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EPIDEMIOLOGICAL AND BACTERIOLOGICAL PROFILES OF PATIENTS WITH MULTIDRUG-RESISTANT TUBERCULOSIS IN THE SOUTHERN REGION OF MOROCCO

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ABSTRACT

Multidrug-resistant tuberculosis (MDR-TB) is a serious public health problem especially in developing countries. Our aim is to determine the bacteriological epidemiological characteristics of MDR TB in Southern Region of Morocco. We conducted a retrospective and descriptive study of MDR-TB cases monitored in the Souss Massa region during the period from January 1, 2017 to December 31, 2021. The study variables were: age, sex, region of origin, period (years), type of tuberculosis, HIV status, and drug resistance. During the study period, 9,111 cases of tuberculosis of all forms were recorded in the Souss Massa region, of which 50 cases were confirmed to be multidrug-resistant. The MDR TB rate was 0.55% of which 10% were pre XDR. The average age of patients was 39 years. The age group most affected was 20-40 years (44%). A male predominance was noted (sex ratio of 3.08). The distribution of tuberculosis drug resistance cases in the different prefectures and provinces of the Souss Massa region was: TAROUDANNT 46%, INEZGANE 30%, AGADIR 10%, CHTOUKA AIT BAHA 8%, TIZNIT 4% and TATA 2%. The location of tuberculosis was pulmonary in 100% of cases and three patients had positive HIV serology. The prevalence of resistant TB has been increasing in recent years due to advances in molecular diagnostic tests offering results within hours.

KEYWORDS: Tuberculosis, multidrug resistance, Souss Massa, COVID.

INTRODUCTION

Tuberculosis is a real public health problem in the world. Until the emergence of the COVID 19 pandemic, tuberculosis was the leading cause of death due to a single infectious agent, ahead of HIV/AIDS [1]. The World Health Organization estimated the number of people with TB disease at 9.9 million in 2020, which equates to 127 cases per 100,000 populations.[1] Despite efforts to improve screening, diagnosis and access to treatment, the problem of tuberculosis is far from being controlled. It is complicated by three main events: the AIDS epidemic, the relative ineffectiveness of BCG (Calmette's bacillus and Guérin's bacillus) and the emergence of resistant or multi-resistant strains of Mycobacterium tuberculosis to TB drugs.[2]

Multidrug-resistant TB (MDR-TB) is a particularly dangerous form of the disease. It is defined by the WHO as resistance to the 2 main antibiotics, rifampicin and isoniazid.[3] The extension of resistance to the other two major classes of second-line anti-tuberculosis agents (fluoroquinolones, aminosides) defines ultra-resistance (XDR). Patients with resistance to isoniazid, rifampicin and fluoroquinolones or aminosides are defined as having pre-XDR TB.[4] The detection of drug resistance requires bacteriological confirmation by molecular biology tests, culture methods or sequencing technologies. Treatment of MDR-TB should consist of a course of second-line medication for at least 9 months and up to 20 months.[5]

The aim of this work is to determine the bacteriological epidemiological characteristics of MDR-TB in the Souss Massa region of Morocco.

MATERIALS AND METHODS

It is a retrospective and descriptive study. It concerned cases of tuberculosis in the Souss Massa region recorded in the database at the level of the Regional Directorate of Health and Social Protection, in the context of epidemiological surveillance of the National Tuberculosis Control Programme (PNLT), during the period from 1 January 2017 to 31 December 2021. All cases of pulmonary or extrapulmonary tuberculosis

confirmed by culture or approved rapid molecular diagnostic tests were included in the study.

The diagnosis of multi-resistance was made for all patients using the GeneXpert MTB/RIF test. It is a real-time polymerase chain reaction (PCR) based system that detects Mycobacterium tuberculosis DNA and mutations that confer resistance to RIF in less than 120 minutes from clinical samples.[6] Then the positive cultures of rifampicin-resistant patients underwent a resistance study to other anti-tuberculosis drugs by the MTBDRplus (Hain Lifescience) GenoType test which is a second-line molecular test containing probes specific to the M. tuberculosis complex, as well as probes for rifampicin-common mutations (RIF) and a subset of isoniazid-resistant (INH) mutations.[7]

The study variables were: age, sex, region of origin, period (years), type of tuberculosis, HIV status, and drug resistance.

The manuscript submitted to your journal has never been published before and is not being reviewed by other journals. It has been approved by all authors for publication in your journal, and the authors do not declare any conflict of interest. The patient data was used with strict confidentiality and is available for any inquiries you may have.

RESULTS

Between January 1, 2017 and December 31, 2021, 9,111 cases of tuberculosis of all forms were recorded in the Souss Massa region, of which 50 cases were confirmed to be multidrug-resistant. The MDR TB rate was 0.55%, of which 10% were pre-XDR (Table I).

The average age of patients was 39 years [10—67 years]. The age group (Figure 1) most affected was 20-40 years (44%) followed by 41-60 years (41%). A male predominance was noted (sex ratio of 3.08). The distribution of cases according to the prefectures and provinces of the region (Figure 2) was: 46% in the province of TAROUDANNT, 30% in the prefecture of Inezgane Aït Melloul, 10% in the prefecture of Agadir Ida Outanane, 8% in the province of Shtuka Ait Baha, 4% in the province of TIZNIT and 2% in the province of TATA.

The anatomical location of tuberculosis was pulmonary in 100% of cases and three patients had positive HIV serology.

Table I: Resistance rate by years of study.

Indicator	2017	2018	2019	2020	2021	Total
Number of cases	1910	1741	1898	1832	1730	9111
Situation of the MDR/XDR	7	8	13	14	8	50
MDR rate	0.36%	0.45%	0.68%	0.76%	0.46%	0.55%

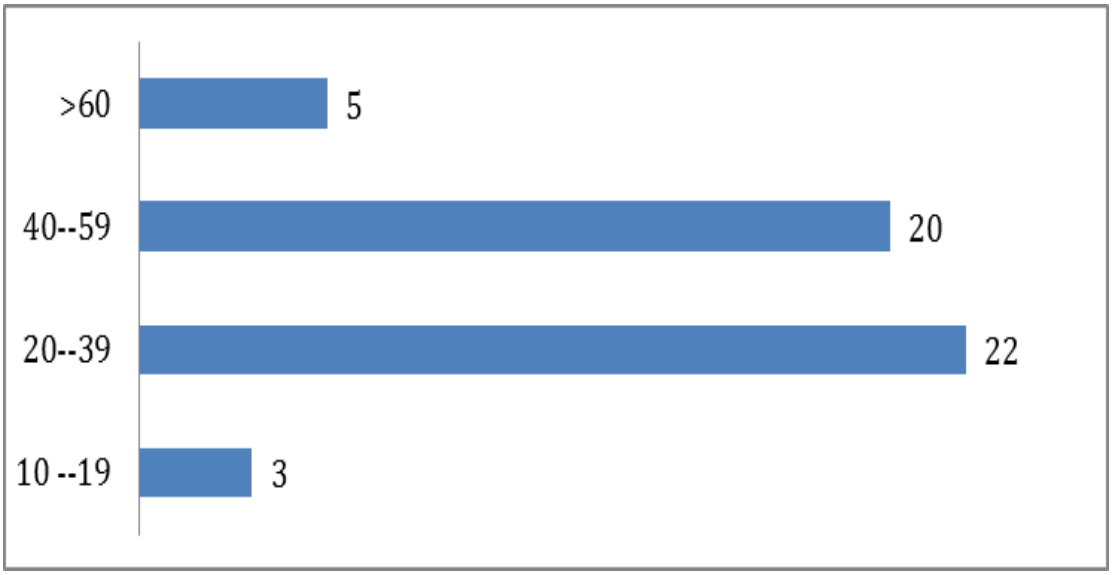

Figure 1: Distribution of MDR-TB cases by age group.

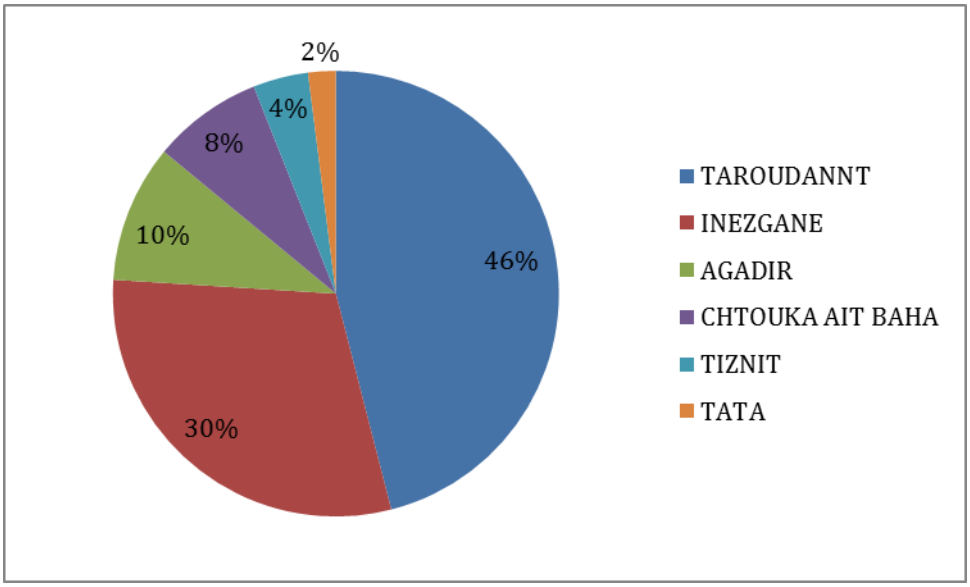

Figure 2: Distribution of MDR-TB cases by geographical origin.

DISCUSSION

The emergence of anti-TB drug resistance in many countries has become a major public health problem and an obstacle to effective TB control. The MDR-TB rate in our study was 0.55% in the Souss-Massa region of which 10% of cases were pre-XDR.

Nationally, 37,263 cases of tuberculosis were recorded in 2021, of which 385 cases of MDR-TB and 39 XDR cases were reported in 2021, i.e. a rate of 1% of MDR-TB cases, 10% of which were XDR.[8]

Internationally, the WHO estimated that there are 630,000 cases of MDR-TB worldwide, or 5.3% of the total prevalent cases. Almost 60% of these cases are in India, China and the Russian Federation. It is estimated that 6% of these multi-resistant TB cases are actually ultra-resistant TB.[9]

In our study, MDR-TB affects young adults aged 20 and 40 with a rate of 44% and an average of 39 years, i.e. the economically productive age group in a precarious situation. Rabah et al. 's study in Tunisia shows results consistent with an average age of 40 years for MDR-TB cases. Also in Europe, according to Faustini et al. young people under the age of 45 are the most susceptible to MDR-TB.[10] The WHO confirms these results by reporting that the majority of those infected with MDR-TB are between 25 and 44 years of age.[11] These results can be explained by the frequency of tuberculosis in general in young adults. Several studies in developing countries show a prevalence of tuberculosis among young adults in active socioeconomic life, among them Morocco, which recorded a 64% rate of tuberculosis cases among people aged 15 to 45.[9,12,13]

Men are most affected by TB drug resistance in our study with a sex ratio of 3.08. Nationally, the male/female sex ratio is 1.5 of tuberculosis.[8] This male predominance is similar in several studies in the literature that showed ratios ranging from 1.5 to 8 in favor of men.[2,14] In contrast, in Western Europe, Faustini et al. found that male dominance was verified in eight studies but denied in three others. He therefore concluded that gender does not influence the acquisition of TB resistance.[10] The male predominance of MDR-TB can be explained by the predominance of tuberculosis in male individuals, so it can be explained by the assumption that women are more adherent to treatment and therefore less likely to receive inadequate treatment.

The majority of patients in our MDR-TB series came from the province of TAROUDANNT (46% of cases) and the prefecture of Inezgane Aït Melloul (30% of cases). These results are consistent with the distribution of tuberculosis cases; all cases combined in 2021 in the same study region at a rate of 56% recorded in Inezgane and Taroudant. This can be explained by the fact that the most affected areas are characterized by unfavourable and precarious living conditions (promiscuity and a low socioeconomic level), as well as the delay in consulting patients due to ignorance of the seriousness of this disease and the predominance of traditional medicinal culture in these areas. The area least affected by MDR-TB (2% of cases) was Tata. The same rate was recorded for tuberculosis in all cases in the Tata area. Tuberculosis cases may be underestimated due to limited access to care in this region.

The MDR-TB and HIV co-infection rate in our study was 6% (3/50 cases of MDR-TB) while the rate of all-case TB and HIV co-infection in the same region and over the same study period was 3% (280 HIV cases/ 9111 TB cases); it is noted that HIV TB co-infection may be a risk factor for developing TB drug resistance. Several authors agree that being HIV-positive is a factor in acquiring MDR-TB.[10,15] Others deny the influence of serological status on the resurgence of this event.[2,16,17]

Regarding the evolution of multidrug-resistant tuberculosis cases during the COVID pandemic, we note that the number of recorded cases remains stable in 2020 and strongly decreased in 2021 compared to the case recorded in 2019. This can be explained by the decrease in the number of tuberculosis cases, all cases combined, reported mainly in 2021 in this region. This decrease in TB case reports during the COVID pandemic is likely due to a decline in the ability of health systems to continue service delivery, lower willingness and ability to seek care in situations of confinement and travel restrictions, concerns about risks to health care facilities during a pandemic, and stigma induced by the similarity of TB and COVID 19 symptoms.[1] Internationally, COVID had a notable impact on the drop in the number of newly diagnosed and reported TB cases worldwide. This number has decreased from 7.1 million in 2019 to 5.8 million in 2020, a decrease of 18%, a return to the 2012 level and far below the estimated 10 million people who developed TB in 2020. Sixteen countries recorded 93% of this decline, with India, Indonesia and the Philippines being the worst affected countries.[1] The COVID-19 pandemic has slowed down the expected progress towards eliminating TB by 2030. There is an urgent need for action to mitigate or reverse these impacts by restoring access to essential TB care services.

DECLARATIONS

- **Ethics approval and consent to participate**: Not applicable.
- **Consent for publication**: We affirm that this manuscript has not been previously disseminated and is not currently under review by any other publication. Furthermore, it has garnered unanimous approval from all authors for submission to your journal, with no conflicts of interest to declare.
- **Availability of data and materials**: The data analyzed in this article will be available upon request.
- **Competing interests**: The authors declare that they have no competing interests as defined by Springer, or any other interests that might be perceived to influence the results and/or discussion reported in this paper.
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Authors' contributions

- **N.E.** is the principal author of this article. She wrote the entire manuscript, supervised the organization of the content, and coordinated the finalization of the article.
- **A.L.** contributed to the collection of epidemiological data on tuberculosis, leveraging his position at the Regional Directorate of Health and Social Protection, where the data is centralized.
- **A.G.** participated in the statistical analysis of the data, interpreted the results, and made significant contributions to the writing of the results section.
- **M.A.** initiated and designed the study, coordinated the efforts among the authors to ensure consistency in the manuscript, and contributed to the critical revision of the manuscript.
- **Z.L.** supervised the entire writing process, revising the various versions of the manuscript, and approved the final version for publication.

All authors have read and approved the final version of the manuscript.

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CONCLUSION

The emergence of multidrug-resistant TB has increased the threat to progress in TB control. Most studies emphasize that previous irregular treatment by poor adherence is the main risk factor found, hence the need for increased vigilance with regard to the monitoring of cases under treatment. Other risk factors such as age, male gender and immunosuppression have been reported by several studies. Late diagnosis of TB drug resistance increases the risk of contamination of the environment and health workers. The control of MDR TB remains essentially preventive. It is based on real preventive strategies planned according to local data and updated in each region.

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