ORIGINAL RESEARCH

Clinical and epidemiological evaluation of Tuberculosis in Albania during the period 2009-2018

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Abstract

Aim: To estimate the clinical and epidemiological pattern of Tuberculosis (TB) in Albania over the period 2009-2018.

Methods: A retrospective analysis of clinical and epidemiological data based on TB individual notification forms during the period 2009-2018.

Results: During the 10-years period, TB incidence increased from 14 to 15.5, but without a significant increasing trend. The total number of TB cases increased from 440 to 447. The proportion of extra-pulmonary TB decreased from 32% to 25% in 2018 (p=0.015), with and average mean change of 29 cases. Males prevail among TB cases and male-to-female ratio ranges from 2:1 to 3:1. Drug susceptibility testing (DST) was carried out depending on the availability of the reagents and there were 54%, 18% and 96% culture cases confirmed positive in 2009, 2014 and 2019, respectively. The overall treatment completion rate was 85% and 88.2% in 2009 and 2018, respectively. However, there was a significant drop in cured cases from 26% in 9.3%, whereas the percentage of deaths has increased from 0.5% in 4.1%. All treatment outcomes exhibited a significant change (p<0.001).

Conclusion: TB continues to be a public health challenge in Albania regardless of the seemingly generally stable epidemiological situation.

Keywords: drug resistance, epidemiology, incidence, treatment outcomes, tuberculosis.

Conflicts of interest: None declared.

Introduction

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS). TB affects more than 10 million people, causing 1.6 million deaths worldwide and about a quarter of the world's population is infected with *M. Tuberculosis* (1).

Geographically, most TB cases in 2018 were in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%) (2).

Drug-resistant TB continues to be a public health threat. In 2018, there were about half a million new cases of Rifampicin-resistant TB, of which 78% had multidrug-resistant TB (MDR) (3).

Despite the notable progress achieved in the fight against TB, countries still face a variety of challenges in reaching the goal to end the epidemic. Proper and fast diagnosis of TB is essential. The sooner a patient is diagnosed, the faster their treatment can begin, easing suffering and preventing further disease transmission.

Since 1994, the World Health Organization (WHO) has developed three main strategies for TB prevention and control: directly observed treatment short course (DOTS), Stop TB and End TB (4,5). Those strategies focused on case notification and monitoring of treatment outcome as the essential measures to evaluate the effectiveness of interventions and identify potential gaps in TB control (6). The efficacy and successful management of any national tuberculosis control program requires reliable clinical and bacteriological diagnosis. In order to provide these data, a national tuberculosis surveillance system was implemented based on individual data since 2008.

Trend in case notification rate, age group affected by TB, bacteriological resistance, treatment outcomes and clinical form are the main indicators used to evaluate the National TB Program. All these indicators were analysed in the current study (7-9). The aim of the present study was to estimate the clinical and epidemiological pattern of TB in Albania over the period 2009-2018.

Methods

The data were obtained from the register at the National Tuberculosis Control Program (NTBP) at the University Hospital of Lung Diseases "Shefqet Ndroqi" (SUSM), Tirana, Albania. Data on tuberculosis patients are recorded and reported individually and in accordance with the guidelines of the World Health Organization and the European TB Supervision Centre (6).

The data are collected and reported for each individual patient in accordance with the notification reporting form designed in 2001. The notification form includes detailed data on TB and other related factors. The study analyse the data reported, recorded and evaluated at NTBP and included general patient data, address, sex, occupation, age, diagnosis, direct sputum and culture results, as well as anti-tuberculosis drug sensitivity results and treatment outcomes.

Statistical analysis was performed in SPSS 25.0 (Statistical Package for Social Sciences). Categorical variables were presented in absolute numbers and corresponding percentages.

Arithmetic averages were calculated for all numerical variables. Differences between groups for discrete variables, nonparametric data, were performed using the Hi-square test. The values of $p \leq 0.05$ were considered

significant. Population estimates were based on 2002 census data, with extrapolation.
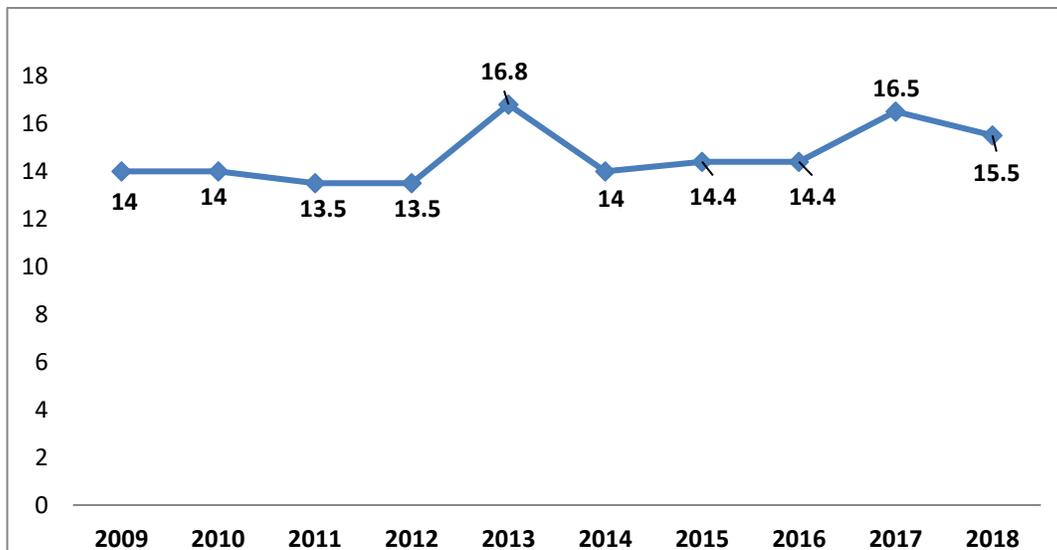
Results

Trends analysis of tuberculosis incidence
In the study period, the incidence rate of TB per 100,000 inhabitants/year went from 13.4 in 2009 to 14.2 in 2018 (Figure 1); there is no evidence of any significant linear trend in the incidence rate of tuberculosis in Albania in the past decade (P>0.05).

The mean percentage of annual changes of TB notification rate from 2009 to 2018 was 6.6%.

**Figure 1. TB incidence during the period 2009-2018**

Tuberculosis cases by site of disease
The number of reported cases of pulmonary TB in Albania varies by about 5.3% on average each
year, from 2009 to 2018. As a result, the proportion of total cases with extra pulmonary

decreased from 32% in 2009 to 25% in 2018 (p=0.015, difference between 2009 *vs* 2018).The average mean change is 29 cases, which shows a stable trend. Figure 2 shows the total number of cases related to site of disease.

Figure 2. Total cases with TB, pulmonary and extra-pulmonary cases
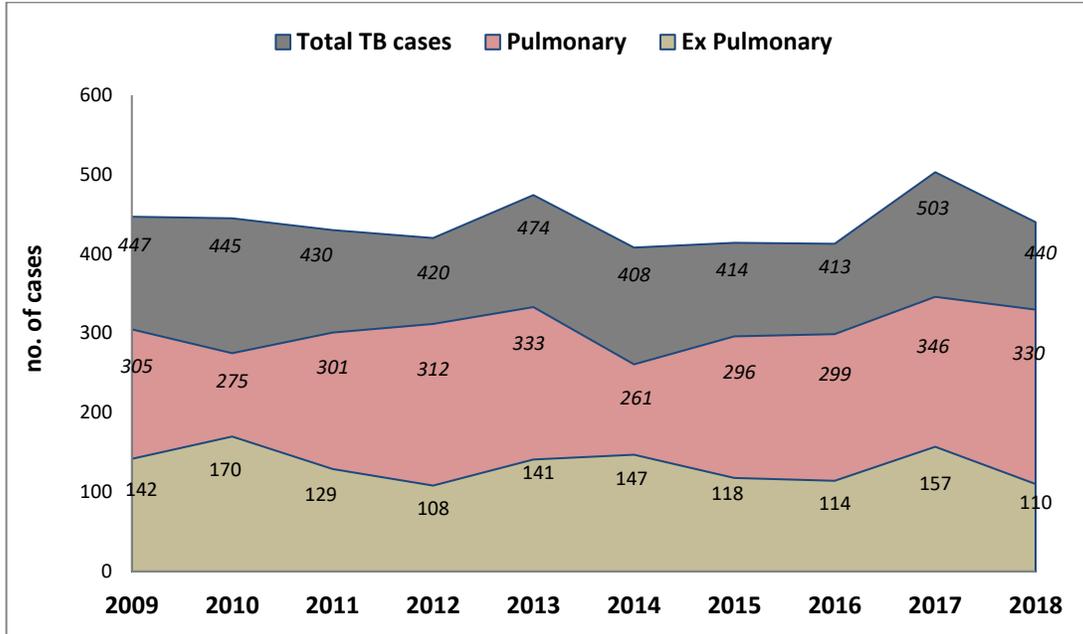
Sex and age distribution

Males predominate among TB cases in all study period and male: female ratio ranges from 2:1 to 3:1.

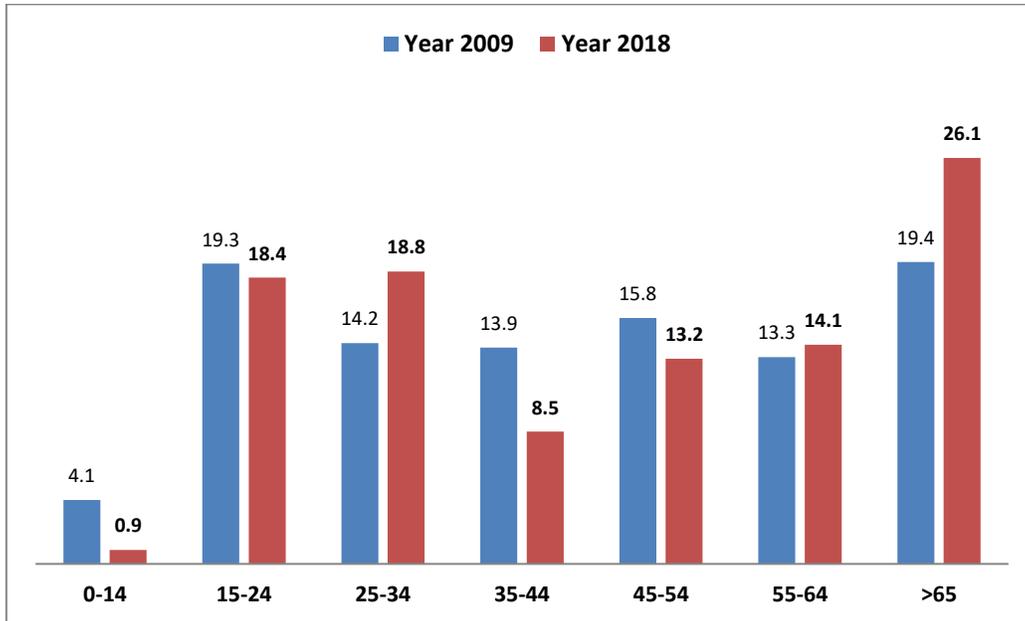Young adults (15-44) and the middle-aged (45-64) together represented 76.5% of all cases and respectively 47.4% and 29.1% in 2009. Young adults and the middle-aged represented 73% in 2018, but there was a significant increase in the age group>65 from 19.7% in 2009 to 26.1% in 2018(p=0.014).

Table 1. TB by age groups

	Years		
	2009	2018	
Age groups	N (%)	N (%)	P-value*
0-15	18 (4.03)	4 (0.91)	0.002
15-25	86 (19.24)	81 (18.41)	0.409
25-35	63 (14.09)	83 (18.86)	0.034
35-45	62 (13.87)	37 (8.41)	0.006
45-55	71 (15.88)	58 (13.18)	0.148
55-65	59 (13.20)	62 (14.09)	0.386
>65	88 (19.69)	115 (26.14)	0.014

*Chi-square test.

Figure 3. Distribution (in %) according to age groups

There was an increase in the age group 25-34 from 14.2% to 18.8% and in the age group over 65 from 19.4% to 26.1%, while there was a decrease in the age group 35-44 from13.9% to 8.5%. Children accounted respectively for 4.1% and 0.9% in 2009 and 2018.

Young adults (15-44) and the middle-aged (45-64) together represented 76.5% of all cases and respectively 47.4% and 29.1% in 2009. Young adults and the middle-aged represented 73% in 2018, but there was a significant increase in age group >65 in 2018(p=0.014).

Bacteriological confirmation and drug susceptibility testing

The proportion of bacteriologically confirmed cases remained high during the study period and there was not great variation annually in smear confirmation cases. Average mean change was 17 ± 13 cases per year, which shows a constant trend.

Drug susceptibility testing (DST) was carried out in a small proportion of pulmonary TB cases, only for 30% of cases in 2018 due to shortage of reagent. The number of cultures tested dropped from 201 in 2009 to 63 in 2018, but starting from 2013 the number of tests was reduced dramatically, and consequently the MDR data are not reliable for our country.

Table 2. Proportion of smear positive cases, MDR and number of drug susceptibility testing

Year	PTB	Smear positive	% of smear positive	MDR cases	DST
2009	305	192	63%	0	201
2010	275	165	60%	2	182
2011	301	190	63%	5	203
2012	312	206	66%	0	163
2013	333	212	64%	1	27
2014	261	175	67%	2	29
2015	296	209	71%	3	13
2016	299	206	69%	1	40
2017	346	210	61%	0	79
2018	330	208	63%	2	63

Treatment outcomes

The overall treatment success rate was 85% and 88.2% in 2009 and 2018, respectively. There is a significant drop in cured cases in 2009 from 26% to 9.3% in 2018. Also, the percentage of deaths increased from 0.5% to 4.1%. All treatment outcomes displayed a significant change (p<0.001).

Figure 4. Treatment outcomes (in percent)
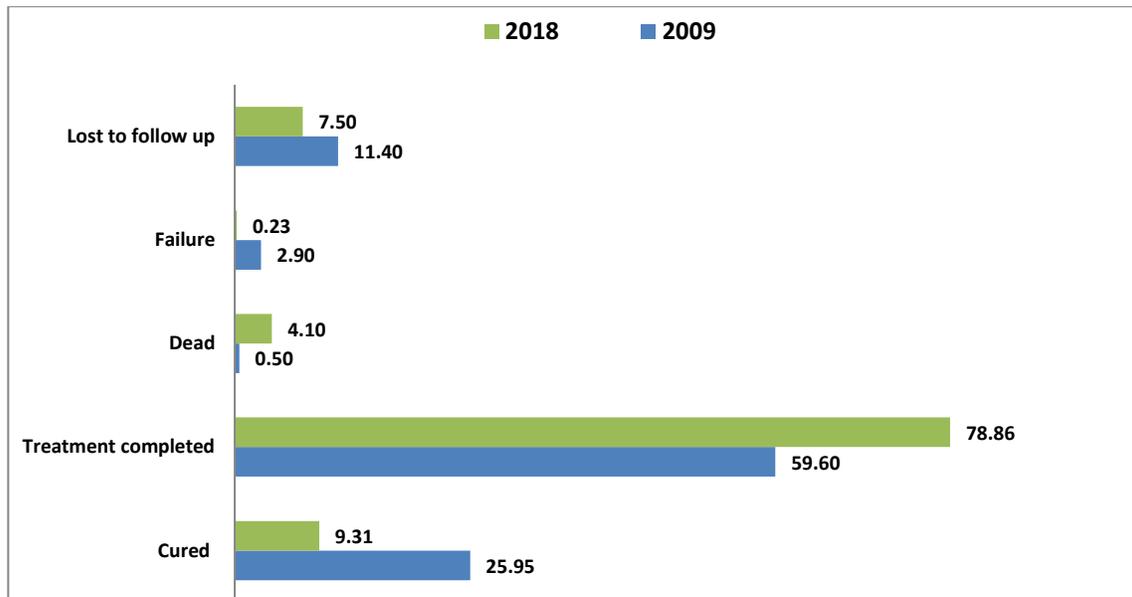
Discussion

The number of patients diagnosed with tuberculosis in the study period had a slight oscillation with an insignificant trend of increase in TB incidence. The incidence increased from 13.4% in 2008 to 15.3% in 2018. There was no evidence of a trend and a statistically significant change in the incidence rate over the study period. The incidence of TB appears to be more or less stable, but if we compare it with the neighbouring countries or other European countries, we notice that Albania is the only country in the region with increased TB incidence and a positive mean annual change (Table 3). There is a wide variation in TB incidence in the Balkan region from 4 (Greece) to 39 (Kosova) cases per 100,000 population.

Table 3. TB incidence in the Balkan region

Country	TB incidence 2009 (cases per 100,000)	TB incidence 2018	MACH* 2014-2018
Albania	13.4	15.3	2.0%
Kosova	60	39.2	-4.6%
Montenegro	19.2	13.4	-7.2%
North Macedonia	23.2	10.4	-6.6%
Serbia	17.2	9.4	-7.0%
Grecee	5.2	4	-4.1%

This indicates that stability of TB incidence over the years in Albania is not a good TB programme indicator and the National TB Programme has to analyse the cause of this stagnation. Furthermore, despite the stable incidence, the proportion of pulmonary TB cases increased to 75% in 2018, posing a serious risk of spreading cases with infectious TB and consequently increasing TB incidence in coming years.

The proportion of extra pulmonary TB continues to be high despite the significant decrease during the last years. The lowest proportion 25% was in 2018 and the higher was 38% in 2010. There is a stable trend in decreasing the proportion of extra pulmonary cases, although the proportion remains high compared to the region. The proportion of extra-pulmonary TB was 14% in Greece, 11% in Serbia, 12% in Monte Negro, 24% in North Macedonia and 29% in Kosovo in 2019. The variances in the reporting of extra-pulmonary TB may result from different diagnostic practices across the country in the region or epidemiological factors and the prevailing M. TB strains (10).

Males predominate among TB cases in all study period and male: female ratio ranges from 2:1 to 3:1.

There were twice as many males as females reported among all incident TB cases in European region, but large variation was observed for male predominance in the sex distribution of TB cases, ranging from almost an even distribution to over three times greater in Armenia and Albania. There are few publications on TB gender differences worldwide and it is not clear whether the differences in morbidity between the sexes are due to biological factors, socioeconomic context, or under diagnosis of TB in women who are

likely to have the least access to health care (11,12). In Albania, the disease of tuberculosis continues to be an important cause of morbidity in women.

The differences between the sexes have been constantly ascertained, but there is no study to assess these changes (13).

Bacteriological confirmation of TB diagnosis was high during the study period, over 60%, and there was not great variation annually in smear confirmation cases.

A high proportion of bacteriologically confirmed PTB cases might imply a delay in diagnosis and may reflect several gaps in diagnosis, such as lack of capacity by the program to accurately diagnose TB through bacteriological examination (14).

The proportion of bacteriologically confirmed cases among pulmonary TB varied considerably among the countries in the region from 45% in Kosovo to 95% in Serbia. The increasing proportion in other countries in the region is due to the implementation of the new technology in these countries, specifically GeneXpert. Thus, the proportion of bacteriologically confirmed cases before and after application of GeneXpert in Monte Negro was 59% and 86% respectively, in Bosnia and Herzegovina 42% and 74% and in North Macedonia 65% and 90%, respectively. Albania has installed last year two GeneXpert and we expect an increase in the bacteriological confirmation like in other neighbouring countries (15).

MDR-TB is a major issue in the Balkan region with the percentage of MDR-TB among all TB cases increasing over the last 10 years from 4.3% to 7.5% (16). Drug susceptibility testing was carried out in a small proportion of pulmonary TB cases (only for 30% of the cases) and we cannot analyse this important indicator, but the proportion of MDR resistance remains low (less than 3% over the study period). Albanian government must provide the necessary reagent for performing drug susceptibility test and evaluating the real situation of MDR in Albania.

Over the study period, the treatment success rates continued to improve, but the cure rate decreased significantly due to the lack of bacteriological confirmation during the follow up treatment phase. The number of deaths increased, but there are only few numbers to draw a valid statistical conclusion.

Conclusion

Despite the stagnation of the total number of TB cases during the study period, the epidemiological situation should not be assessed as stable, but deteriorating. MDR situation is unknown due to the shortage of reagent and pose a threat to TB control. The other epidemiological indicators like treatment outcomes and age group improved during the study period.

References

1. World Health Organization (WHO). Global tuberculosis report 2018. Geneva: WHO; 2018. Available from: https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?sequence=1&isAllowed=y (accessed: August 1, 2019).

2. World Health Organization. Moscow Declaration to End TB; First WHO global ministerial conference on ending TB in the sustainable development era: a multisectoral response. Geneva: World Health Organization and the Ministry of Health of the Russian Federation; 2017. Available from: https://www.who.int/tb/features_archive/Moscow_Declaration_to_End_TB_final_ENGLISH.pdf?ua=1(accessed: June 28, 2019).

3. World Health Organization.Thirteenth General Programme of Work, 2019–2023. Geneva: WHO; 2018. Available from: https://apps.who.int/iris/bitstream/handle/10665/324775/WHO-PRP-18.1-eng.pdf(accessed: August 1, 2019).

4. World Health Organization (WHO) and Stop TB Partnership. The Stop TB Strategy. Building on and enhancing DOTS to meet the TB-related millennium development goals. Geneva: WHO;2006.

5. World Health Organization (WHO). Implementing the end TB strategy: the essentials. Geneva: WHO; 2015.

6. European Centre for Disease Prevention and Control (ECDC). Tuberculosis surveillance and monitoring in Europe, 2017. Stockholm: ECDC; 2018.

7. Schwoebel V, Lambregts-van Weezenbeek CS, Moro ML, Drobniewski F, Hoffner SE, Raviglione MC, et al. Standardization of anti-tuberculosis drug resistance surveillance in Europe. Recommendations of a World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) Working Group. Eur Respir J 2000;16:364-71.

8. World Health Organization/International Union Against Tuberculosis and Lung Disease. Guidelines for surveillance of drug resistance in tuberculosis. Int J Tuberc Lung Dis 1998;2:72-89.

9. Veen J, Raviglione M, Rieder HL, Migliori GB, Graf P, Grzemska M, et al.Standardized tuberculosis treatment outcome monitoring in Europe.Eur Respir J 1998;12:505-10.

10. Uplekar M, Rangan S, Ogden J. Gender and Tuberculosis control: towards a strategy for research and action. Geneva: WHO; 1999:6-10

11. Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. Tuber Lung Dis1996;77:391-400.

12. Caws M, Thwaites G, Dunstan S, Hawn TR, Lan NT, Thuong NT, et al.The influence of host and bacterial genotype on the development of disseminated disease with Mycobacterium tuberculosis. PLoS Pathog 2008;4:e1000034.

13. Hafizi H, Dilika E, Bardhi D, Shehu E. The treatment outcomes for TB patients in Albania from 2001-2006.Gender differences in TB disease in Albania. AJMHS 2008;2.

14. Desikan P. Sputum smear microscopy in tuberculosis: is it still relevant? Indian J Med Res 2013;137:442-4.

15. Agrawal M, Bajaj A, Bhatia V, Dutt S. Comparative Study of GeneXpert with ZN Stain and Culture in Samples of Suspected Pulmonary Tuberculosis. J Clin Diagn Res 2016;10:9-12.

16. World Health Organization. Tuberculosis surveillance and monitoring in Europe 2020: 2018 data. WHO; 2020.