strategy for health care interventions, a broader understanding of the potential risk factors linked to MDR-TB infection is extremely essential.

However, most of MDR-TB studies has been investigated, mainly in United States and Europe [10]. Indeed, it is quite interesting and important to clarify the prevalence of MDR-TB, which has not been well studied in Malaysia. The purpose of this study is to determine the prevalence of MDR-TB and highlight the relevant health risk factors accountable for the developing MDR-TB infection in Malaysia.

2. Methods

2.1 Study design

The occurrence of MDR-TB infection in patients with TB were identified between year 2009 to year 2019. All registered TB patients who have been infected with MDR-TB are retrieved from National TB Information System (TBIS), Malaysia. Socio-demographic characteristic such age, gender, ethnicity, marital status and employment, followed by clinical characteristics were recorded into a Microsoft excel data sheet.

The Malaysia TB Information System is a TB patient tracking system in the country that was introduced in 2003 [11]. MDR-TB data were collected and reported regularly by these TB clinics or treatment centers throughout the country using a uniform method [11]. Throughout this process, all MDR-TB cases which reported to Health Department Office, serves as a data center for the collection, surveillance, monitoring and recording of all MDR-TB events in the state [11]. This data will be used to monitor cases involving MDR-TB not only in treatment facilities but also at national level [11]. This helps in evaluating data produced at national and global level through annual reports to the World Health Organization (WHO) [11]. The TBIS 10A1 (Initial Information on TB Treatment) were used to collect data in this study. The TBIS 10A1 form provides data for individuals with MDR-TB and is intended for enrolment of individuals with TB as well as input information's into the national TBIS database [12]. This shall include accurate details on individual with MDR-TB, including details of socio-demographic, clinical data and initiation of TB therapy [13].

2.2 Statistical and Data Analysis

Data obtained from TBIS is used to approximate the prevalence of MDR-TB as well to identify the possible risk factors among TB patients. The data collected from TBIS has been cleaned and converted into an excel spreadsheet. The statistical software (SPSS version 20) was used to analyze data. A 95% confidence interval was used to describe the frequency of MDR-TB. Prevalence is a term used to describe the overall number of incidents in which the disease is transmitted by the population at risk. In comparison, cases that were not MDR-TB were selected randomly as control measures. The total proportion of population at risk of TB is MDR-TB and non-MDR-TB. In order to calculate the prevalence, the following formula equitation (1) was used. [14]:

$$\text{Prevalance} = \frac{\text{Count of MDR_TB patients}}{(\text{Count of MDR_TB patients} + \text{Count of Non_MDR_TB patients})} \quad \text{Equitation. (1)}$$

Seven risk factors for MDR-TB infected patients in Malaysia are evaluated: gender, marital status, ethnicity, employment status, alcohol consumption, diabetic status, and smoking status. For each risk factors, Pearson's chi-square analysis is performed. The analysis involves the following steps: (a) Extraction of observed values, (b) Formulation of hypothesis, (c) Calculation of expected values and (d) Calculation of Chi-square test significance. Once the observed values and expected values are calculated, the excel formula equitation (2). To calculate the significance level, p-value, of the Pearson Chi-square test, CHISQ.TEST is used [14].

$$= \text{CHISQ.TEST (Observed-values / Expected-values)}$$

$$\chi_c^2 = \sum \left(\frac{o_i - E_i}{E_i} \right)^2 \quad \text{Equitation. (2)}$$

3.0 Results

Total of 989 MDR-TB cases reported in Malaysian national TB surveillance from 2009 to 2019, respectively. The MDR-TB cases from 2009 to 2019 including with the seven independent risk factors: gender, marital status, ethnicity, employment status, alcohol consumption, diabetic status, and smoking status shown in Table 1.

Table 1.0
MDR-TB cases from year 2009 to 2019.

Risk factors / Years	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
MDR-TB	55	64	141	74	124	104	101	74	116	64	72
Male	37	45	92	57	92	84	82	61	77	51	54
Female	18	19	49	17	32	20	19	13	33	13	8
Single	35	26	43	24	46	42	13	25	48	29	26
Married	20	38	98	50	78	62	88	49	62	35	46
Malay	35	45	94	51	88	71	70	52	86	38	55
Chinese	5	5	7	6	6	5	4	4	5	4	4
Indian	11	10	35	13	28	25	24	17	22	21	12
Others	4	4	5	4	2	3	3	2	3	1	1
Working	10	12	49	26	35	12	24	16	29	15	11
Not Working	45	52	92	48	89	92	77	58	87	49	61
Alcoholic	8	16	37	7	22	29	30	10	30	21	9
Non-Alcoholic	47	48	104	67	102	75	81	64	78	43	63
Diabetic	42	55	72	65	78	52	70	48	77	53	60
Non-Diabetic	13	9	69	9	46	52	31	26	39	11	12
Non-Smoker	4	2	7	4	5	6	5	3	2	3	4
Smoker	51	62	134	70	119	98	96	71	114	61	68
Note. ***Total of (MDR-TB) cases from year 2009 to year 2019: 989 MDR-TB incidents are reported to be the highest in 2013 and the lowest in 2009.											

Meanwhile the total number of TB cases from 2009 to 2019 are 287,092 respectively. The TB cases from 2009 to 2019 together with the seven independent risk factors: gender, marital status, ethnicity, employment status, alcohol consumption, diabetic status, and smoking status shown in Table 2.

Table 2.0
TB cases from year 2009 to 2019.

Risk factors / Years	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
TB	25241	27450	27500	29021	29221	25031	24220	25240	26168	24300	23700
Male	15210	17720	16245	17510	16731	14500	13100	14620	14084	14150	12850
Female	10031	9730	11255	11511	12490	10531	11120	10620	12084	10150	10850
Single	2241	1675	2408	1825	2135	1772	1670	1665	1872	2438	1782
Married	23000	25775	25092	27196	27086	23259	22550	23575	24296	21862	21918
Malay	14855	17135	17137	17832	19601	15670	15437	16375	17618	15789	15556
Chinese	2996	3702	3501	3224	3102	3017	3275	3070	2972	3021	2752
Indian	5870	4872	5241	6423	5020	4772	4100	4370	4200	4172	4090
Others	1520	1741	1621	1542	1498	1572	1408	1425	1378	1318	1302
Working	4527	4383	4272	4307	4772	4326	3966	5271	4788	4624	4613
Not Working	20714	23067	23228	24714	24449	20705	20254	19969	21380	19676	19087
Alcoholic	5201	3724	4672	4407	4328	4269	4432	4170	3983	4007	4002
Non-Alcoholic	20040	23726	22828	24614	24893	20762	19788	21070	22185	20293	19698
Diabetic	15201	17720	16358	15520	15366	15201	15179	15073	14788	14702	14585
Non-Diabetic	10040	9730	11142	13501	13855	9830	9041	10167	11380	9598	9115
Non-Smoker	3856	2129	2277	2539	2867	2729	2614	3729	1484	4088	5216
Smoker	21385	25321	25223	26482	26354	22302	21606	21511	24684	20212	18484
Note. ***Total of (TB) cases from year 2009 to year 2019: 287,092											
TB cases reported to be the highest in 2013 and the lowest cases of TB was reported in 2019.											

Based on National TB Surveillance data for Malaysian TBIS, the overall estimate of the MDR-TB occurrence among TB infected individuals in Malaysia is determined based on the count, (MDR-TB patients / MDR-TB patients count + non-MDR-TB patients count) as shown in Table 3.

Table 3.0
Overall incidence of MDR-TB cases from 2009 to 2019

Risk factors / Years	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
MDR-TB/Total TB	0.22%	0.23%	0.51%	0.25%	0.42%	0.41%	0.42%	0.29%	0.44%	0.26%	0.30%	0.34%
Male	0.24%	0.25%	0.56%	0.32%	0.55%	0.58%	0.62%	0.42%	0.54%	0.36%	0.42%	0.44%
Female	0.18%	0.19%	0.43%	0.15%	0.26%	0.19%	0.17%	0.12%	0.27%	0.36%	0.07%	0.20%
Single	1.54%	1.53%	1.75%	1.30%	2.11%	2.32%	0.77%	1.48%	2.50%	1.18%	1.44%	1.63%
Married	0.09%	0.15%	0.39%	0.18%	0.29%	0.27%	0.39%	0.21%	0.25%	0.16%	0.21%	0.24%
Malay	0.24%	0.26%	0.55%	0.29%	0.45%	0.45%	0.45%	0.32%	0.49%	0.24%	0.35%	0.37%
Chinese	0.17%	0.13%	0.20%	0.19%	0.19%	0.17%	0.12%	0.13%	0.17%	0.13%	0.15%	0.16%
Indian	0.19%	0.20%	0.66%	0.20%	0.55%	0.52%	0.58%	0.39%	0.52%	0.50%	0.29%	0.41%
Others	0.26%	0.23%	0.31%	0.26%	0.13%	0.19%	0.21%	0.14%	0.22%	0.08%	0.08%	0.20%
Working	0.22%	0.27%	1.13%	0.60%	0.73%	0.28%	0.60%	0.30%	0.60%	0.32%	0.24%	0.48%
Not Working	0.22%	0.22%	0.39%	0.19%	0.36%	0.44%	0.38%	0.29%	0.41%	0.25%	0.32%	0.32%
Alcoholic	0.15%	0.43%	0.79%	0.16%	0.51%	0.67%	0.45%	0.24%	0.75%	0.52%	0.22%	0.44%
Non-Alcoholic	0.23%	0.20%	0.45%	0.27%	0.41%	0.36%	0.41%	0.30%	0.35%	0.21%	0.32%	0.32%
Diabetic	0.28%	0.31%	0.44%	0.42%	0.51%	0.34%	0.46%	0.32%	0.52%	0.36%	0.41%	0.39%
Non-Diabetic	0.13%	0.09%	0.62%	0.07%	0.33%	0.53%	0.34%	0.26%	0.34%	0.11%	0.13%	0.27%
Non-Smoker	0.10%	0.09%	0.31%	0.16%	0.17%	0.22%	0.19%	0.08%	0.13%	0.07%	0.08%	0.13%
Smoker	0.24%	0.24%	0.53%	0.26%	0.45%	0.44%	0.44%	0.33%	0.46%	0.30%	0.37%	0.37%
Note. ***Incidence of (MDR-TB) from year 2009 to 2019: 0.34%												

Overall prevalence of (MDR-TB / Total TB) from 2009 to 2019, shown in Fig. 1.

For 2011, the cumulative incidence of MDR-TB over total TB was highest compared to other years. In 2012 and 2018 majority of MDR-TB incidence dropped drastically. The frequency of MDR-TB among Malaysian TB patients is still relatively low, which is approximately 0.34% between 2009 and 2019. In addition, independent risk factors, such as socio-demographic characteristics, are also linked to MDR-TB occurrence in Malaysia. Table 4 shows the association of independent factors which contribute to the incidence of MDR-TB in Malaysia.

Table 4.0
Independent risk factors related to MDR-TB prevalence.

Independent Risk Factors	Number (Prevalence)	P-value
Gender	166,720 (0.44%)	< 0.001
Male	120,372 (0.20%)	
Female		
Marital Status	21,483 (1.63%)	< 0.001
Single	256,609 (0.24%)	
Married		
Ethnic Groups	183,008 (0.37%)	< 0.001
Malay	34,632 (0.16%)	
Chinese	53,130 (0.41%)	
Indian	16,325 (0.20%)	
Other		
Working Status	49,849 (0.48%)	< 0.001
Working	237,243 (0.32%)	
Not Working		
Alcohol Consumption	47,195 (0.44%)	< 0.001
Alcoholic	239,897 (0.32%)	
Non-Alcoholic		
Diabetic Status	169,693 (0.39%)	< 0.001
Diabetic	117,399 (0.27%)	
Non-Diabetic		
Smoking Status	253,564 (0.13%)	< 0.001
Smoking	33,528 (0.27%)	
Non-Smoking		

The frequencies of MDR-TB cases in male patients is 732 and in female patients is 241. For TB patients the frequency for male patients is 166,720 accompanied by female patients is 120,372. Within the MDR-TB group, the number of males is equal to females. Pearson's chi-square showed that there is a substantial difference in the occurrence of MDR-TB between male and female individuals (0.44% and 0.20% respectively, with $p < 0.001$) as depicted in Fig. 2.

The estimated MDR-TB cases are 357 in single patients and 626 in married patients. For patients with TB, the frequency for single patients is 21,483, followed by married patients is 256,609. The proportion of singles in the MDR-TB group is equal to that of married couples in the MDR-TB group. Pearson's chi-square showed that there is a substantial difference in occurrence of MDR-TB between single and married patients (1.63% and 0.24%, $p < 0.001$) outlined in Fig. 3.

The frequencies of MDR-TB cases among Malay patients are 685, Chinese patients are 55, Indian patients are 218 and others are 32. The frequencies for Malay patients are 183,005, Chinese patients are 34,632, Indian patients are 53,130 and others are 16,325. The proportion of all ethnic's groups in the MDR-TB group is equal. Pearson's chi-square suggested that there is a substantial difference in the frequency of MDR-TB among different ethnicity ($p < 0.001$) as shown in Fig. 4.

The frequencies of MDR-TB incidence among working individuals are 239 and not working are 750 individuals. The frequencies for working individuals are 49,849 and not working individuals are 237,243. The proportion of working individuals in the MDR-TB group is equal to the proportion of not working individuals in the MDR-TB group. Pearson's chi-square exhibits that there is a substantial difference in the prevalence of (MDR-TB) between working and not working individuals (0.48% and 0.32%, $p < 0.001$) shown in Fig. 5.

The frequencies of MDR-TB incidence among alcoholic patients are 209 and non-alcoholic are 772 patients. For TB patients the frequencies for alcoholic patients are 47,195 and non-alcoholic patients are 239,897. The proportion of alcoholic patients in the MDR-TB cluster is equal to the proportion of non-alcoholic patients in the MDR-TB cluster. Pearson's chi-square proves that there is a significance difference in the prevalence of MDR-TB between alcoholic patients and non-alcoholic patients (0.44% and 0.32%, $p < 0.001$) as illustrated in Fig. 6.

The frequencies of MDR-TB incidence among diabetic patients are 672 and non-diabetic patients are 317. For TB patients the frequencies for diabetic patients are 169,693 and non-alcoholic patients are 117,399. The proportion of diabetic patients in the MDR-TB cluster is equal to the proportion of non-diabetic patients in the MDR-TB cluster. Pearson's chi-square found that there is a significance difference in the prevalence of MDR-TB between diabetic and non-diabetic patients (0.39% and 0.27% respectively, with $p < 0.001$) as outlined in Fig. 7.

The frequency of MDR-TB cases among the smoking patients is 944 and 45 are non-smoking patients For TB patients the frequencies for smoking patients are 253,564 and non-smoking patients are 33,528. The proportion of smoking patients in the MDR-TB group is equal to the proportion of non-smoking patients. Pearson's chi-square reveals that the prevalence of MDR-TB between smoking and non-smoking patients differs significantly (0.13% and 0.27% respectively, with $p < 0.001$) as shown in Fig. 8.

Discussion

In Malaysia, the MDR-TB frequency is low and can be attributed to patients' positive response to first-line antibiotics such as isoniazid and rifampicin. According Chien et al. [15] TB patients with isoniazid-resistant can be cured at a risk of relapse of less than 5%. Men are at greater risk of being infected with MDR-TB compared to the women identified in this study. One potential explanation, according to Caminero et al. [16], that men primarily smoke, drink alcohol and use drugs compared to women. According to Skrahina [17], younger and single individuals tend to be more vulnerable to MDR-TB due to their high participation in social behaviors which includes alcohol intake and smoking compared to older and married individuals. Evidence from this study indicates that MDR-TB infections between different ethnicities may rely on their behavioral activities. Malaya and Indian ethnic groups have a higher incidence of MDR-TB relative to other ethnic groups in Malaysia, and this may be attributed to social behavioral factors such as smoking habits, substance use of drugs and alcohol consumption. Jobless TB infected individuals are more vulnerable to transmission of MDR-TB than those working due to their poverty line, which prevents them from follow up with routine health checks with clinicians in TB centers and purchasing medicines. Study revealed a 3.54-fold higher likelihood of MDR-TB transmission between alcoholics compared to non-alcoholics, indicating the possibility of disease recurrence [18]. The substantial proportion of MDR-TB multidrug-resistant tuberculosis among diabetic patients appears to be growing steadily compared to non-diabetic patients [19]. Smoking is associated with the cessation of (TB/ MDR-TB) treatment and it has been found that this association is independent of alcohol or illicit drug usage [20].

Conclusion

To date, (MDR-TB) cases in Malaysia is relatively low ($< 0.34\%$) compared to global notification. Although all Malaysians are free to diagnose and treat, some MDR-TB patients still have a heavy financial burden on them. Multi-drug resistance TB develops either due to infection with a resistant strain, or as a result of inadequate treatment and poor patient compliance. Proper patient care and commitment to the completion of anti-TB therapy are recommended. The results of the study revealed that all contributing risk factors including age, gender, ethnicity, marital status, smoking, job, diabetic and alcohol intake are associated significantly with MDR-TB prevalence and relatively low ($< 2.0\%$) in Malaysia. Reliable MDR-TB prevalence

estimates will theoretically help to improve prevention measures, guide successful intervention and follow-up interventions in vulnerable populations, and assist in overall clinical decision-making. In public health perspective, priority actions to develop national guideline for surveillance and monitoring of MDR-TB and engagement with non-profit organization, civil society and communities for treatment support should be strengthened.

Declarations

Conflict of Interest.

The authors declare no conflict of interest, financial or otherwise.

Note

***Total of (MDR-TB) cases from year 2009 to year 2019: **989**

Note

***Total of (TB) cases from year 2009 to year 2019: **287,092**

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Informed consent

Informed consent is not applicable.

Ethical approval

National Institutes of Health and Medical Research Ethics Committee. NMRR-19-1460-46943

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Figures

Figure 1

Overall prevalence of MDR-TB/ Total TB

Figure 2

Prevalence of MDR-TB by gender between 2009-2019.

Figure 3

Prevalence of MDR-TB by marital status between 2009-2019.

Figure 4

MDR-TB prevalence between different ethnic groups during the period 2009-2019.

Figure 5
The frequency of working and non-working individuals in the MDR-TB group between 2009-2019.

Figure 6
Prevalence of MDR-TB by alcohol consumption among patients between 2009-2019.

Figure 7

Prevalence of MDR-TB among diabetic patients between 2009-2019.

Figure 8

MDR-TB prevalence by smoking status among patients between 2009-2019.

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