

The epidemiology of tuberculosis in Greece.

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ABSTRACT: Tuberculosis is the infection caused by *Mycobacterium tuberculosis* complex species that usually affects the lungs but can also occur as extrapulmonary or disseminated disease. According to the recently published report by the ECDC and WHO, the case notification rate in Greece was 6.0 cases per 100.000 population in 2008, while underreporting is an important problem for TB control.

Key Words: Tuberculosis, Epidemiology, Greece.

INTRODUCTION

Tuberculosis (TB) is the infection caused by *Mycobacterium tuberculosis* complex species that usually affects the lungs but can also occur as extrapulmonary or disseminated disease. TB in humans, is mainly caused by *M.tuberculosis*, (with a small fraction of disease caused by *M.bovis* and *M.africanum*)¹. This report presents the epidemiological data of TB in Greece during 2004-2010.

Tuberculosis remains one of the most devastating and widespread infections and a major public health issue world wide. It is estimated that in 2004 there were 8.9 million new cases of TB globally². One-third of the world's population has been infected with *Mycobacterium tuberculosis* and 2 million deaths are attributed to tuberculosis each year^{3,4}.

The WHO Global tuberculosis control report shows that the greatest burden of TB is in sub-Saharan Africa and Asia, with TB case notifications in the WHO European region constituting less than 10% of worldwide notifications.² In Europe a huge disparity in the rates of TB between the western and eastern countries exists and it appears to be worsening⁵. Both Ireland and UK had notification rates for all cases of <13/100.000 population. On the contrary, in Romania

and the Russian Federation rates are >100/100.000 while Kazakhstan reports a rate of 216/100.000. TB notifications in Central European countries are somewhere in between these two extremes⁶. Young children are the most likely to develop disease after infection and are significantly more likely to develop extra-pulmonary and severe disseminated disease than adults⁷. Moreover, according to the more recent data from ECDC/WHO surveillance report, a decreasing trend of mean annual rate between 2005-2010 is noticed. In 2010, 73.996 TB cases were reported by the 27 EU countries, Iceland and Norway, representing a decrease of 7% compared with 2009 and a mean five-year decline of 4,4% for the period 2006-2010. The overall notification rate in 2010 was 14,6 per 100.000 population and for the first time all EU/EEA countries have notification rates below 100 per 100.000 population⁸.

In June 2005, a new Stop TB Strategy was approved by the World Health Organization (WHO) aiming in drastically reducing the global burden of TB by 2015. What this strategy intends to accomplish is to cure at least 85% of sputum smear-positive cases and to reduce the TB prevalence and mortality by 50% compared to the rates in 1990, so that by 2050 it is not a public health problem anymore⁹.

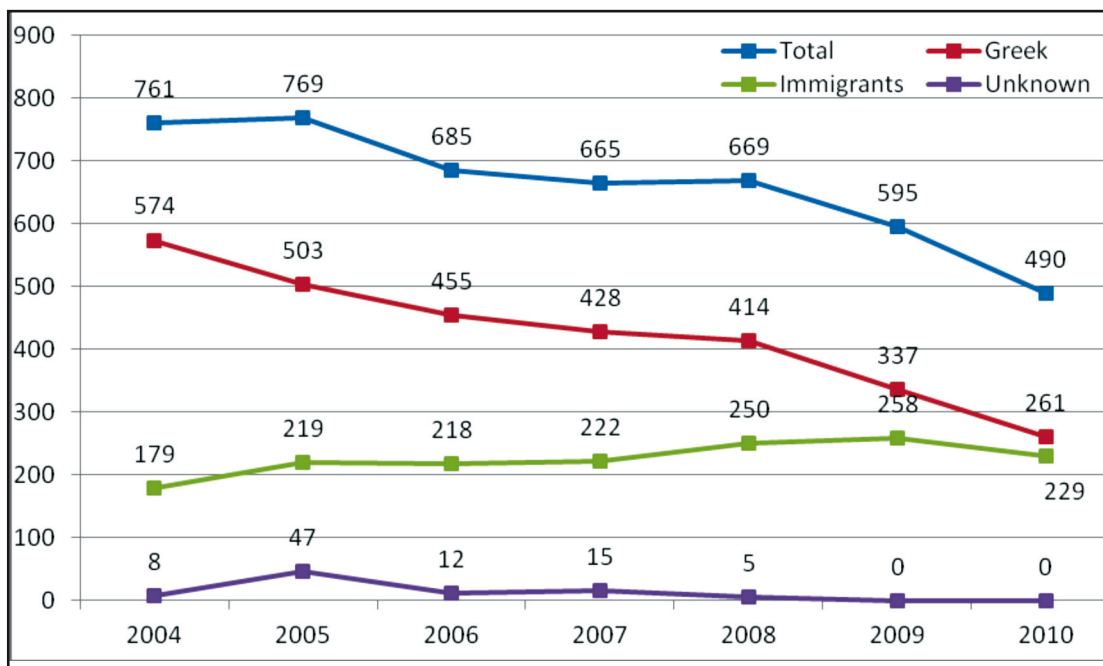


Figure 1. Frequency Distribution of reported cases of tuberculosis by nationality in Greece, 2004-2010 (www.keelpno.gr).

TB surveillance in Europe is co-ordinated by EuroTB, which is a network of national institutions in charge of TB surveillance in the 53 countries of the WHO European region. The organization collects information on TB case surveillance, drug resistance and treatment outcomes⁵.

In Greece the National Reference Laboratory for Mycobacteria (NRLM), sited in Sotiria Chest Disease Hospital in Athens, has provided a variety of reference services for both the public and the private healthcare sector in the field of mycobacterial disease¹⁰. Additionally, the Mandatory Notification System (MNS) of the Hellenic Centre for Diseases Control and Prevention (HCDCP) records all necessary data, so as to enable the epidemiological recording of the disease through data analysis and implement public health measures for the TB cases' immediate environment¹¹. The systematic surveillance of the disease is necessary to monitor the indicators set by WHO and European Centre for Disease Control (ECDC), in order to control TB on a European and international level.

According to the recently published report by the ECDC and WHO Regional Office for Europe, the case notification rate in Greece was 6.0 cases per 100.000 population in 2008, while only 37,7% of all reported

TB cases were confirmed by bacterial culture¹². Underreporting is an important problem for TB control in Greece, where various limitations in the national TB monitoring system exist¹³. Furthermore, migration from regions with high TB incidence (Iraq, Afghanistan, India, Africa etc.) possibly leads to further underestimation of the TB burden and facilitates further spread of the disease. Additionally, a 3-year period prospective study, conducted in Central Greece in 2008, reports that the incidence rate of Mycobacterium tuberculosis complex (MTC) infections of the lung was 5.7, 5.28 and 5.1 cases/100.000 in 2004, 2005 and 2006 respectively¹⁴.

An analysis of data collected annually through the MNS of the HCDCP for the period 2004 - 2010 shows that in our country an average of 600 cases is reported each year. In the country of 11 million people is 5,45/100.000. In addition there is a gradual reduction of notified cases, specifically from 761 in 2004 to 490 in 2010. The average incidence rate per 100.000 population by geographic region (NUTS-I, Nomenclature of Territorial Units for Statistics) was higher in Central Greece and Attica, while the lower incidence rate was recorded in the area of the Aegean Islands and Crete. With regard to the reported cases in Greeks

and the percentage of all reported cases, a decreasing trend is observed. On the contrary, the reported cases in immigrants are increasing (Figure 1). However, it should be noted that studies calculating the number of new TB cases through the consumption of anti-TB drugs, have shown significant underreporting of the disease¹⁵. Moreover, the exact rate of TB increase in the number of persons with foreign nationality, from 2004 to 2010 is not actually known. Hence it is rather impossible to determine exactly how much of the decrease trend of cases between 2004 and 2010 is due to underreporting and in what extent the increased trend in immigrants is due to a possible recent increase in their population¹⁵. Overall, during the period 2004-2010 the 64.1% of the total number of reported cases were Greeks, 34% were of foreign nationality, while in 1.9% of cases the nationality is not determined¹⁵. The results of a study, which evaluated the epidemiological and clinical features of childhood TB in the Greater Athens area in the last decade, showed that the average annual TB incidence was estimated at 5,37 per 100.000 for children aged <14 years. Time trend analysis for the 20-year period revealed a significant reduction in the total number of TB cases and in TB among children from low-incidence countries¹⁶.

Most TB cases in Greeks occurred in persons aged 65 and older, while most TB cases in foreigners occurred in those aged 25 to 34 years. The difference in the age distribution between Greeks and foreigners is consistent with the fact that the majority of immigrants in our country are people of working age. Regarding the type of the disease, the largest proportion (66.4%-74.9%) of cases was pulmonary, whereas the rate of the extra pulmonary locations was low. Additionally, cavities were observed on chest x-rays in 20.4% of the reported cases in Greeks and in 16.2% of cases occurring in foreign-born persons. The presence of cavities is important in the epidemiology of the disease since these cases are more contagious¹⁵. These data should be interpreted with caution, because there are indications of under-reporting.

Apart from the epidemiology of TB in general it is noteworthy that the percentage of cases due to resistant strains is increasing worldwide. According to WHO resistance to any of the anti-tuberculosis drugs has reached 20% in 2008 globally and was significantly higher in Eastern (48.8%) than Western Europe

(8.9%). Moreover, there appears to be an increase of multidrug-resistant TB (MDR-TB) - defined as TB resistant to at least isoniazid and rifampin - and of extensively drug-resistant TB (XDR-TB) - defined as disease caused by MDR strains that are also resistant to at least one fluoroquinolone and one or more injectable agents^{3,4}. MDR cases accounted for 5.3% in 2008 globally and for 22.6% and 1.5% in Eastern and Western Europe respectively. Recently totally drug-resistant TB (TDR-Tb) i.e. TB due to strains that are resistant to all first- and second-line agents has emerged¹⁷. In Greece resistance to first-line TB drugs remains higher than in most other countries in western Europe¹⁸. According to a study conducted in 2010 by the Greek National Reference Laboratory for Mycobacteria, RIF resistance was also higher in Greece (4%) compared with other western European countries, while MDR-TB was much higher in Kazakhstan (14,2%), Estonia (13,3%), Russia (12,5%), Latvia (10,8%), Lithuania (9,8%) and Georgia (7,6%) than in Greece (4%) and the rest Europe (median European MDR rate 1,0%)¹⁰.

The species of mycobacterium responsible for tuberculosis in Greece is mostly *M. tuberculosis*, while *M. bovis* is following¹⁹. It is also very interesting the fact that there have been cases in whom disease was caused by intravesical instillation of *M. bovis*-derived BCG vaccine strain^{20, 21}.

In conclusion, tuberculosis is one of the most serious infectious diseases, with incalculable financial impact on health systems all over the world. Even though, since 2004, the incidence of the disease has been reduced globally, the total number of deaths from tuberculosis and the percentage of resistant strains continue to increase. Additionally, in our country an important underreporting of the disease has been observed. Co-operation among all parties involved in the diagnosis, treatment, prevention and epidemiological surveillance of the disease, through implementation of national TB control programs, seems to be the only way to control the disease, both in Greece and internationally.

Νεότερα επιδημιολογικά δεδομένα της φυματίωσης στον ελλαδικό χώρο.

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ΠΕΡΙΛΗΨΗ: Φυματίωση ονομάζεται η λοίμωξη από είδη του *Mycobacterium tuberculosis* complex, που κατά κανόνα προσβάλλει τους πνεύμονες, αλλά μπορεί να εμφανιστεί και ως εξωπνευμονική ή γενικευμένη νόσος. Σύμφωνα με τα στοιχεία τόσο του ECDC όσο και του WHO, η επίπτωση της νόσου στην Ελλάδα το έτος 2008 ήταν 6,0 νέα κρούσματα ανά 100.000 πληθυσμού. Η ελλιπής αναφορά νέων κρουσμάτων αποτελεί πρόβλημα για τον έλεγχο της φυματίωσης στην Ελλάδα.

Λέξεις Κλειδιά: Φυματίωση, Επιδημιολογία, Ελλάδα.

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