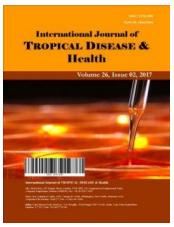

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# Epidemiological Profile of Tuberculosis and Investigation of Some Risk Factors in the Province of Larache, Morocco (2000-2012)

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Authors AS and AA collected the data, designed the study, wrote the protocol. Authors NAO and SEK wrote the first draft of the manuscript. Author HJ managed the literature searches. Author AQ managed the analyses of the study. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aim:** Tuberculosis (TB) remains a topical health issue all over the world. The present work aims to bring out the epidemiological profile of TB and to investigate some risk factors associated with this pathology in the province of Larache, Morocco.
**Methodology:** It consists in a retrospective study based on 7671 cases of tuberculosis, all forms combined, reported to the Centre for Diagnosis and Treatment of Respiratory Diseases of Larache during a period of 13 years from January 2000 to December 2012.
**Results:** The results showed that pulmonary tuberculosis represents two thirds of all cases (58%), Pleural TB comes second and Ganglionic TB comes third with 18% and 12% respectively. Moreover, 45% of patients completed their treatment and 34% are cured (smear negative). We reported 89 cases of death during the period of study. The evolution of the annual rate of success knew a remarkable increase from 95.6% in 2000 to 98.4% in 2012.
On the other hand, we demonstrated that death occurs preferentially in older patients (55.9 ±19.7

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years old). Ganglionic and cerebral TB occur preferentially in younger patients (26.6 ± 17.7 years old) whereas urogenital and pericardial TB occur in older patients especially (45.7 ± 18.8 years old). As for localization, we found that patients suffering from pulmonary TB display a significantly higher risk of death compared to other patients (RR = 1.58; $CI_{95\%}$= 1.01 - 2.467). In contrast, the risk of death is significantly lower in patients with ganglionic TB (RR= 0.08; $CI_{95\%}$= 0.01- 0.56).
Furthermore, females present a significantly higher risk to contract ganglionic, peritoneo-intestinal and pericardial TB compared to males. In contrast, the risk of contracting pulmonary TB is almost two times higher in males compared to females.
**Conclusion:** In conclusion, much effort should be made to fight against tuberculosis in Morocco.

*Keywords: Tuberculosis; epidemiology; age; gender; localization; Morocco.*

## 1. INTRODUCTION

Tuberculosis (TB) remains a topical health issue all over the world despite the implementation of preventive means such as BCG vaccination (1921) and efficient therapies since 1950. Indeed, the WHO estimates at 10.4 million of people affected by TB in 2014 and 1.8 million of people who died from it [1].

All the countries are affected but most cases occur in Asia (55%) and Africa (30%), especially India and China that contain 35% of all TB cases. TB control could be achieved if each patient was diagnosed and treated quickly [2].

In Morocco, in 2015, there were 30,636 cases of all types of TB (28,955 new cases and 1,681 relapses), that makes an incidence of 89 per 100,000 inhabitants. The number of deaths due to TB in the same year was 656 [3].

Moreover, eradication of TB by 2030 is among health objectives the United Nations have put as priorities for the sustainable development.

In this context, the present study took place in the province of Larache located at the north of Morocco, during the period between 2000 and 2012. It had two objectives; the first is to bring out the epidemiological profile of TB, the second is to investigate some risk factors associated with this pathology. The results of the present work could contribute to the improvement of the application of the WHO Anti-Tuberculosis Program and to a better control of this contagious disease in this province.

## 2. MATERIALS AND METHODS

The present work covers the province of Larache, located in the region of "Tanger-Tétouan-Al Hoceima" in north of Morocco, whose population came close to 481,000 inhabitants in 2000 and became about 494,000 inhabitants in 2012. This was a retrospective study based on 7671 cases of tuberculosis, all forms combined, reported to the Centre for Diagnosis and Treatment of Respiratory Diseases (CDTRD) of Larache during a period of 13 years from January 2000 to December 2012.

In fact, patients go for the first consultation to the provincial hospital of Larache, the hospital of Ksar El Kbir, the health centers, the public and private pulmonologists and the general practitioners in this province. Those suspected of having TB are directed towards the provincial CDTRD for microbiological analyses in order to confirm the presence or absence of TB. Subsequently, TB patients undergo treatment and are followed up during the full course of treatment period in the CDTRD.

All the details of reported cases (e.g. age, gender, affected organ, radiological and clinical examination findings, treatment and follow-up) are stored in individual records of patient treatment and in a register in the CDTRD.

The variables we included in our study were gender, age, localization (affected organ), evolution, admission year and the season.

The population data used for the calculation of incidence rates originated from the estimations of the High Commissioner for Planning on a provincial level. The rate of incidence was obtained by multiplying the number of cases by 100,000 and dividing by the population of the province.

The specific lethality for each age group was obtained by dividing the number of deaths among this age group by the number of cases in the same age group.

In order to compare numbers between different groups, *chi-square test* was used with an error risk consented to 5%. Furthermore, *Relative Risk* (RR) was used in order to investigate the association between death and localization, and gender and localization. The test value is considered significant when the confidence interval (CI) does not contain the value 1.

On the other hand, *One Factor Analysis of Variance* (Anova) was used in order to analyze the relation between age and localization. Indeed, if the Anova test is statistically significant, that means that TB localization depends on the age of patients. In this case, an additional analysis, called *means multiple comparison* is applied to distinguish localizations' groups with statistically different age, i.e. patients with localizations belonging to the same group are statistically the same age, whereas patients with localizations belonging to different groups are not the same age.

The same statistical method was used to investigate the relation between age and TB evolution.

## 3. RESULTS

Among the 7671 cases of TB studied, 4757 were men (62%) while 2914 were women (38%). The difference was statistically significant ($\chi^2$=442.8; p<0.001), the sex-ratio was 1.63.

The annual incidence of tuberculosis decreased slightly between 2000 and 2004, from 130 to 102 cases per 100,000 inhabitants, and then it increased gradually to reach its maximum, which is 139 per 100,000 inhabitants, in 2012.

Similarly, the study of annual changes in incidence by gender showed that TB incidence remained much higher in men than in women throughout the study period. In fact, it went from 131cases per 100,000 in 2004 to 172 in 2012 among men and from 74 cases per 100,000 in 2004 to 107 in 2011 among women (Fig. 1).

Moreover, the average age of TB patients was 33.93 ± 17.97 years, while the median age was 28 years. In men, the average age was 33.6 ± 17.1 years while 34.4 ± 19.2 in women, the gender difference was statistically not significant (F= 3.6 ; p>0.05).

The repartition by age groups showed a predominance of cases who were between 15 and 24 years (30.4%) followed by those who were between 25 and 34 years and those who were between 35 and 44 years respectively (Fig. 2). That showed that the disease had affected preferentially the most active population.

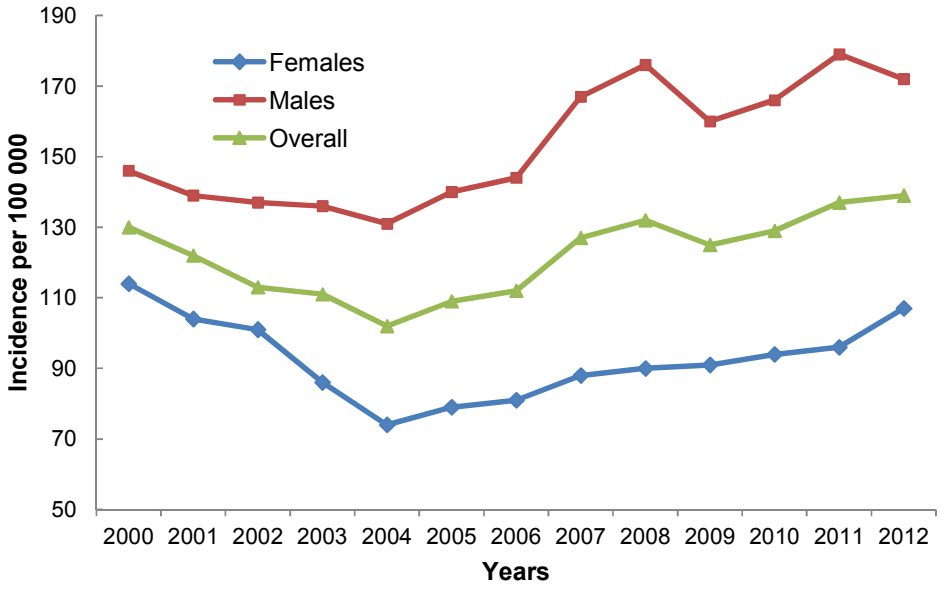


**Fig. 1. Evolution of the annual incidence of TB from 2000 to 2012**

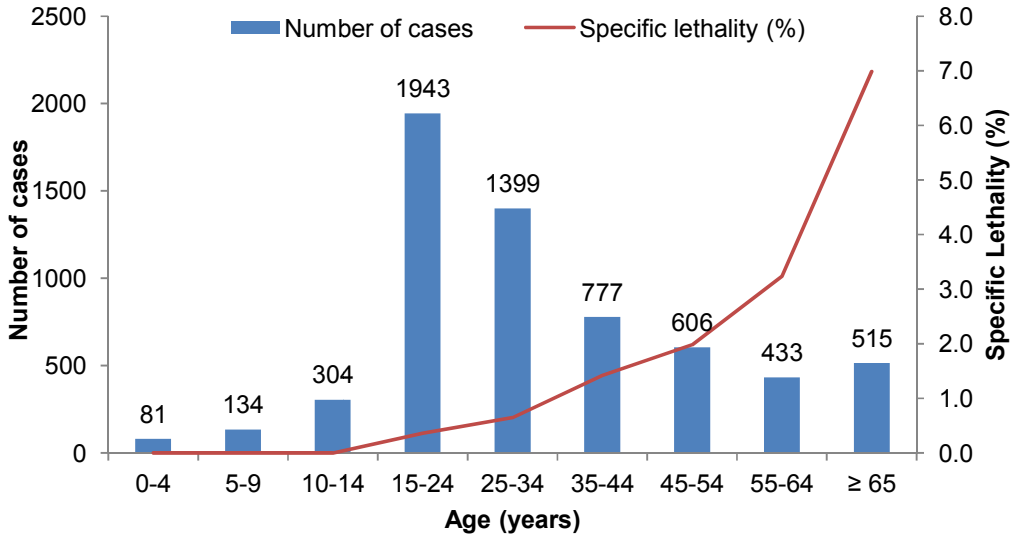


**Fig. 2. Repartition of TB cases number and specific lethality by age group**

On the other hand, the specific lethality became important after the age of 45 years. It reached a maximum value of 7% in more than 65 years age group (Fig. 2).

The repartition of patients according to the type of tuberculosis showed that pulmonary tuberculosis represented two thirds of all cases (58%) while pleural TB was the second and ganglionic TB was the third with 18% and 12% respectively (Fig. 3). It should be noted that Smear Positive Pulmonary Tuberculosis (PTB+) represented 88% of pulmonary TB cases.

As far as season is concerned, we found that the number of cases was higher during spring and summer with 2196 and 1940 cases respectively, compared to autumn and winter with 1851 and 1684 cases respectively. The difference between seasons was statistically significant ($\chi^2$=71.4; p<0.001).

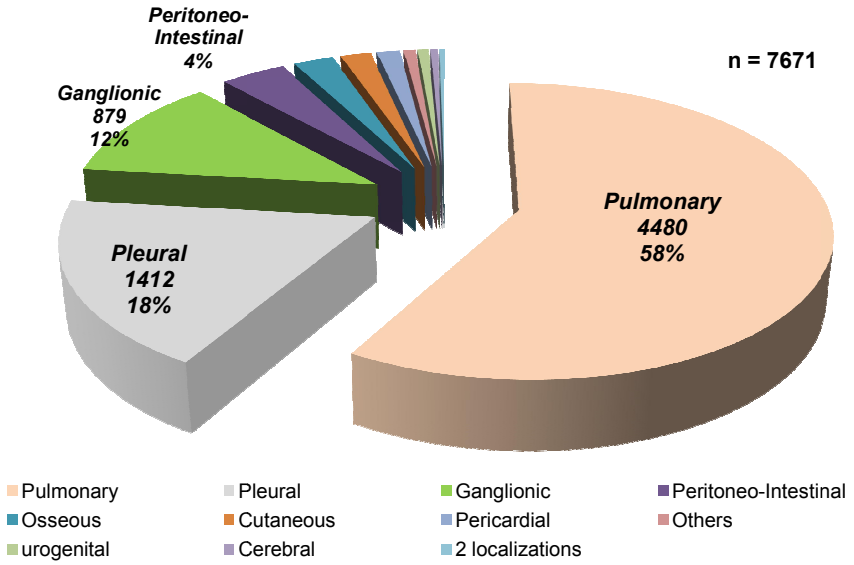


**Fig. 3. Repartition of tuberculosis cases according to the affected organ**

The evolution of patients was also investigated and the Fig. 4 shows that 45% of patients completed their treatment, with disappearance of all signs of the disease and improvement of the health (but without sputum bacilloscopy), and that 34% of patients were cured (sputum smear negative). In addition, 89 deaths were reported during the period of study. It should be noted that 14% of patients were lost to follow-up, so their evolution was unknown (Fig. 4).

Furthermore, the annual change according to the evolution of patients displayed a remarkable and steady increase of the annual rate of success (completed treatment and recovery) from 95.6% in 2000 to 98.4% in 2012.

As for the impact of age on the evolution of patients, the *one factor Anova* revealed a significant association ($F=54.2$; $p<0.001$). This means that the evolution depends on the age of the patient. The means comparison method led to three groups of evolution according to the age (Fig. 5).

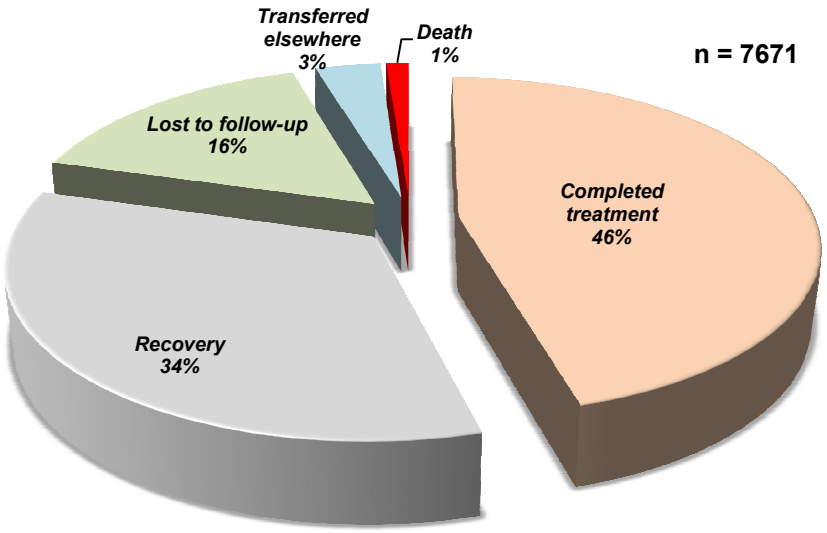


**Fig. 4. Repartition of tuberculosis cases according to the evolution**

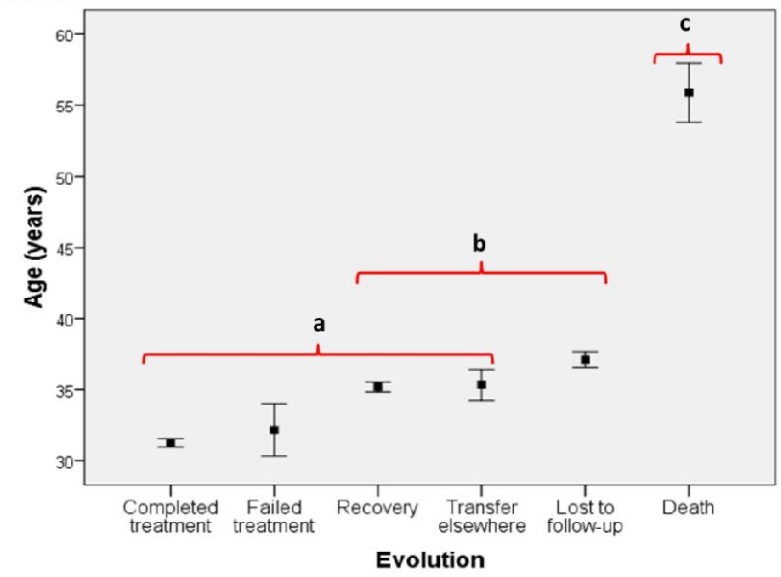


**Fig. 5. Repartition of means of age according to the evolution**

Indeed, the Fig. 5 shows that death occurs preferentially in older patients (c), the average age of dead patients was 55.9 ±19.7 years.

On the other hand, we investigated the implication of age in the repartition of TB localizations using one factor Anova. The results displayed a statistically significant relation between TB localization and the patient age ($F=46.6$; $p<0.001$). The means comparison method led to seven groups of localizations according to the age (Fig. 6).

The results of Fig. 6 implied that ganglionic and cerebral TB occur preferentially in the younger patients (a), with an average age of 26.6 ± 17.7 years, whereas urogenital and pericardial TB occur in the older patients especially, with an average age of 45.7 ± 18.8 years.

So as to study the association between TB localization and death, we calculated the relative risk of death for each localization (Table 1). The results showed that patients suffering from pulmonary TB displayed a significantly higher risk of death compared to other patients (RR= 1.58; $CI_{95\%}$= 1.01 – 2.467). In contrast, the risk of death was significantly lower in patients with ganglionic TB (RR= 0.08; $CI_{95\%}$= 0.01- 0.56).

Furthermore, we calculated the relative risk of gender (females being exposed) for each TB localization in order to analyze the association between the gender of patients and the TB localization (Table 2). The results showed that women presented a significantly higher risk to contract ganglionic, peritoneo-intestinal and pericardial TB compared to men with respective risks of 2.49, 2.29 and 1.55. In contrast, the risk of contracting pulmonary TB was almost two times higher in men compared to women (Table 2).

**Table 1. Repartition of relative risks (RR) of death according to the localization**

| Localizations | RR (Dead exposed) | 95% confidence interval | |
|---|---|---|---|
| Pulmonary | 1.579* | 1.011 | 2.467 |
| Ganglionic | 0.078* | 0.011 | 0.562 |
| Cerebral | 22.490 | 0.401 | 3.004 |
| Cutaneous | 1.019* | 1.015 | 1.022 |
| Osseous | 1.279 | 0.400 | 4.088 |
| Peritoneo-intestinal | 1.399 | 0.563 | 3.480 |
| Urogenital | 1.008* | 1.005 | 1.010 |
| Pericardial | 3.143 | 0.969 | 10.187 |
| Pleural | 0.880 | 0.503 | 1.538 |
| 2 Localizations | 1.003* | 1.002 | 1.005 |
| Others | 1.464 | 0.200 | 10.731 |

*The RR is statistically significant when the $CI_{95\%}$ does not include the value 1*

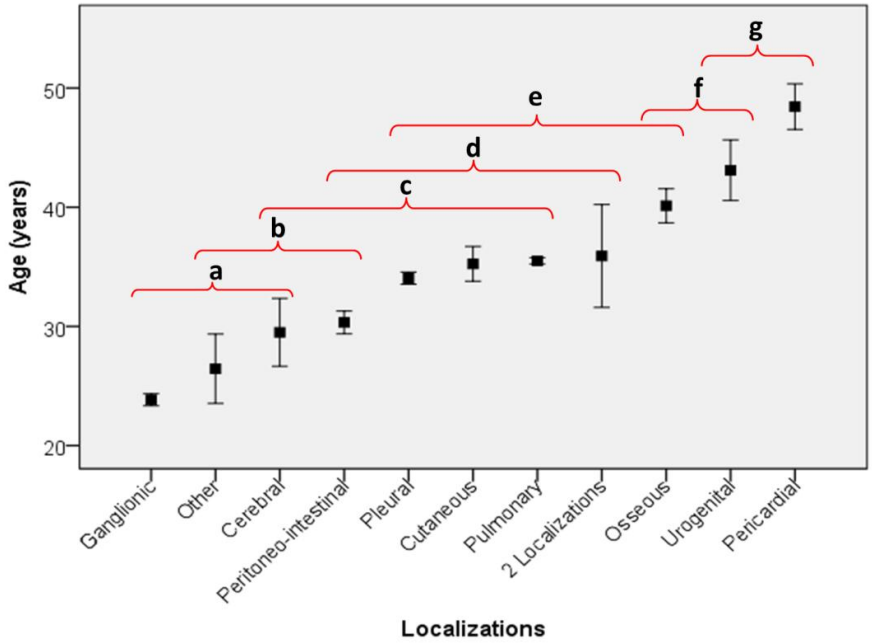


**Fig. 6. Repartition of means of age according to the localization**

**Table 2. Repartition of relative risks (RR) of gender according to the localization**

| Localizations | RR (Females exposed) | 95% confidence Interval | |
|---|---|---|---|
| Pulmonary | 0.534 | 0.487 | 0.587 |
| Peritoneo-intestinal | 2.489 | 1.972 | 3.142 |
| Ganglionic | 2.294 | 1.990 | 2.644 |
| Pericardial | 1.553 | 1.060 | 2.276 |
| Cerebral | 1.842 | 0.938 | 3.617 |
| Cutaneous | 1.110 | 0.790 | 1.559 |
| Osseous | 1.173 | 0.874 | 1.574 |
| Urogenital | 1.333 | 0.758 | 2.344 |
| Pleural | 1.010 | 0.897 | 1.137 |
| 2 Localizations | 5.577 | 2.055 | 15.133 |
| Others | 2.213 | 1.288 | 3.803 |

*The RR is statistically significant when the $CI_{95\%}$ does not include the value 1*

## 4. DISCUSSION

This work showed that males are by far the most affected by TB throughout the period of the study with a sex-ratio of 1.63 which remains lower than that found in south of Morocco (1.73) [4] and in Belgium (1.82) [5]. This result is comparable to that found by studies in France (1.63) [6]. Other studies reported a lower sex-ratio in favor of men, particularly in Madagascar (1.52) [7], in Switzerland (1.43) [8] in Congo (1.42) [9], in Tunisia (1.4) [10] and in Algeria (1.1) [11].

The fact that TB affects males more than females could be due to tobacco consumption which constitutes a risk factor for this disease and which is predominant in males [12,13].

Moreover, we found that median age of patients is 28 years, which is lower than that reported in south of Morocco [4], in Tunisia [10], in Cameroun [14], in Madagascar (40 years) [7], in France (44 years) [15] and in Belgium (37 years) [5]. The average age which is 34 years is similar to that found by other studies in south of Morocco [4] and in Congo [9].

The present study also showed that the most affected age group is 15-44 years with 66.4%, this result is in perfect accordance with those obtained in south of Morocco [4] and elsewhere [9,16,17].

As for TB localization, we showed that pulmonary TB is the most frequent with 58%. This percentage is higher than that found in south of Morocco, Tunisia and Congo [4,9,10] but considerably lower than that reported in France (73%), Madagascar (65.9%) and Netherland (62%) [6,7,18]. Moreover, the present study showed that 88% of pulmonary TB patients were TPM+ whereas another study carried out in Belgium reported 44% only, which indicates a greatly higher risk of contagiousness in Morocco [5].

Regarding the evolution of tuberculosis cases, this work showed a significant improvement in the success rate, which would be due to the effort of the nursing staff and/or the introduction of combined forms of medication. This success rate is prominent compared to that found in other countries [19-21]. In addition, we found that death occur preferentially in older patients which is likely due to their frail health. This result is reported by several studies [8,15].

On the other hand, we reported by the present study that patients with pulmonary TB display higher risk to die compared to other patients, which agrees with the results of other studies [9]. We also reported that males have higher risk to contract pulmonary TB compared to females. Indeed, gender aspects of TB have been a neglected research area, and little attention has been given to these aspects of TB control. However, certain studies demonstrated that males are biologically more vulnerable to pulmonary TB [22]. In addition, other studies, including in Bangladesh, Malawi and South Africa, argue that TB is more difficult to diagnose in women [23-25]. Some studies have found that women with pulmonary TB have a different immune response to TB than men [26] resulting in different symptoms, signs and outcomes, and that women with TB may not test positive on microscopic examination of the sputum [27]. One study found that TB lung lesions might not be as severe in women as in men, which can reduce the severity of symptoms in women and make diagnosis more difficult [28].

## 5. CONCLUSION

In conclusion, even if the TB management success rate has known an important increase in the province of Larache, the incidence of TB there remains high. Then, Moroccan health authorities should make more effort to the successful implementation of the national anti-tuberculosis strategy in this province, and particular attention should be paid to old patients, male patients and pulmonary TB patients.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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