Journal of Scientific Research & Reports
9(5): 1-7, 2016; Article no.JSRR.22247
ISSN: 2320-0227

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Trends in Tuberculosis/Human Immunodeficiency Virus Comorbidity, Latvia, 2012-2014

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Authors' contributions

This work was carried out in collaboration between all authors. Author JI designed the study and formed a group of patients. Authors SA and SJ wrote the protocol, author JV gathered statistical analysis, author EJ managed the literature searches, author HE wrote the first draft of the manuscript, Authors LA and RB managed the experimental process. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JSRR/2016/22247
Editor(s):
(1) Viroj Wiwanitkit, Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
Reviewers:
(1) Nelida Virginia Gomez, Buenos Aires University, Argentina.
(2) Ketan Vagholka, D.Y. Patil University School of Medicine, India.
(3) Shweta Sharma, Dr. Ram Manohar Lohia Hospital and PGIMER, New Delhi, India.
Complete Peer review History: http://sciencedomain.org/review-history/12224

Short Research Article

Received 24th September 2015
Accepted 27th October 2015
Published 10th November 2015

ABSTRACT

Aims: To describe the rates of HIV cases and Tuberculosis co-infection in Latvia from 2012 through 2014.
Methodology: This retrospective study was conducted by Riga Eastern Clinical Univesity Hospital(RECUH) Latvian Center of Infectology (LCI) HIV datebase. 2293 TB-patients were reported. 288 (12,6%) of all TB patients were HIV-infected. All patients had TB epidemiology during the last years and define variables predicting TB/HIV co-infection. In the same time between January 1, 2012 and December 31, 2014 were diagnosed tuberculosis with HIV co-infection. Temporal trends were estimated by Statistical (SPSS) version 22.0 for Windows.

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Results: In this study were reported 2 293 TB-patients from 2012 to 2014. 288 (12,6%) of all TB patients were HIV-infected. By years 2012-2013-2014, the rate of tuberculosis had been 43,0-38,3-31,8 per 100 000 population accordingly. Most cases of tuberculosis represented new disease (86%, n = 249). Most of patients had extra-pulmonary disease (54%, n = 87/162), closely followed by pulmonary TB alone (46%, n = 75/162). We identified a trend toward increase in tuberculosis prevalence and mortality.

Conclusion: Incidence rate of TB is positively correlated with HIV prevalence. Social inequality and the advent of AIDS are the major factors that aggravate the current situation of tuberculosis. We recommend for Latvian Ministry of Health use complete guidelines for the best management of HIV-infected patients and especially for those who co-infected TB, by targeting all health care personnel in a concerted educational outreach.

Keywords: TB; HIV; co-infection; AIDS.

1. INTRODUCTION

Tuberculosis (TB) is a public health problem worldwide [1] and remaining unresolved in the 21st century [2]. The increasing of tuberculosis is linked to human immunodeficiency virus (HIV) infection. It was estimated that 11% of all adults with tuberculosis in 2001 were co-infected with HIV or had AIDS.[3] Tuberculosis patients who are co-infected with HIV are at greater risk of mortality. The World Health Organization (WHO) estimated that 1.1 million (13%) of the 9.0 million people who developed TB worldwide were HIV-positive, globally there were still 360 000 deaths from HIV-associated TB in 2013, equivalent to 25% of all TB deaths (among HIV-negative and HIV-positive people) in 2013 and around 25% of the estimated 1.5 million deaths from HIV/AIDS [4].

The increase in the prevalence of HIV has serious implications for tuberculosis control programs, particularly in countries with high tuberculosis incidence. HIV has been a major factor responsible for increased mortality among TB co-infected patients [5]. Poverty is a major reason why tuberculosis remainsa public health problem. But since the 1980s, HIV has been a major factor contributing the return of tuberculosis in developed and developing countries alike [6,7]. For 2013, Latvia is listed 48th on the Human Development Index and as a high income country until 1 July 2014. [8,9] Latvia is one of 122 countries,that accounted for 95% of the global number of TB cases reported in 2013 [10] Although there are ways for the prevention and control of tuberculosis, the virus has modifyed the balance between human beings and Koch's bacillus, as well as having a marked effect on the epidemiology, natural history, and clinical evolution of tuberculosis. [11,12] Co-infection with tuberculosis in HIV results in higher mortality rates than in HIV infection alone [5-7]. There are increased risk of latent tuberculosis infection reactivation in HIV-infected and AIDS patients. In co-infected patients, mortality is commonly related to delayed diagnosis [13]. Not all countries achieved sustainable TB and HIV collaboration to describe the global burden of both diseases at a national scale.

1.1 Objective

To evaluate the impact of the HIV epidemic on tuberculosis in Latvia. We have analyzed the incidence and prevalence of tuberculosis with HIV co-infection, as well as of the associated mortality, identify variable associated with TB/HIV co-infection from 2012 through 2014 in Latvia.

2. DATA AND METHODS

2.1 Study Population

We have collected data (review of data on all cases) related to tuberculosis, with HIV co-infection registered from January 1, 2012 to December 31, 2014, in Latvia. Also, systematic study of HIV seroprevalence among tuberculosis patients in 2012 and 2014. We included HIV-infected patients with TB, aged 18 years old or older. All patients receiving care for TB were seen by chest specialist physicians. Direct smear examination with Ziehl-Neelsen (ZN) staining for the diagnosis of tuberculosis (TB), three direct sputum examinations were systematically performed for all patients who could produce a sputum sample, as well as a standard chest X-ray. Investigation for extra-pulmonary involvements is an integral part of the routine workup of patients with tuberculosis, and chest X-ray is systematically equested for all patients

with EPTB. The diagnosis of EPTB was based on radiological examinations; bacteriological, cytological, biochemical and histological examinations of fluids or pathological tissue samples collected from the involved organs; or strong clinical evidence consistent with active EPTB, followed by a clinician decision to treat with a full course of anti-tuberculosis chemotherapy.

Molecular techniques, which rapidly identify mycobacterial DNA in sputa, stool, BAL, urina have been performed too.

Statistical Package for Social Science (SPSS) version 22.0 for Windows [14]. This retrospective study was conducted by RAKUS LIC HIV Registries to describe TB/HIV epidemiology during the last years and define variables predicting TB/HIV co-infection.

2.2 Data Collection

This study was conducted through extensive analysis of existing TB and TB/HIV data at the LCI databases, reporting new cases, relapses, and reentries after treatment dropout (included medical records of hospitalized TB/HIV co-infected patients). The data was managed using Excel to create graphs depicting trends. TB and HIV diagnosis, treatment, testing, and management during this period were done according to the national guidelines.

2.3 Statistical Analysis

Dates were analysed using the Statistical Package for Social Science (SPSS) version 22.0 for Windows [14].

3. RESULTS

3.1 Detailed Estimate of Tuberculosis Incidence Stratified by HIV Status. Demographic, clinical, and laboratory profile of the study population

Between 2012 and 2014, 2 293 TB-patients were reported. 288 (12,6%) of all TB patients, were HIV-infected. Amoung our study cohort there were slightly more man than women 71,5% (n = 206). In 28% (n=79/281) cases TB diagnosis had been performed relatively in shorter time (< 1 year) after HIV infection diagnosed. In 72% (n=202/281) cases TB diagnosis had been performed in time > 1 year after HIV infection diagnosed, the mean duration of known HIV infection at the time of TB diagnosis was 7 years. TB diagnosis had been performed in the age group 30-59 predominantly. Most cases of tuberculosis represented new disease (86%, n = 249).

Most patients had pulmonary TB alone (PTB) (48%,n=85/176), followed by miliary TB (MTB) (including mixed forms of TB - both PTB and EPTB) (41%, n=71/176), closely followed by extra-pulmonary TB alone (EPTB) (11%, n = 20/176). Fig. 1. have shown details the distribution of the forms of tuberculosis in our patients. HIV-induced immunosuppression modifies the clinical presentation of TB, resulting in atypical signs and symptoms, that more frequent leads to extrapulmonary or miliary dissemination. Fig. 2. have shown the distribution of the forms of extra pulmonary tuberculosis in our patients. TB/HIV co-infected patients with extra-pulmonary TB had a higher proportion of infection in miliary sites than those with extra-pulmonary TB who were HIV-negative. Miliary tuberculosis (multifocal/disseminated TB) represents a second great part of all tuberculosis form. Amoung patients with miliary TB, disease involvs organs other than lungs - pleura, lymph node, abdomen, genito-urinary system, skin, joints and bones, meninges, etc. Pulmonary involvement was found in 58/71 (82%) patients with miliary TB, among this patients in addition 19/58 (34%) had pleural involvement and 15/58 (26%) patients had lymph node involvment. The median CD4 count were 189 cell/mm3 (min 1-max 1254). TB diagnosis had been performed by bacteriologycal examination as culture positive. In 61/288 (21%) cases was found multi-drug resistant strains. TB with HIV coinfection had worse treatment outcomes and mortality had been higher 37/288 (13%) than HIV-negative tuberculosis patient. To manage treatment of TB is more difficult in HIV-infected patients, particularly regarding to pharmacological interactions between rifampicin and protease inhibitors, or rifabutin and protease inhibitors. Finally, immune restoration induced by highly active anti-retroviral therapy (HAART) in developed countries may be responsible for a paradoxical worsening of TB manifestations. In 1991, several years before any health consequences of HIV were discernible in Latvia, the incidence of tuberculosis was 28,7 per 100 000. By years 2012-2013-2014, the rate of tuberculosis had been 43,0-38,3-31,8 per 100 000 respectively. Newly diagnosed cases of tuberculosis among HIV-infected persons by years 2012-2013-2014 was 110- 94 – 84 per 100 000 (Fig. 3).

3.2 Trends in Antiretroviral Therapy Uptake

We obtained dates of adults receiving antiretroviral therapy (ART) in Latvia during the year, from RECUH LCI HIV database. Regarding HIV treatment, ART had been prescribed in 163/288 (57%) patients. In years 2012-2013-2014 ART received 59%-51%-60% of HIV/TB coinfected patients respectively.

4. DISCUSSION

We have identified a trend toward the rise in tuberculosis prevalence and mortality. There was also a trend toward the rise in the incidence of tuberculosis/HIV co-infection, as well as in the rates of detection of new cases of active and latent tuberculosis. Tuberculosis (TB) incidence rates correlated positively with HIV incidence rates.

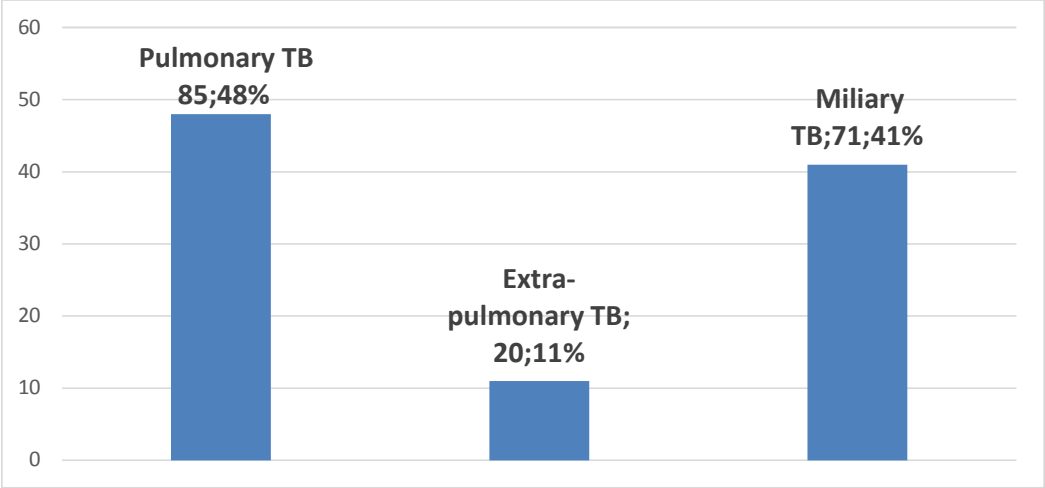

Fig. 1. Prevalence of the clinical form of tuberculosis amoung TB/HIV infected patients in Latvia from 2012 to 2014 (n=176)

Data are: clinical form;n; proportion (%)

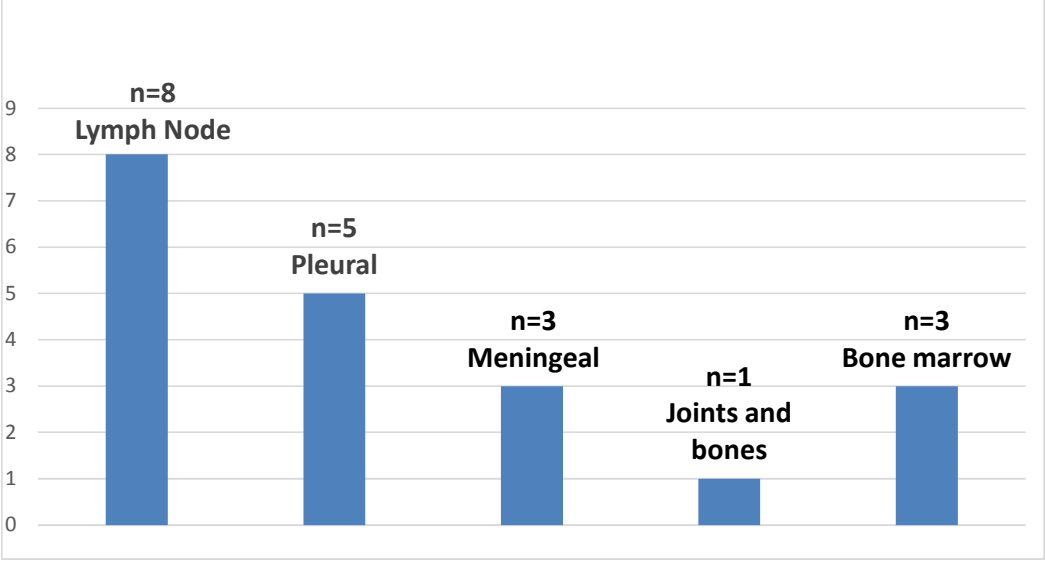

Fig. 2. Prevalence of the clinical forms of extra pulmonary TB among TB/HIV infected patients in Latvia from 2012 to 2014 (n=20)

Data are: clinical form;n

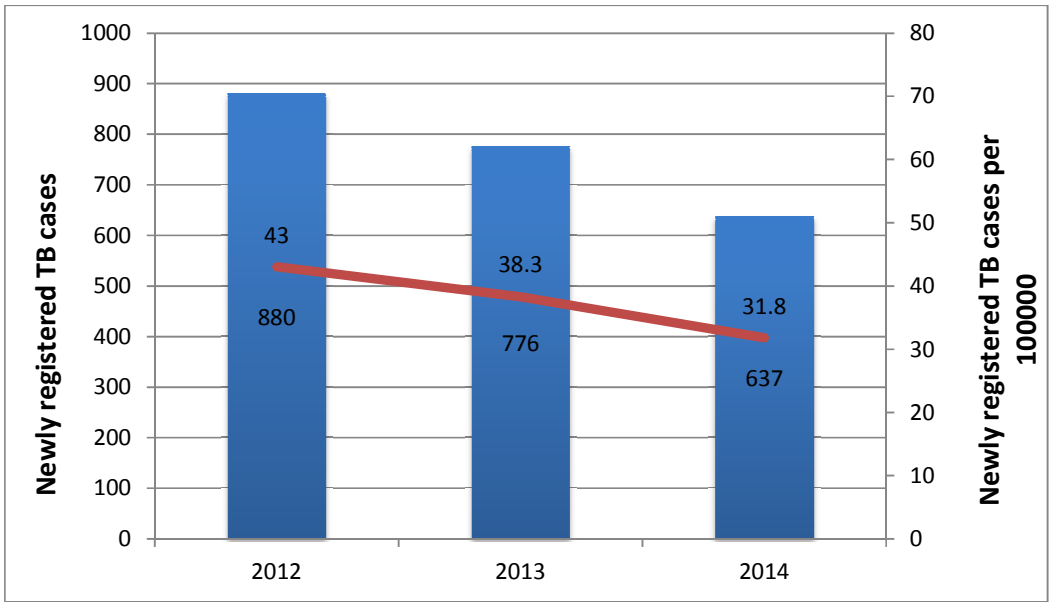

Fig. 3. Incidence of tuberculosis in Latvia 2012-2014

Ggender analize inequalities have been reported in TB case notification , with the male to female ratios ranging from 1.5 -2.2:1, but in contrast, lower male to female ratios were reported in Asia [15,16]. The male to female ratios in our study was 3.3:1. The decline in male to female ratio in our data could be due to access of health services, biological-, socio-economic- and cultural factors as well as poor man education and diagnosis delays [8].

Social inequality and the advent of AIDS are the major factors that aggravate the current situation of tuberculosis. Most TB/HIV co-infected patients were borned in high-burden city of Latvia. This study illustrates the importance of integrating TB with HIV in preventing treatment, which should be entered in other countries with high TB exidences, as it has a positive impact on disease control. The HIV pandemic presents a massive challenge to global TB control. World Health Organization (WHO), the Joint United Nations Programme on HIV/Acquired Immunodeficiency Syndrome (UNAIDS), the US Census Bureau, and the US Centers for Disease Control and Prevention published that in 2000 were regestrated 8.3 million new TB cases (137/100,000 population; range, 121/100,000-151/100,000). Tuberculosis prevalence rates were highest in the African Region (290/100,000 per year; range, 265/100,000-331/100,000). Nine percent (7%-12%) of all new TB cases in adults (aged 15-49 years) were attributable to HIV infection, but the proportion was much higher in African Region (31%) and some industrialized countries, notably the United States (26%). There were an estimated 1.8 million (1.6-2.2 million) deaths from TB, of which 12% (226 000) were attributable to HIV. Tuberculosis was the cause of 11% of all adult AIDS deaths.

Our study have showen the most frequent clinical presentation smear-positive pulmonary TB in patiens with TB and HIV coinfection. The majority of our cases represented newly diagnosed TB in an advanced state of immune deficiency, with low CD4 T-cell counts. We have founded low frequencies of AIDS with other (non-AIDS and non-TB) opportunistic infections.

The prevention of HIV and TB, the extension of WHO DOTS programs, and a focused effort to control HIV-related TB in areas of high HIV prevalence are matters of great urgency. The most common TB presentation was smear-positive pulmonary TB, closely followed by extra-pulmonary TB. Most of our TB cases were new cases; there were few other AIDS-related opportunistic diseases and few non-AIDS related comorbidities. An analysis of trends and differentials in case notifications and treatment outcomes of TB may help improve our understanding of the performance of TB and HIV co-infection control services. Recommendations of TB and HIV co-infection was suboptimal and needs to be improved.

5. CONCLUSIONS

We have reported that over the past 3 years, TB/HIV co-infected patients notification rates were invariable high, poor treatment outcomes were reduced. Understanding the epidemiology of TB in such settings is important for resource planning. In the light of this study, we urge clinicians to prescribe ART for all persons co-infected with TB and HIV, as per the most recently issued treatment guidelines. We further recommend that the Ministry of Health continue promoting and implementing guidelines for the best management of HIV-infected patients and especially for those with TB complicating HIV, by targeting all health care personnel in a concerted educational outreach.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/12224