

The Epidemiological and Clinical Aspect of Pulmonary Tuberculosis in Elderly: A Comparison with None-elderly in Yazd

Mohammad Shahradian^{1, 4}, Seyedeh Mahdiah Namayandeh^{2*}, Masuda Mojahed³,
Mohammad Ali Morowatisharifabad^{4, 1}, Vahid Barzegarpour⁵

1. Department of Ageing Health, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Research Center of Prevention and Epidemiology of Non-Communicable Disease, Department of Statistics and Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
3. Department of infectious diseases, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
4. Elderly Health Research Center, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
5. Department of Health Education, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

ARTICLE INFO

Original Article

Received: 16 Apr 2018

Accepted: 6 May 2018



Corresponding Author:

Seyedeh Mahdiah
Namayandeh
drnamayandeh@Gmail.com

ABSTRACT

Introduction: The nature of life course, with aging, triggers changes in the respiratory and immune system of the elderly, which increases the susceptibility to Tubercle Bacilli (TB) in the elderly. Clinical characteristics and the natural course of TB in older adults are different. This study aimed to compare the epidemiological and clinical features of pulmonary TB in elderly and non-elderly patients over 16 years old in Yazd city in a five-year period.

Methods: Within this historical cohort study, recorded of patient's data, including age, gender, clinical symptoms of the disease, history of treatment, drug resistance, and treatment results examined during 2012-2016.

Results: From 177 patients with pulmonary TB, who admitted to this study, 107 were 65 years and older (60.5%), and 70 were aged 16-64 (39.5%). Elderly experienced fever significantly fewer ($p = 0.02$), nonetheless they are more complaining about dyspnea ($p = 0.01$) and anorexia ($p = 0.04$) than non-elderly people. The incidence of drug complications was significantly higher among the elderly. Drug side effects, especially dermal itching ($p = 0.001$), are higher for older people. The number of drug resistance associated with larger mortality and recurrence in the elderly, which is not significant. Mantel-Haenszel evaluation showed that irrespective of drug resistance, the elderly died more than non-elderly ($OR = 1.37 \pm 0.88$) ($p = 0.85$).

Conclusion: Clinical symptoms, diagnostic criteria and treatment outcome and complications of TB in the elderly are significantly different from others. Elderly people are considerably more likely to anorexia than non-elderly. Fever is not common among elderly people. The incidence of drug complications was significantly higher among the elderly. Considering these differences will help us to diagnose and treat them more effectively.

Keywords: Epidemiology, Tuberculosis, Elderly, Treatment Outcome, Yazd

How to cite this paper:

Shahradian M, Namayandeh M, Mojahed M, Morowatisharifabad MA, Barzegarpour V. The Epidemiological and Clinical Aspect of Pulmonary Tuberculosis in Elderly: A Comparison with None-elderly in Yazd. J Community Health Research. 2018; 7(2): 119-126.

Copyright: ©2017 The Author(s); Published by Shahid Sadoughi University of Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Tuberculosis (TB) is one of the oldest known human diseases. TB appears in both pulmonary and extra-pulmonary forms. People get infected by inhaling the TB bacillus. After entrance into the lung, TB germ makes the primary lesion and can spread to other parts of the body through bloodstream, lymphatic vessels, and bronchi.

The World Health Organization (WHO) considered it a global health emergency ⁽¹⁾. Each case of TB with cavity can infect 20 people ⁽²⁾. According to WHO report, by the end of 2020, one billion people will develop a new infection with *Mycobacterium tuberculosis*, and 35 million TB patients will be died ⁽³⁾. In 2015, Iran according to the WHO report the incidence rate of tuberculosis was 16 cases per 100000 populations ⁽⁴⁾.

The population aged 60 or over is expected to go quickly double, however, growth in the number of older people is more rapidly in the least developed countries. Between 2015 and 2030, the projected 70 percent increase in the population aged 60 years or over is nearly identical with that projected in the other less developed countries. Thus, the challenges of age-related diseases are higher in these countries ⁽⁵⁾.

The results of general census of population and housing in 2011 in Iran shows that, about 2.8 percent (more than 6 million) of our population aged 60 years and over. Therefore, Iran is changing the demographic trend towards aging as other countries. It is expected that by 1406, the 60 years old or more of the population will reach 10 percent ⁽⁶⁾.

In general, non-behavioral risk factors of TB include age, homelessness, renal failure, diabetes, HIV infection, immunodeficiency, imprisonment, and behavioral risk factors, including malnutrition, alcohol, and smoking ^(7, 8). Risk factor is varying in societies with different climatic and economic conditions ⁽⁹⁻¹⁴⁾.

The nature of life course, with aging, triggers changes in the respiratory and immune system of the elderly, which increase the susceptibility to TB in the elderly. In the elderly, they are susceptible to increase to infectious diseases, especially

respiratory diseases ⁽¹⁵⁾. Aging has a significant effect on Inherent immunity and acquired active immunity ⁽¹⁶⁻¹⁸⁾, which can increase the risk of TB in this group. Improving the life expectancy and the number of elderly people increases the use of immunosuppressive drugs that can increase the incidence of pulmonary tuberculosis in the elderly. ⁽¹⁹⁾. Cellular immunity against disease through phagocytic cells and T- cells against the bacterium ⁽²⁰⁾. T-cell production lessened in the thymus gland in aging ^(21, 22). A large proportion of TB population occurs between the ages of 45 and 55, but in the West Pacific region, the eastern and southeastern Mediterranean, ascents are increasingly occurring in people over the age of 65 ⁽²³⁾. Recent studies show, there has been an increasing trend for the incidence of TB in people aged 65 and over in Asian countries. There are reports of upper incidence in the United States, especially in Central and South America ⁽¹³⁾ and North America ⁽²⁴⁾. Two or more Co-morbidity and their treatment in advanced age are associated with an increased risk of TB. Several comorbidities were common in the aging may increase the risk of active TB. Overall, compared to younger ones, aging can lead to changes in simple symptoms, diagnosis, treatment and drug resistance.

TB Control Program integrated into the healthcare services in Iran and has been active. Treatment of patients and care based on the DOTS (Directly Observed Treatment Short Course) strategy, the complete treatment of patients with a goal of 70% detection and 85% recovery after treatment ⁽²⁵⁾. This study aimed to compare the epidemiological and clinical characteristics of pulmonary TB in elderly and non-elderly in Yazd city during the years 2012-16.

Methods

The survey was a historical cohort type and had approved by the ethics committee of Yazd University of Medical Sciences (no.1395.159). Patients divided into 2 groups based on their age at diagnosis, as elderly (65 years and older) and non-elderly, including 2 subgroups of young and adults respectively 16-29 and 30-64 years old. The

patients selected according to the WHO protocol, which included the hilar lymphadenopathy, the sputum cultures result, and clinical symptoms⁽¹⁸⁾. Patient entered this study according to inclusion and exclusion criteria. Inclusion was: residence in Yazd city confirmed as TB patient by a laboratory or clinical diagnosis (sputum smear results, sputum culture, and positive bronchial lavage). Patients lived in other provinces or those who referred to Yazd for diagnosis or periodic monitoring of treatment excluded. Patients with clinical diagnosis of TB without a positive test excluded from this study. According to immune system development during the puberty and complexity of infectious diseases in children, patient under the age of 16 years old excluded from this study.

Based on the importance of TB and the implementations of the DOTS strategy, Nikpoor clinic selected as a referral center of TB in Yazd province. Patients' data is collected contain; age, sex, clinical signs of the disease, including fever, sweating, cough and sputum, anorexia, hemoptysis, dyspnea, weight loss chest pain, blindness, bronchoscopy and sputum culture, chest radiography and comorbidity such as diabetes, renal failure, chronic obstructive pulmonary disease and immune deficiency, HIV, cancer, history of TB, history of treatment, drug resistance. TB patient monitored at least four times in two

months and during maintenance four times in four months. The drug treatment response of pulmonary TB in a patient's case (including improved, died). This information collected and entered into SPSS 16 software. Chi-square and Mantel-Haenszel test analyzed the clinical signs and diagnosis and outcome.

Results

In this five-year period of study, we used census for including of TB patient. The studied population composed of 177 patients. The number of males was 95 (53.7%), and 82 (46.3%) were females. The mean age for the None-elderly 42.89 ± 12.20 (range from 18 to 63 years) and that of the elderly group was 76.99 ± 7.04 years (age range of 65-93 years).

The Nikpoor clinic is a referral center in Yazd province, the number of tuberculosis patients was censused and computed the incidence rate of positive-smear pulmonary TB, negative smear TB and the annual incidence of TB in hundred thousand people in a five-year period. From including of TB patient, 107 people were 65 years and old (incidence rate =3.05 in 100,000) and 70 patients aged 16-64 years (incidence rate =59.42 in 100,000). The incidence rate of TB was more significant in the elderly ($P < 0.0001$). The incidence rate is shown in Figure 1.

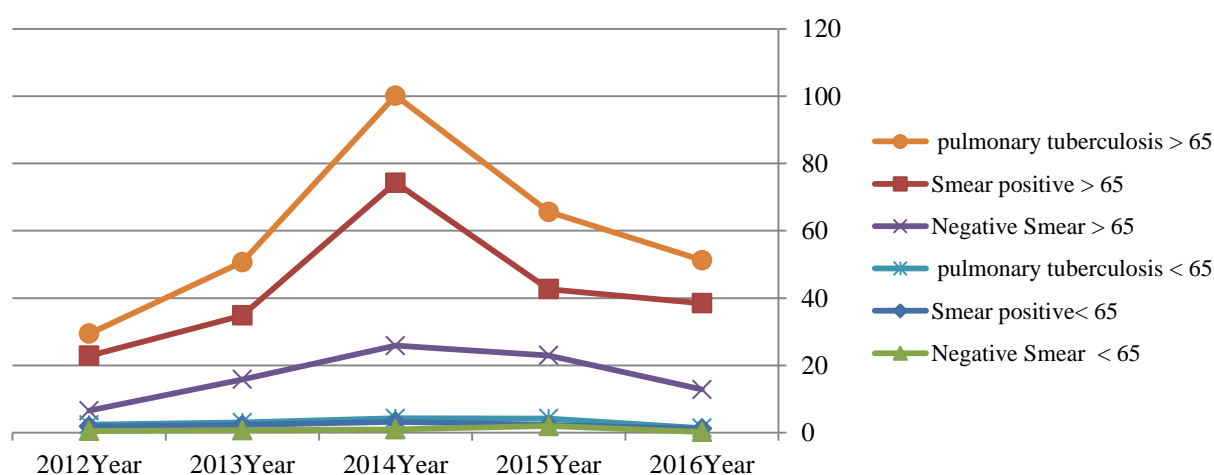


Figure 1. Trends in the incidence in each 100,000 persons of TB in elderly and non-elderly in Yazd province.

According to respiratory hospitalization before the diagnosis of TB, a higher percentage of elderly (72.9%) compared to the none-elderly group (47.1%) has been seen ($P < 0.001$).

The mean length of hospitalization in the elderly group (14.41 ± 8.88 days) was longer than the other group (10.32 ± 6.85 days) ($P < 0.01$).

Table 1 shows the history of TB treatment, although with increasing age the incidence of

recurrence was higher than those groups, but was not statistically significant.

Clinical symptoms were evaluated in 2 groups, and we found that they had chief complain of dyspnea ($p = 0.01$) and anorexia ($p = 0.04$) than non-elderly people. As it can be seen, the elderly fever was seen significantly less than the non-elderly ($p = 0.02$). (Table1).

Table 1. Shows the Study history of TB treatment and clinical symptoms between 2 groups of elderly and non-elderly patients.

Variables	Elderly		None-elderly		P value	
	N	%	N	%		
History of TB treatment	New case	92	86	61	87.2	0.270
	Relapse	11	10	4	5.7	
	Cure after failure	2	2	4	5.7	
	Resistant cases	2	2	1	1.4	
Clinical symptoms	Fever	23	21.50	26	37.14	0.026
	Sweating	8	7.48	7	10	0.372
	Cough	81	75.70	52	74.29	0.483
	Purulent sputum	31	28.97	22	31.43	0.426
	Hemoptysis	3	2.80	6	8.57	0.089
	Dyspnea	50	46.73	20	28.57	0.011
	Recent weight loss	48	44.86	33	47.14	0.442
	Chest pain	7	6.54	2	2.86	0.234
	Anorexia	20	18.69	6	8.57	0.047
	Weakness	15	14.02	6	8.57	0.203

Two main risk factors for pulmonary TB were smoking and opium addiction. These were significantly higher in none-elderly groups than another group ($p < 0.001$) ($P=0.03$), respectively.

The patients' side effect of the drug analyzed. The elderly drug side effects is significant ($p = 0.01$). The incidence of skin itching in the elderly is statistically significant ($p = 0.001$).

In 2 groups, there was no difference in the frequency of comorbidity, But In the none-elderly group, history of Corticosteroid use was significantly more than other ($p = 0.02$).

Furthermore, although the number of elderly people Who Non adherence with medication was slightly higher ($p > 0.05$).

At the end of the treatment, the rate of completed treatment in 2 groups was similar.

Mantel-Haenszel analysis showed that, regardless of drug resistance, older people died more than non-elderly ($OR = 1.37 \pm 0.88$) ($p = 0.85$). At the same time, the rate of Completed treatment in both groups has reached a strategic goal of more than 85% (Table 3).

Table 2. Shows evaluation of drug side effects in both elderly and none-elderly patients.

Drug side effect	elderly(%) n		None-elderly		P value	
	N	%	N	%		
Side effect	No one	72	67.3	55	78.6	0.014
	Moderate	2	1.9	5	7.1	
	Severe	33	30.8	10	14.3	
Nausea	10	9.3	7	10	0.540	
Burning feet	0	0	1	1.4	0.395	
Skin spot	5	4.7	0	0	0.078	
Itching	24	22.4	3	4.3	0.001	
Hearing loss	1	0.9	1	1.4	0.636	
Dizziness	6	5.6	2	2.9	0.320	
Jaundice	6	5.6	4	5.7	0.610	
Medicinal Hepatitis	3	2.8	5	7.1	0.161	
Visual impairment	1	0.9	0	0	0.605	
Renal failure	1	0.9	0	0	0.605	

Table 3. Shows the Comparison of the results of treatment of TB between 2 groups of elderly and non-elderly patients.

Outcome	Elderly		None-elderly		P value	
	N	%	N	%		
Remission	86	86	55	88.7	0.448	
Expired	TB related	10	10	5		8.1
	Other diseases	4	4	2		3.2

Discussion

The incidence of pulmonary tuberculosis in this study shows that tuberculosis occurs significantly among elderly. Clinical symptoms, diagnosis, and treatment of TB in the elderly are substantially different from others. Elderly people are significantly more likely to anorexia than non-elderly. Fever in the elderly isn't common. Other studies showed TB occurs in elderly people with nonspecific appearance⁽²⁶⁾. These differences can be explained through physiological changes that occur during aging.⁽²⁷⁾ The results of this study showed that young people have a significant fever and hemoptysis symptoms than older people. In similar studies, fever, hemoptysis^(26, 28), and nighttime sweats⁽²⁶⁾, cough^(26, 29) have been significantly observed in young adults. On the other hand, the elderly were less likely to have the fever and also had symptoms of dyspnea and anorexia^(28, 29) more than others. A study conducted in Iran by Talebi Taher et al. showed

that in patients admitted to Rasool Akram Hospital was associated with lower incidence of fever, sweating, hemoptysis, anorexia and chest pain in older patients.^(26, 27, 30) however, comparing the results from the study confirmed their result except chest pain, and anorexia was more common in Yazd elderly. The cause of the prevalence of hemoptysis in young patients, the higher prevalence of cavity lesions in young people than in the elderly can be pointed out. Increasing the intensity of inflammatory reactions in the alveolar wall of young people leads to capillary laceration alveolar, thus bleeding is more than the elderly⁽³¹⁾. Concerning the cause of decreasing the prevalence of fever and anorexia in elderly patients, it can be said that with age, the immune system's response decreases and inflammatory responses to microorganism's decrease and inflammatory mediators such as IL-6 and TNF- α Cause less fever and other inflammatory appearance⁽³²⁾. The results from this study and

other studies indicated that the elderly significantly increased the prevalence of dyspnea⁽²⁷⁾ In relation to the risk factors associated with TB, a study done by Jeon, diabetes increased the risk of active TB by about three-fold (relative risk = 3.11, 95%) (CI :2.27-4.26) in all age groups. One reason for the high rate of TB in the elderly be increased the prevalence of diabetes⁽³³⁾. Furthermore, the study was similar to the underlying disease, such as diabetes mellitus, and renal failure^(27, 30). Although these two diseases were more frequent in Yazd's elderly but not significant. The study by Van Den Brande. In Belgium also showed a significant increase in smoking in young people⁽²⁹⁾. In a study by Maurya, there was a significant relationship between smoking and TB⁽¹⁶⁾. The study by Brode on individuals with the rheumatoid disease has shown that the use of immunosuppressive drugs increases the risk of Mycobacterium infection⁽³⁴⁾. Among anti - TNF - mediated immunosuppressive therapies, increases particularly the risk of active TB⁽³⁴⁻³⁶⁾. Corticosteroids (oral prednisolone > 7.5 mg/day) in other diseases are also an independent risk factor for active TB^(37, 38). In another study, the use of suppressor drugs was more closely observed in the elderly group⁽²⁹⁾. The results from this study, similar to the study by Yee and Schaberg, showed that more side effects had been

observed in the elderly^(28, 39, 40). As seen in this study, the elderly is almost three times as likely to develop the Sid effect⁽⁴¹⁾. In this study, the recovery rate (87%) has reached the goal of the strategy. However, as we can see in this study, the death rate from TB in the elderly is higher similar to other studies^(1, 28, 42, 43). In another study, six times more deaths from TB in the elderly occurred, and postmortem morbidity was more than twenty times higher than that of young people⁽⁴¹⁾.

Conclusion

TB presentation diagnostic criteria and treatment outcome and complications in the elderly are a significant difference with non-elderly. This study has shown the fundamental differences between the elderly and non-elderly. Knowing these differences will help us diagnose and treat them more effectively.

Acknowledgments

The authors acknowledge the ongoing friendly contributions from the Nikpoor clinic personnel especially Dr. Azam Mirshamsi and Mr. Mosayeb Rajabzade, staff of Shahid Sadoughi University of Medical Sciences.

Conflict of interest

The authors declare that they have no conflict of interests.

Reference

1. World Health Organisation (WHO). Tuberculosis (TB). Global Tuberculosis Control Surveillance, Planning, Financing, Who Report. 2008. Available at: http://www.who.int/tb/publications/global_report/2008/en.
2. Mandell G, Bennett J, Dolin R. Principles and practice of infectious diseases. 5th ed, Philadelphia: Churchill Livingstone. 2000.
3. Siribaddane S, Wigesundera A. Autoimmune Haemolytic Afaemia Responding to Anti-Tuberculous Treatment. Trop Doc. 1997;27:243-4.
4. World Health Organization (WHO). Global tuberculosis report 2015 -2016. Available at: www.who.int/tb/publications/global_report/
5. World Health Organization (WHO). World report on ageing and health: World Health Organization; 2015. Available at: <http://www.who.int/ageing/events/world-report-2015-launch/en/>
6. Statistical Center of Iran. The detailed results of general census of population and housing in 2006. Available at: <https://www.amar.org.ir/>. 2015.
7. Fitzgerald DW, Sterling TR, Haas DW. Mycobacterium tuberculosis. In: Mandell GL, Bennett JE, Dolin R, editors. Principle and practice of infectious diseases. 7th ed. Philadelphia, USA: Churchill Livingstone; 2010: 3129-63.

- 8.,Kasper DL, Braunwald E, Hauser S, et al. Harrison's principles of internal medicine. 16th. New York: McGraw-Hill Professional. 2004.
- 9.Alavi SM, Salami N. The causes of death among patients with tuberculosis in Khuzestan, Iran. *Pakistan Journal of Medical Sciences*. 2008;24(2):217.
- 10.den Boon S, Borgdorff MW, Verver S, et al. Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area. *Thorax*. 2005;60(7):555-7.
- 11.Lemos AC, Matos E, Bittencourt CN. Prevalence of active and latent TB among inmates in a prison hospital in Bahia, Brazil. *Journal Brasileiro de Pneumologi*. 2009 Jan;35(1):63-8.
- 12.Leung CC LT, Chan WM, Yew WW, et al. Diabetic control and risk of tuberculosis: a cohort study. *American Journal of Epidemiology*. 2008;167(12):1486-94.
- 13.Organisation PAH. Tuberculosis in the Region of the Americas Regional Report 2011: Epidemiology CaFIPAHO, Washington DC. 2011.
- 14.Quantrill SJ WM, Bell CE, Hutchison AJ, et al. Peritoneal tuberculosis in patients receiving continuous ambulatory peritoneal dialysis. *Nephrol Dial Transplant*. 2001; 16(5):1024-7.
- 15.Hocking WG, Golde DW. The pulmonary-alveolar macrophage. *New England Journal of Medicine*. 1979;301(11):580-7.
- 16.Maurya V ,Vijayan V, Shah A. Smoking and tuberculosis: an association overlooked. *The International Journal of Tuberculosis and Lung Disease*. 2002;6(11):942- 51.
17. Tuberculosis. Center for Diseases Control (CDC), Iranian Ministry of Health and Medical Education, 2004 [Persian].
- 18.World Health Organisation (WHO).Tuberculosis (TB).Global Tuberculosis Control Surveillance P, Financing, Who, Available at: URL: http://www.who.int/tb/publications/global_report/2008/en/.
19. Dutt AK, Stead WW. Tuberculosis in the elderly. *Med Clin North Am* 1993;77:1353–1368.
- 20.Rezaei-talab F ,Akbari H, Rezaei-talab GH. Smooking associated with pulmonary TB. *Med J Mashhad Univ Med Sci* 2007;50(95):75-80. [Persian].
- 21 Guya M, editor Diabetes and hypothyroidism. Annual Conference of Diabetes and Hypothyroidism Screening Center for Diseases Control (CDC), Iranian Ministry of Health and Medical Education; 2006 Persian].
22. Nissapatorn V, Kuppusamy I, Josephine FP, et al. Tuberculosis: a resurgent disease in immunosuppressed patients. *The Southeast Asian Journal of Tropical Medicine and Public Health*. 2006; 37sup: 153-160.
23. World Health Organisation (WHO). World Population Aging 2013. In United Nations. Available at : URL: <http://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing; 2013>
24. CDC Reported tuberculosis in the United States 2013. Available at : URL: <https://www.cdc.gov/tb/statistics/reports/2013/pdf/report; 2013>
- 25.Mirhaghani L, Nasehi M. National tuberculosis program in Iran. Iran, Tehran: Ministry of Health, Nashre Seda; 2002 [Persian].
- 26.Korzeniewska-Kosela M, Krysl J, Müller N, et al. Tuberculosis in young adults and the elderly: a prospective comparison study. *Chest Journal*. 1994;106(1): 28-32.
- 27.Pérez-Guzmán C, Vargas MH, Torres-Cruz A, et al. Does aging modify pulmonary tuberculosis?: A meta-analytical review. *Chest Journal*. 1999; 116(4): 961-967.
- 28.Lee JH, Han DH, Song JW, et al. Diagnostic and therapeutic problems of pulmonary tuberculosis in elderly patients. *Journal of Korean Medical Science*. 2005; 20(5): 784-789.
- 29.Van Den Brande P, Vijgen J, Demedts M. Clinical spectrum of pulmonary tuberculosis in older patients: comparison with younger patients. *Journal of Gerontology*. 1991; 46(6): 204-209.
30. Talebi-Taher M, Javad-Moosavi SA, Pourghasemian M. Comparing pulmonary tuberculosis between elderly patients and young adults. *Razi Journal of Medical Sciences*. 2011; 18(88): 30-35[Persian].
- 31.Rizvi N, Shah RH, Inayat N, et al. Differences in clinical presentation of pulmonary tuberculosis in association with age. *Journal of Pakistan medical Association*. 2003; 53(8).
- 32.Evans JG. General medicine and geriatrics, where is the difference? The example of infective disease. *Schweizerische Medizinische Wochenschrift*. 1995; 125(40): 1847-1854.

33. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS Medicine*. 2008; 5(7): 1091-1101.
34. Brode SK, Jamieson FB, Ng R, et al. Increased risk of mycobacterial infections associated with anti-rheumatic medications. *Thorax*. 2015; 70(7): 677-682.
35. Dixon WG, Hyrich KL, Watson KD, et al. Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR). *Annals of the Rheumatic Diseases*. 2010; 69(3): 522-528.
36. Tubach F, Salmon D, Ravaud P, et al. Risk of tuberculosis is higher with anti-tumor necrosis factor monoclonal antibody therapy than with soluble tumor necrosis factor receptor therapy: The three-year prospective French Research Axed on Tolerance of Biotherapies registry. *Arthritis & Rheumatology*. 2009; 60(7): 1884-1894.
37. Jick SS, Lieberman ES, Rahman MUM et al. Glucocorticoid use, other associated factors, and the risk of tuberculosis. *Arthritis & Rheumatology*. 2006; 55(1): 19-26.
38. Lai CC, Lee MT, Lee SH, et al. Risk of incident active tuberculosis and use of corticosteroids. *The International Journal of Tuberculosis and Lung Disease*. 2015; 19(8): 936-942.
39. Schaberg T, Rebhan K, Lode H. Risk factors for side-effects of isoniazid, rifampin and pyrazinamide in patients hospitalized for pulmonary tuberculosis. *European Respiratory Journal*. 1996; 9(1): 2026-2030.
40. Yee D, Valiquette C, Pelletier M, et al. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. *American Journal of Respiratory and Critical Care Medicine*. 2003; 167(11): 1472-1477.
41. Teale C, Goldman J, Pearson S. The association of age with the presentation and outcome of tuberculosis: a five-year survey. *Age and Ageing*. 1993; 22(4): 289-293.
42. Alvarez S, Shell C, Berk SL. Pulmonary tuberculosis in elderly men. *The American journal of medicine*. 1987; 82(3) :602-606.
43. Counsell SR, Tan JS, Dittus RS. Unsuspected pulmonary tuberculosis in a community teaching hospital. *Archives of Internal Medicine*. 1989; 149(6): 1274-1278.