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ASSESSMENT OF MYCOBACTERIUM TUBERCULOSIS DRUG-RESISTANCE PATTERNS IN A PUBLIC HOSPITAL OF LIMA, PERU DURING 2022

EVALUACIÓN DE LOS PATRONES DE FARMACORRESISTENCIA DE MYCOBACTERIUM TUBERCULOSIS EN UN HOSPITAL PÚBLICO DE LIMA, PERÚ DURANTE 2022

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ABSTRACT

Background: Tuberculosis is a public health problem considered to be the world's leading cause of death from an infectious disease among adults. Diagnosis is often challenging and is based on clinical, epidemiological, radiological, bacteriological, histological and biochemical findings. Timely diagnosis, identification of the susceptibility profile and follow-up compliance is important to enable more effective treatment and avoid severe forms of the disease. **Objective:** Describe the resistance patterns of Mycobacterium tuberculosis identified in the period of the year 2022 at Hospital María Auxiliadora. **Material and Methods:** This is an observational, cross-sectional study of patients diagnosed with tuberculosis throughout the year 2022 in the Tuberculosis Center of Excellence (TB COE), division of the respiratory medicine department at the Hospital Maria Auxiliadora, Lima, Peru. Data was collected from the medical records which was then included for the statistical analysis. The clinical and demographic characteristics were described by absolute frequencies and percentages. Chi-square test and Fisher's exact test were used to evaluate the association between the sensitivity profile of tuberculosis and the independent variables. A p-value < 0.05 was considered as statistically significant. **Results:** A total of 261 medical records were included in the present study. The most frequent age group was 17-59 years old, the majority were male (62.1%) and 15.7% were relapses, as established on national technical standard. Of the total, 89.7% were sensitive to first line drugs; 6.1% of the patients were multidrug-resistant (MDR), and 0.8% presented extensively drug-resistance (XDR); likewise, 0.8% and 2.7% presented resistance for rifampicin only and resistance for isoniazid only respectively. HIV infection was found at 14.2%. The most common form of tuberculosis was pulmonary (49%) followed by pleural tuberculosis (21.8%). **Conclusion:** Tuberculosis is a worldwide condition whose drug-resistance patterns continue evolving. However, in our hospital, a southern Peru reference Center, most TB patients are still sensitive to first line drugs. Only a small amount of MDR and XDR patients were found. Moreover, the most common clinical presentation was pulmonary followed by pleural tuberculosis.

Keywords: Tuberculosis; Mycobacterium tuberculosis; Drug Resistance; Infections. (Source: MESH-NLM)

RESUMEN

Antecedentes: La tuberculosis es un problema de salud pública considerado la principal causa mundial de muerte por una enfermedad infecciosa entre los adultos. El diagnóstico suele ser difícil y se basa en hallazgos clínicos, epidemiológicos, radiológicos, bacteriológicos, histológicos y bioquímicos. El diagnóstico oportuno, la identificación del perfil de susceptibilidad y el cumplimiento del seguimiento son importantes para permitir un tratamiento más eficaz y evitar formas graves de la enfermedad. **Objetivo:** Describir los patrones de resistencia de Mycobacterium tuberculosis identificados en el periodo del año 2022 en el Hospital María Auxiliadora. **Material y métodos:** Se trata de un estudio observacional, transversal, de pacientes diagnosticados de tuberculosis durante todo el año 2022 en el Centro de Excelencia en Tuberculosis (COE-TB), división del servicio de medicina respiratoria del Hospital María Auxiliadora, Lima, Perú. Los datos fueron recolectados de las historias clínicas que luego fueron incluidas para el análisis estadístico. Las características clínicas y demográficas se describieron mediante frecuencias absolutas y porcentajes. Para evaluar la asociación entre el perfil de sensibilidad de la tuberculosis y las variables independientes se utilizó la prueba de Chi cuadrado y la prueba exacta de Fisher. Un valor p < 0,05 se consideró estadísticamente significativo. **Resultados:** Se incluyeron en el presente estudio 261 historias clínicas. El grupo de edad más frecuente fue el de 17-59 años, la mayoría eran varones (62,1%) y el 15,7% eran recidivantes, según lo establecido en la norma técnica nacional. Del total, el 89,7% eran sensibles a fármacos de primera línea; el 6,1% de los pacientes eran multirresistentes (MDR), y el 0,8% presentaban resistencia extensiva a fármacos (XDR); asimismo, el 0,8% y el 2,7% presentaban resistencia sólo para rifampicina y resistencia sólo para isoniazida respectivamente. La infección por VIH se detectó en el 14,2%. La forma más frecuente de tuberculosis fue la pulmonar (49%), seguida de la tuberculosis pleural (21,8%). **Conclusiones:** La tuberculosis es una afección mundial cuyos patrones de farmacorresistencia continúan evolucionando. Sin embargo, en nuestro hospital, un centro de referencia del sur del Perú, la mayoría de los pacientes con TB siguen siendo sensibles a los fármacos de primera línea. Sólo se encontró una pequeña cantidad de pacientes MDR y XDR. Además, la presentación clínica más frecuente fue la tuberculosis pulmonar seguida de la pleural.

Palabras clave: Tuberculosis; Mycobacterium tuberculosis; Farmacorresistencia; Infecciones. (Fuente: DeCS- BIREME)

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INTRODUCTION

Tuberculosis (TB) infection continues to be a worldwide public health issue in which its incidence and mortality numbers have been declining in the last decade, apparently not fast enough for the targets set by the World Health Organization (WHO) [1]. During 2021, an increase of 4.5% in the worldwide incidence of TB compared to the previous year was reported, where 10.6 million people got infected and a mortality rate of 20 per 100 000 population was evidenced[1]. One of the main possible causes of the increasing number of cases, is the impact of the COVID-19 pandemic on the unprepared healthcare systems for a crisis of this magnitude mirrored in a lack of TB related services[2].

As for Latin America, other aspects must be taken into account such as the ongoing political, economic, and social crises, a setback in poverty reduction, in addition to the increasing rates of homelessness and prisoners[3,4] which reflects in two south American countries with a position in the three global lists of high-burden countries for TB [5] Brazil accounts for the only south American country included in two of them, the high burden TB list itself as well as in the HIV-associated TB one. In addition, Peru is the other south American country that has gained a spot in the third one, the Multidrug-resistant (MDR) / Rifampicin-resistant (RR) TB list [6] which keeps bringing nothing but concern in all aspects for disease control. It is worth mentioning that following the worldwide trend, Peru also experienced an increase of 5.1% in the incidence of TB between the years mentioned.

Alongside the growth in TB infection and death numbers, drug-resistant TB (DRTB), continues to be a rising problem. Reflected on the steady increase of these cases, several factors play a critical role on the risk to develop DRTB, including demographic and socioeconomic ones such as psychiatric illness, alcohol or drug addiction, homelessness, comorbidities and ages between 18 to 45 [7]. On another hand, but still interrelated, history of previous treatment has been more strongly associated 8 with its different scenarios ranging from inadequate treatment for specific situations, as in wrong choice of new drugs for an unsuccessful treatment, discharge of still infected patients, cases of undetected underlying resistance and non-adherence, to genetic predisposition due to permanent or temporary mutations on efflux pump, propionate catabolism, glycerol kinase encoding associated genes, to name a few [9]. It is worth mentioning that Mycobacterium was found as one of the most important multi-antibiotic resistant bacteria (MAR) with the presence of 14 MAR genes[10].

The development of different drug resistance patterns impacts socially and economically as it requires a prolonged and a more expensive treatment regimen involving investment in more resources and infrastructure, which are lacking in the context of low-income countries [11] due to poor investment from the government in quantity or quality alongside different social factors[12]. This causes a great impact on morbidity and mortality especially in vulnerable communities for the access to health services in general [11]. From this study we intend to describe the drug resistance patterns of Mycobacterium tuberculosis identified in the period of the year 2022 in our locality and to compare them with those existing in other realities.

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MATERIAL AND METHODS

Study design and participants

The present study was of an observational, cross-sectional design. The population was made up of patients of any age who have been diagnosed with tuberculosis involving anybody organ throughout the year 2022, in which their treatment follows up was monitored by the Maria Auxiliadora Hospital. Patients were excluded from the study in the case of incomplete clinical-epidemiological data and those without an antituberculous drug sensitivity test.

Data collection and endpoints

Data was collected from the medical records of patients with a diagnosis of tuberculosis in any of its clinical forms who started an antituberculosis treatment scheme during the period of January 1 of 2022 to December 31 of the same year, which were provided by the registry of the Tuberculosis Center of Excellence (TB COE), area of the hospital in charge of monitoring these

patients that belongs to the Pulmonology Department of the María Auxiliadora Hospital. In addition, the results of the antituberculous drugs sensitivity profiles of these patients were also taken from the NetLab information system of the National Institute of Health. Medical records that did not have a sensitivity profile or other registered clinical-epidemiological data were excluded.

Ethics statements

International ethical standards for biomedical research with human subjects, present in the Declaration of Helsinki will be followed. Informed consent was not required since only specific information from medical records were obtained and evaluated. All data was handled with total confidentiality and used for research purposes only. Finally, the final manuscript will be published in a journal indexed in Scopus and PubMed. No financial support was provided for this study.

Statistical analysis

A database was generated in Microsoft Excel ® v. 2010 (Microsoft Corporation, CA, USA) which was then to the statistical program STATA version 15.0 (StataCorpLP, TX, USA) to carry out the statistical analysis. All the variables were reported in absolute frequencies and percentages as they were all categorical, including age which was then categorized before the analysis. On another hand, we performed a bivariate analysis, in order to indicate significance between sensitivity and some degree of resistance, the Chi-square test and Fisher's exact test were used according to the evaluation of the assumptions based on the expected values. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 294 medical histories of patients with a diagnosis of tuberculosis in all its clinical forms were reviewed, of which 18 were excluded for having incomplete clinical-epidemiological-radiological data, in addition to 15 medical histories that did not have sensitivity profile data in the NetLab information system of the National Institute of Health; finally, 261 patients were included for the statistical analysis. (Figure 1)

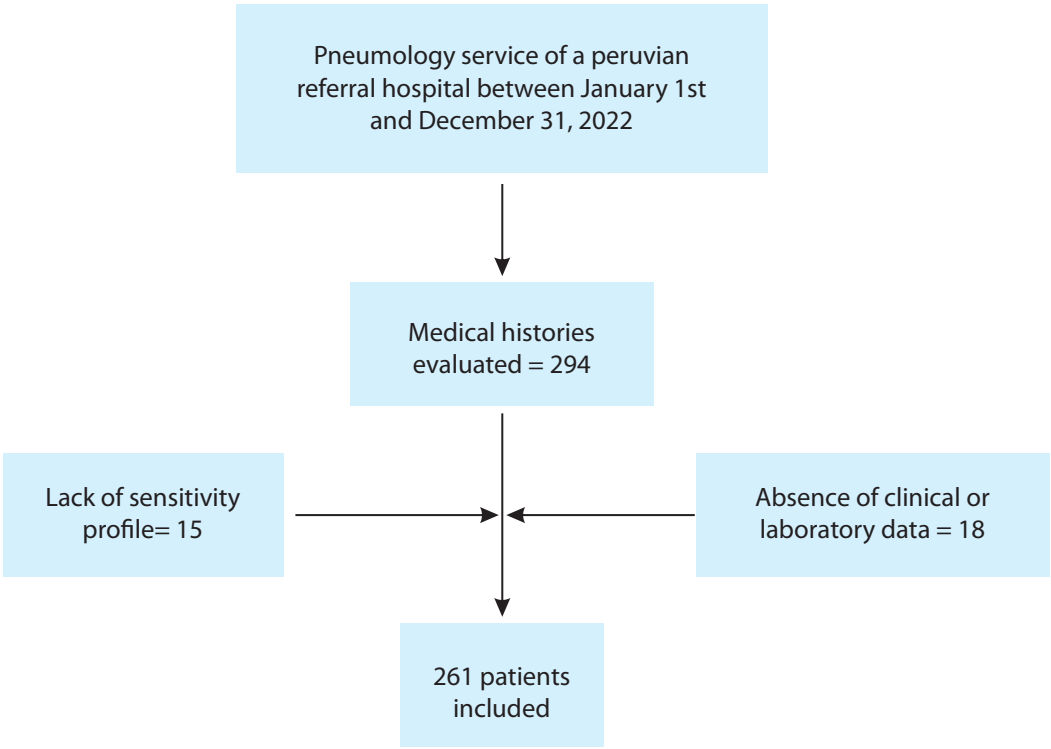

Figure 1. Flow chart

Table 1. Clinical and demographics characteristics.

	TUBERCULOSIS N=261	
EDAD	**Frequency**	**%**
0-5 y	1	0.38
6-11 y	5	1.92
12-18 y	12	4.6
19-26 y	37	14.18
27-59 y	160	61.3
>60 y	46	17.62
SEX	**Frequency**	**%**
Feminine	99	37.93
Masculine	162	62.07
NATIONALITY	**Frequency**	**%**
Peruvian	253	96.93
Venezuelan	8	3.07
CRITERIA	**Frequency**	**%**
Bacteriological	129	49.43
Clinical/Epidemiological/Radiological	73	27.97
Histopathological	43	16.48
Biochemical	16	6.13
DX TEST	**Frequency**	**%**
Genotype	125	47.89
Genexpert	128	49.04
MODS	8	3.07
SENSITIVITY PROFILE	**Frequency**	**%**
Sensible	234	89.66
Mono rifampicin resistant	2	0.77
Mono isoniazid resistant	7	2.68
MDR-TB	16	6.13
XDR-TB	2	0.77
CONDITION OF ADMISSION	**Frequency**	**%**
Never treated	217	**83.14**
Relapse	41	15.71
Resumed abandonment	3	1.15
COMORBIDITIES	**Frequency**	**%**
HIV Immunosuppression	37	14.18
Non HIV- Immunosuppression	30	11.5
Other Comorbidities	5	1.91
Unhealthy Habits	18	6.89

None	171	65.52
UNHEALTHY HABITS	**Frequency**	**%**
Alcohol	8	6.13
Smoking	1	0.38
Drug users	12	4.6
None	240	91.95
RISK FACTOR	**Frequency**	**%**
None	206	78.93
Contacts with active tuberculosis	50	19.16
MDR contact	3	1.15
Health workers	2	0.77

MODS: Microscopic observation drug susceptibility; MDR: Multidrug resistant tuberculosis; XDR: Extensively drug resistant tuberculosis; HIV: Human Immunodeficiency virus

As it is reported on table 1, the most frequent age group was the 27-59 years old one and the majority were male (62.1%). Among the diagnostic criteria for patient admission, the most common was bacteriology (49.4%), followed by clinical/epidemiological/radiological (27.97%), histopathology (16.5%), and biochemical (6.13%). Sensitivity profile studies on antituberculosis drugs obtained were performed with Genotype (47.9%), Genexpert (49%), MODS (3.1%) diagnostic tests. Out of the 261 patients evaluated, 89.66% were sensitive to first line antituberculosis drugs; 6.13% were MDR-TB, and 0.77% presented XDR-TB resistance; likewise, 0.77% and 2.68% exhibited monoresistance to rifampicin and isoniazid respectively.

Regarding the condition of admission, 83.14% were considered as new patients, this meaning they have never received treatment for TB infection; 15.71% presented relapse, defined by the Peruvian technical standard as presenting a new diagnosis of tuberculosis 6 months after the last diagnosis; and 1.15% were admitted as patients who resumed their treatment after not receiving it for 30 days or more, as established on the previously mentioned document. Most of the patients had no comorbidities (65,52%), although 14.18% had a diagnosis of HIV, 11.5% patients presented another condition that conditioned immunosuppression (diabetes mellitus, pregnancy, treatment with corticoids and chronic renal disease), 1.91% had another disease that did not condition immunosuppression (history of arterial hypertension, stroke, Parkinson's disease, bulimia, gout, human papillomavirus infection), 6.89% patients had unhealthy habits.

With respect to last, it was observed that 6.13% of the patients consumed alcohol, 4.6% were drug users, 0.38% had a history of smoking and 91.95% had no harmful habits. In relation to risk factors, patients who had contact with active tuberculosis (19.16%), patients with MDR contact (1.15%), health workers (0.77%), and patients who did not present any risk factor (78.93%) were taken into account.

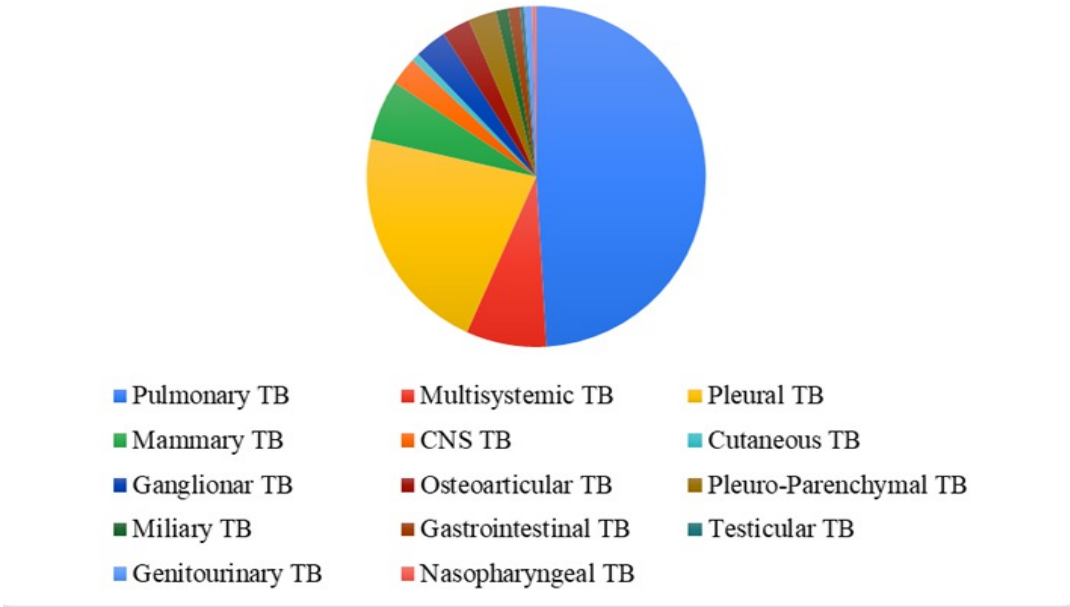

Figure 2. Distribution of clinical forms of tuberculosis.

Distribution of the clinical forms of tuberculosis are shown on Figure 2. Most patients were diagnosed with pulmonary tuberculosis (49.04%), followed by pleural TB (21.84%). It was observed that 7.66% were diagnosed with multisystemic TB, 5.75% with mammary TB, 3.07% with ganglionar TB, TB of the central nervous system, osteoarticular and pleuro-parenchymal each accounting for 2.68% of the population; miliary and gastrointestinal forms where each constitutes 1.15% of the population; cases of genitourinary and cutaneous TB were each amounting to 0.77% and finally only 0.38% presented nasopharyngeal TB.

Table 2. ABivariate analysis.

	OVERALL POPULATION	PULMONARY	EXTRAPULMONARY	P VALUE
	n = 261 (100%)	n = 127 (48.66%)	n = 134 (51.32%)	
AGE				
0-5	1 (0.38)	1 (0.79)	0 (0)	
6-11	5 (1.92)	4 (3.15)	1 (0.75)	
12-18	12 (4.6)	4 (3.15)	8 (5.97)	
19-26	37 (14.18)	18 (14.17)	19 (14.18)	
27-59	160 (61.3)	72 (56.69)	88 (65.67)	
>60	46 (17.62)	28 (22.05)	18 (13.43)	0.158
SEX				
Feminine	99 (37.93)	49 (38.58)	50 (37.31)	0.833

Masculine	162 (62.07)	78 (61.42)	84 (62.69)	
NATIONALITY				
Peruvian	253 (96.93)	125 (98.43)	128 (95.52)	
Venezuelan	8 (3.07)	2 (1.57)	6 (4.48)	0.174
CRITERIA				
Bacteriological	129 (49.43)	95 (74.8)	34 (25.37)	
Clinical/Epidemiological/ Radiological	73 (27.97)	29 (22.83)	44 (32.84)	
Histopathological	43 (16.48)	2 (1.57)	41 (30.6)	
Biochemical	16 (6.13)	1 (0.79)	15 (11.19)	<0.001
DX TEST				
Genotype	125 (47.89)	88 (69.29)	37 (27.61)	
Genexpert	128 (49.04)	38 (29.92)	90 (67.16)	
MODS	8 (3.07)	1 (0.79)	7 (5.22)	<0.001
SENSITIVITY PROFILE				
Sensible	234 (89.66)	108 (85.04)	126 (94,03)	
Mono rifampicin resistant	2 (0.77)	2 (1.57)	0 (0)	
Mono isoniazid resistant	7 (2.68)	4 (3.15)	3 (2.24)	
MDR TB	16 (6.13)	12 (9.45)	4 (2.99)	
XDR TB	2 (0.77)	1 (0.79)	1 (0.75)	0.074
CONDITION OF ADMISSION				
Never treated	217 (83.14)	96 (75.59)	121 (90.3)	
Relapse	41 (15.71)	29 (22.83)	12 (8.96)	
Resumed abandonment	3 (1.15)	2 (1.57)	1 (0.75)	0.003
COMORBIDITIES				
HIV Immunosuppression	37 (14.18)	19 (14.96)	18 (13.43)	0.724
Non HIV- Immunosuppression	30 (11.5)	17 (13.39)	13 (9.7)	0,289
Other Comorbidities	5 (1.91)	2 (1.57)	3 (2.24)	0.488
Unhealthy Habits	18 (6.89)	12 (9.45)	6 (4.48)	0.113
None	171 (65.52)	79 (62.2)	93 (69.4)	0.318
UNHEALTHY HABITS				
Alcohol	8 (6.13)	7 (5,51)	1 (0,75)	0.026
Smoking	1 (0,38)	1 (0,79)	0 (0)	0.303
Drug users	12 (4,6)	7 (5,51)	5 (3,73)	0.492
None	240 (91,95)	114 (89,76)	126 (94,03)	0.113
RISK FACTOR				
None	206 (78,93)	96 (75,59)	110 (82,09)	
Contacts with active TB	50 (19,16)	28 (22,05)	22 (16,42)	
MDR contact	3 (1,15)	2 (1,57)	1 (0,75)	
Health workers	2 (0,77)	1 (0,79)	1 (0,75)	0.641

MODS: Microscopic observation drug susceptibility; MDR: Multidrug resistant tuberculosis; XDR: Extensively drug resistant tuberculosis; HIV: Human Immunodeficiency virus

Table 2 indicates that 65.67% of patients between the ages of 27-59 years were diagnosed with extrapulmonary tuberculosis. Similarly, 62.69% of the patients with extrapulmonary tuberculosis were male. A significant p-value was obtained when evaluating the variables of diagnostic criteria, admission condition, type of diagnostic test used for the sensitivity profile.

Most of the patients with a diagnosis of extrapulmonary tuberculosis had never been treated (90.30%). Regarding the sensitivity profile, 94.03% of patients with extrapulmonary tuberculosis were sensitive to first-line drugs; in contrast, patients with pulmonary tuberculosis presented more cases of MDR tuberculosis (9.45%).

Table 3. Demographic data according to drug susceptibility pattern.

	TUBERCULOSIS					
	SENSIBLE	R RESISTANT	H RESISTANT	MDR	XDR	P VALUE
	n = 234 (89,66%)	n = 2 (0.77%)	n = 7 (2.68%)	n = 16 (6.13%)	n = 2 (0.77%)	p
AGE						
0-5	1 (0,43)	0 (0)	0 (0)	0 (0)	0 (0)	
6-11	4 (1,71)	1 (50)	0 (0)	0 (0)	0 (0)	
12-18	12 (5,13)	0 (0)	0 (0)	0 (0)	0 (0)	0,005
19-26	34 (14,53)	0 (0)	0 (0)	3 (18,75)	0 (0)	
27-59	144 (61,54)	0 (0)	6 (85,71)	10 (62,5)	0 (0)	
>60	39 (16,67)	1 (50)	1 (14,29)	3 (18,75)	2 (100)	
GENDER						
Feminine	92 (39,32)	1 (50)	0 (0)	6 (37,5)	0 (0)	0,213
Masculine	142 (60,68)	1 (50)	7 (100)	10 (62,5)	2 (100)	
NATIONALITY						
Peruvian	227 (97,01)	2 (100)	6 (85,71)	16 (100)	2 (100)	0,462
Venezuelan	7 (2,99)	0 (0)	1 (14,29)	0 (0)	0 (0)	
CLINICAL FORM OF TB						
Pulmonary TB	108 (46,15)	2 (100)	4 (57,14)	12 (75)	2 (100)	0,544
Multisystemic TB	19 (8,12)	0 (0)	0 (0)	1 (6,25)	0 (0%)	
Pleural TB	56 (23,93)	0 (0)	0 (0)	1 (6,25)	0 (0)	
Mammary TB	15 (6,41)	0 (0)	0 (0)	0 (0)	0 (0)	
CNS TB	7 (2,99)	0 (0)	0 (0)	0 (0)	0 (0)	
Cutaneous TB	2 (0,85)	0 (0)	0 (0)	0 (0)	0 (0)	
Ganglionar TB	6 (2,56)	0 (0)	1 (14,29)	1 (6,25)	0 (0)	
Osteoarticular TB	7 (2,99)	0 (0)	0 (0)	0 (0)	0 (0)	

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Pleuro-Parenchymal TB	5 (2,14)	0 (0)	1 (14,29)	1 (6,25)	0 (0)	
Miliary TB	2 (0,85)	0 (0)	1 (14,29)	0 (0)	0 (0)	
Gastrointestinal TB	3 (1,28)	0 (0)	0 (0)	0 (0)	0 (0)	
Testicular TB	1 (0,43)	0 (0)	0 (0)	0 (0)	0 (0)	
Genitourinary TB	2 (0,85)	0 (0)	0 (0)	0 (0)	0 (0)	
Nasopharyngeal TB	1 (0,43)	0 (0)	0 (0)	0 (0)	0 (0)	
CONDITION OF ADMISSION						
Never treated	198 (84,62)	2 (100)	6 (85,71)	10 (62,5)	1 (50)	
Relapse	34 (14,53)	0 (0)	1 (14,29)	5 (31,25)	1 (50)	0,125
Resumed abandonment	2 (0,85)	0 (0)	0 (0)	1 (6,25)	0 (0)	
COMORBIDITY						
HIV Immunosuppression	35 (14,96)	0 (0)	1 (14,29)	1 (6,25)	0 (0)	0,836
Non HIV-Immunosuppression	26 (11,11)	1 (50)	0 (0)	3 (18,75)	0 (0)	0,386
Other Comorbidities	4 (1,71)	0 (0)	0 (0)	1 (6,25)	0 (0)	0,423
Unhealthy Habits	12 (5,13)	0 (0)	3 (42,86)	3 (18,75)	0 (0)	0,006
None	158 (67,52)	1 (50)	3 (42,86)	8 (50)	2 (100)	0,503
UNHEALTHY HABITS						
OH	5 (2,14)	0 (0)	3 (42,86%)	0 (0%)	0 (0%)	0,003
Smoking	1 (0,43)	0 (0)	0 (0%)	0 (0%)	0 (0%)	1
Drug users	9 (3,85)	0 (0)	0 (0%)	3 (18,75%)	0 (0%)	0,087
None	219 (93,59)	2 (100)	4 (57,14%)	13 (81.25%)	2 (100%)	0,02
RISK FACTOR						
None	186 (79,49)	2 (100)	6 (85,71)	10 (62,5)	2 (100)	
Contacts with active TB	44 (18,8)	0 (0)	1 (14,29)	5 (31,25)	0 (0)	0,473
MDR contact	2 (0,85)	0 (0)	0 (0)	1 (6,25)	0 (0)	
Health workers	2 (0,85)	0 (0)	0 (0)	0 (0)	0 (0)	

MDR: Multidrug resistant tuberculosis; XDR: Extensively drug resistant tuberculosis; HIV: Human Immunodeficiency virus.

The sensitivity profile observed in each group of patients is described on Table 3. Overall, the majority of patients were sensitive to first-line antituberculosis drugs. Statistically significant results were obtained when evaluating the sensitivity profile according to age as well as unhealthy habits. Most patients with MDR tuberculosis were between 27-59 years of age; however, 61.5% of patients sensitive to first-line drugs were also in the same age group. 42.86% of the patients who presented resistance to isoniazid consumed alcohol, likewise 18.75% of the MDR patients were drug users.

No statistically significant differences were obtained when evaluating sensitivity in relation to the clinical forms of tuberculosis, sex, nationality and comorbidities; however, it was found that among patients with the diagnosis of MDR tuberculosis, 62.5% were male, 75% were diagnosed with pulmonary tuberculosis and 31.3% had relapsed after previous treatment. Finally, in relation to comorbidities, 50% did not have them and 18.8% had some type of immunosuppression rather than HIV.

DISCUSSION

In the present study we sought to determine the different TB drug resistance patterns of TB diagnosed patients in a public hospital in Lima, Peru. The majority of patients were sensitive to first-line antituberculosis drugs, nevertheless a lower percentage of patients with MDR and XDR tuberculosis and with resistance to rifampicin or isoniazid were also observed. Around the world there are different reports of the prevalence of tuberculosis and their respective sensitivity profiles. A systematic review by Lohiya et al. reported the prevalence of MDR, Any Drug Resistance and XDR patients to be 3.5%, 24.9% and 0.06%, respectively [13]. Likewise, in the study by Ahmad et al. regarding the prevalence of tuberculosis and drug resistance in the Middle East, regions such as Saudi Arabia, had variations in the MDR-TB prevalence according to the time period in which the studies were conducted, with an average of 6.7%[14]. Similarly, Tengan et al. studied the prevalence of MDR-TB in Latin America among never treated patients was 7.0% and previously treated cases was 26.5%[15].

Additionally, as in our study, it has been reported that monoresistance was higher for isoniazid compared to rifampicin[14,15]. Our findings align with those reported in the international literature, likely due to shared local factors associated with tuberculosis. Poverty, for instance, has been identified as a contributing factor, with higher incidence observed in middle and low-income countries by Furin et al.[16] Moreover, under-diagnosis of resistant forms of tuberculosis can delay treatment initiation, potentially explaining the unchanged or increasing prevalence rate of MDR tuberculosis as reported by Tengan et al.[15] The most common age group in the present study was the 17-59 years old one, with a predominance in the male sex, results consistent with those from similar studies that also concluded the adult group to be the most frequently affected, and also the one in which coinfection with HIV is more common [17,18]. Similar findings were reported by Bonin, et al. who found that 76% of the patients they studied were male[18].

We emphasize adequate control over unhealthy habits on TB patients, as 60% of these habits was described on patients admitted in a Brazilian referral hospital with significant correlation of the use of illicit drugs with drug-resistant TB [18]. Despite, finding less frequency than previously described [19], alcohol drinking was found to be associated with drug-resistance. Indeed, it has been related with rising risk of transmission and disease severity, by increasing pulmonary oxidative stress, impairing mucociliary function, alveolar epithelium and macrophage action[20].

Smoking is also described as a major driver of TB. Thereby, De Vargas, et al. concluded that self-reported active smokers, with 32% prevalence, had minor chances to cure and more to abandon treatment[21]. In contrast, despite evaluating more patients, we found less prevalence of smoking habit and could not

establish its association with drug-resistance TB. The impact caused by these conditions, as mentioned by Song W, et al. in their retrospective cohort study, needs to be taken into consideration because of its effect over TB-resistance[22].

Furthermore, most of the patients with a diagnosis of tuberculosis in our study, were sensitive to first-line antituberculosis drugs regardless of the presence of any comorbidity, in contrast to different studies that show HIV infection as a disease that generally conditions patients to present resistance to first-line antituberculosis drugs. Both share predisposing factors such as poverty, which has been shown to be a risk factor for MDR-TB in HIV patients due to overcrowding in the home, overcrowding in transportation and weak immune systems associated with malnutrition[16,23]. That is why studies such as the systematic review and meta-analysis by Sultana et al. reports the odds of MDR-TB infection among HIV-positive cases to be 1.42 times higher[24].

There are other immunosuppressive conditions predisposing the patient to TB infection such as diabetes mellitus which has been reported to triple the risk for disease development and have a 2-fold higher risk of developing MDR TB than patients without it.[25,26] Although the association between comorbidities that generate immunosuppression and MDR TB is still inconsistent as mentioned by Hamada et al, in their review article, there is still a limitation when evaluating the sensitivity profile in different parts of the world[27]. Sensitivity profiles are often performed only when there is first-line treatment failure, and this could be the reason why in our study the results of resistance and comorbidities are not related to the previously mentioned international studies.

Other conditions that generate immunosuppression and consequently are associated with tuberculosis have been described in the international literature[28-30]. In our study we considered other factors such as pregnancy, patients with chronic renal disease, neoplasias and treatment with corticoids[28].

Patients who had no contact with a TB infected person presented a higher prevalence of drug resistance than those who were. However, only one case of TB MDR was reported out of the 3 patients with TB MDR exposure while the other two were susceptible to first line treatment. According to a systematic review which included studies from around the world, the resistance pattern concordance between infected patients and their household contacts was of 54.3% meaning more than half of the secondary cases had the same resistance pattern of the index cases[31]. Out of the 33 articles included, 2 were performed in the Peruvian population. Bayona et.al. studied MDR-TB patients from 1996 to 1999 where 8% of the contacts developed TB infection, and out of those who developed the disease, 84% were MDR-TB with 17% sharing the same drug-resistance pattern[32]. Similarly, Parr included patients from 1996 to 2003 revealing that almost 90% were resistant to isoniazid and rifampin showing the importance of TB contact investigation, which lies in the reduction of its related mortality associated with a late diagnosis especially in high-burden settings[33-35]. On another hand, the relationship between drug-resistance and TB relapse or abandonment.

Our study has inherent limitations that should be considered in its interpretation. We analyzed patients diagnosed with tuberculosis solely in 2022 at María Auxiliadora Hospital, with no data from previous years to determine prevalence tendencies. Furthermore, the transfer of patients to local health centers hindered follow-up and monitoring of treatment response. Additionally, there was a delay in sensitivity profile requests, resulting in resistance evaluations typically occurring only after first-line treatment had failed. Nonetheless, it is important to remark that this study was performed in an academic medical center, a third level and referral hospital in Peru.

CONCLUSIONS

Tuberculosis is a worldwide condition whose drug-resistance patterns continue evolving. However, in our hospital, a southern Peru reference Center, most TB patients are still sensitive to first line drugs.

nly a small amount of MDR and XDR patients were found. Moreover, the most common clinical presentation was pulmonary followed by pleural tuberculosis. Nevertheless, a close follow-up of Mycobacterium tuberculosis-resistance patterns is crucial to prevent the spread of this infection. Monitoring of high-risk patients is required for optimal control because MDR and XDR tuberculosis is a serious public health issue around the world.

As this investigation was done during COVI-19 pandemic, we recommend carrying out some studies that consider pre- and post-COVID-19 pandemic information.

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