

LUCRĂRI ORIGINALE

Is there delay in diagnosis of pulmonary tuberculosis in an intermediate-to-low TB incidence setting

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REZUMAT

Există o întârziere în diagnosticul tuberculozei într-o instituție cu incidență medie a TB

Un studiu transversal asupra întârzierii diagnosticului de tuberculoză într-o instituție specializată cu incidență medie a tuberculozei a demonstrat o întârziere medie datorată pacientului de 44±61,65 zile și o întârziere totală de 103±148 de zile. Alcoolismul, lipsa cazurilor de tuberculoză în familie, diabetul zaharat, recidiva, tusea sau tahicardia ($p<0,01$), absența hemoptiziei, dispneei sau anemiei ($p<0,01$), vârsta ≥ 40 de ani ($p<0,05$), auscultația negativă și sputa pozitivă în microscopie ($p<0,05$) au fost asociate semnificativ cu întârzierea >30 de zile datorată pacientului. Vârsta <40 de ani, auscultația negativă și rezultatul microscopiei sputei ($p<0,01$), genul feminin, mediul urban ($p<0,05$), absența tusei, a sputei, a scăderii în greutate, a febrei, a cavității ($p<0,01$) și transpirațiile nocturne ($p<0,05$) au fost semnificativ asociate cu o întârziere globală de peste 103 zile. Sunt necesare în continuare educația populației și educația medicală continuă.

Cuvinte-cheie: tuberculoză, diagnostic, întârziere, contagiozitate, sănătate publică

ABSTRACT

A cross-sectional study on pulmonary TB diagnosis delay in an intermediate TB incidence setting showed average patient's delay of 44±61.65 days and total delay of 103±148 days. Alcoholism, lack of TB cases in family, diabetes mellitus, relapse, cough or tachycardia ($p<0.01$), absence of hemoptysis, dyspnea and anemia ($p<0.01$), age ≥ 40 ($p<0.05$), negative auscultation and positive sputum smear findings ($p<0.05$) were significantly associated with patient's delay >30 days. Age <40 years, negative auscultation and sputum smear findings ($p<0.01$), female sex, city as residence ($p<0.05$), absence of cough, sputum, weight loss, fever, excavation ($p<0.01$), and night sweats ($p<0.05$) were significantly associated with total delay > 103 days. Further population education and continual medical education are warranted.

Keywords: tuberculosis, diagnosis, delay, infectiousness, public health

Introduction

Early detection of pulmonary tuberculosis (PTB) is crucially important from both clinical and epidemiological view. The prolonged period of infectiousness in undetected PTB cases contributes to further dissemination of the disease in the community, which is an important public health issue^{1,3}. Early detection of TB is dependent upon patients perceiving the need to seek care, then presenting to a health clinic and being properly diagnosed⁴. Misinterpretation of early symptoms may lead to delays in seeking health care but lack of medical knowledge and/or resources may also contribute to delay of medical services⁵. Delay in diagnosis of PTB was recently studied in two high TB incidence countries, and previously in several settings^{4,5-11}.

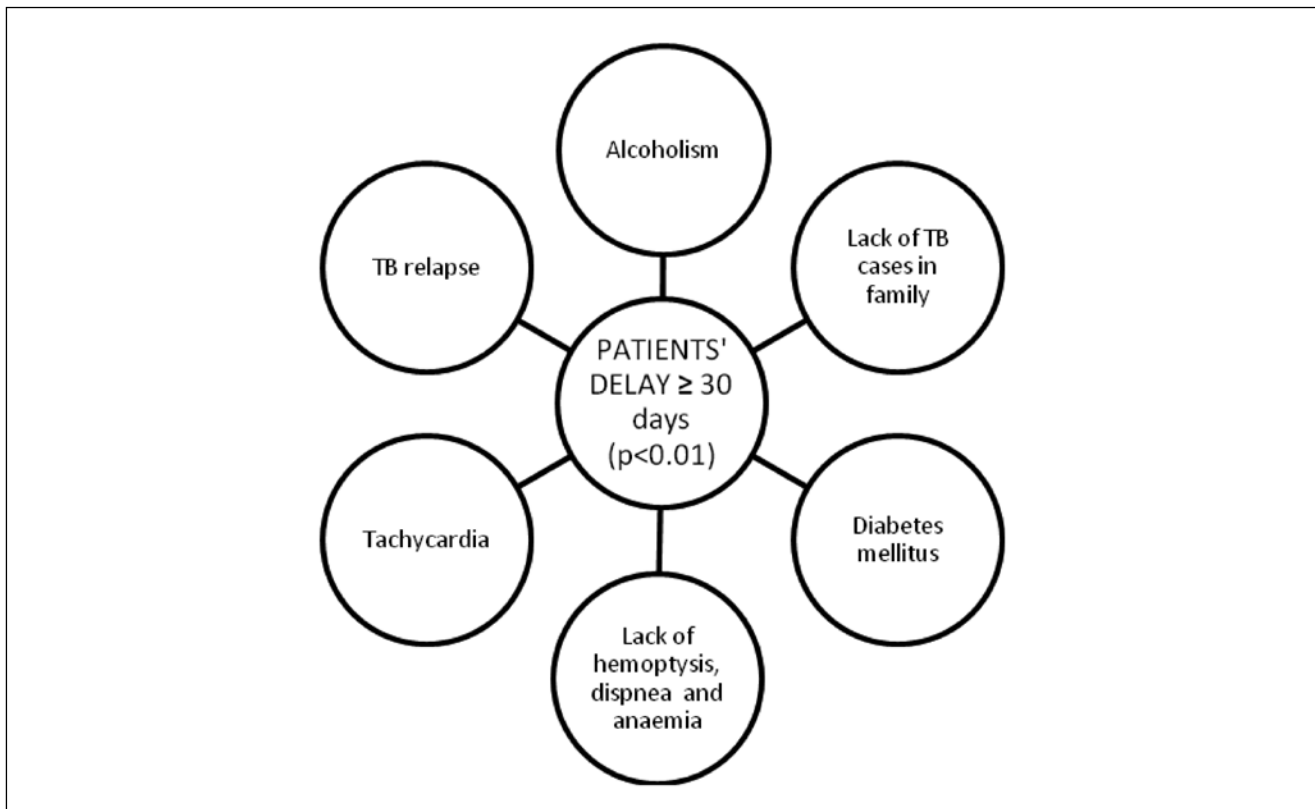
The aim of our study is to investigate if there is delay in diagnosis of PTB at the secondary level facility of an intermediate-to-low TB incidence setting of Serbia, South-East European developing country in transition¹², and to identify associated factors. South Banat County is situated at the North of the Serbian capital Belgrade district, and reports stable

intermediate TB incidence rates during the five-year study period.

As a part of former Yugoslavia, Serbia is a country in socioeconomic transition period with slight decrease in over-all TB incidence rate during the past decade, low-medium HIV-infection prevalence and dramatically increased TB incidence time trend in the elderly¹³. Serbian national anti-tuberculosis program was established in 1952, following the recommendations of the World Health Organization, and regularly improved thereafter. Apart from passive case finding, certain effort has been done in active approach to case detection^{2,3}.

Methods

A cross sectional study included PTB patients with bacteriologically confirmed diagnosis between January 2006 and December 2010 at the second level facility of the South Banat County, Pancevo, Serbia. The study was approved by the facility body and the School of Medicine University of Belgrade, Medical Students Research Centre to be performed under the

Figure 1. The most significant associations with patients' delay of ≥ 30 days ($p < 0.01$)

guidance of mentor at the Teaching Hospital of Lung Diseases in Belgrade.

Using a semi-structured questionnaire, we analyzed i) period between the onset of symptoms and the first seeking of medical care (patient's delay) and ii) period between the first medical consultation and diagnosis of TB (delay of medical services) in correlation with demographic and clinical features. The acquired data were based on review of available medical documentation. The methods of descriptive and analytical statistics (χ^2 -test and McNemar test) were applied.

Results

Out of 62 patients (34 male, 28 female), aged 50 ± 18 years (67.74% aged ≥ 40 years), 77.42% were sputum smear positive for acid fast bacilli (AFB), and smokers were significantly more sputum smear positive than non smokers ($p < 0.01$); none was HIV-seropositive; 85.48% patients had cough and 66.13% chest pain as initial symptoms; 74.19% presented with positive auscultation finding (table I). Average patients' delay was 44 ± 61.65 days. Alcoholism, lack of TB cases in the family, diabetes mellitus, TB relapse, presence of cough or tachycardia ($p < 0.01$), then, the absence of hemoptysis, dyspnea and anemia ($p < 0.01$), age ≥ 40 ($p < 0.05$), a negative finding on auscultation and the presence of AFB positive sputum ($p < 0.05$) were significantly associated with the patient's delay of > 30 days (figure 1).

Average total delay was 103 ± 148 days. Age < 40 years, negative auscultation findings and AFB negative sputum smear ($p < 0.01$), then, female sex, city as place of residence ($p < 0.05$), absence of: cough, sputum, weight loss, fever, excavation ($p < 0.01$), and night sweats ($p < 0.05$) were significantly associated with total delay of > 103 days (table II and figure 2).

Discussion

The results of our study showed that there is diagnostic delay in PTB. It is a consequence of both delay in seeking of medical care in symptomatic, and delay of medical services during diagnostic procedures, the latter being longer on average. While total delay in our study is similar to that found in Brazil and Malaysian studies, contrary to our results, the patient delay was dominant component in Malaysian study compared to delay of medical services^{4,6}. Due to well developed medical services and relatively small territory of the South Banat County (not more than 20 km radius), we assumed that problem to access to medical care could not be important contributing factor in patients' delay as it was in some other countries, thus it was not a matter of the analysis^{8,9}.

The average doctor's delay, which is longer than the patient's delay (59 vs 44 days) is a common observation in countries where TB is a rare disease⁸. Positive correlation of absence of excavation on chest x-ray and medical services' delay in diagnosis of PTB might appoint that excavation itself suggest TB as a radiographic differential diagnosis better compared to TB initial forms like initial nodules, round infiltrate, caseous pneumonia etc. This potential lack of knowledge or experience is important since TB diagnosis includes special request for staining and culturing of the patient's material, which means the presence of TB in clinician's mind first.

Cough, the most common symptom of PTB is also common in smokers and elderly patients with a variety of pulmonary and cardiac diseases. Undetected PTB patient, whose cough can be perceived related to the other diseases, may be a source of TB infection, especially for the close contacts¹³ and health care workers as well¹⁴. A recent study has shown that knowledge about TB was not satisfactory in the general

Table I. Pulmonary TB patients' characteristics and delay to see a doctor in South Banat County, Serbia, 2006-2010

Parameter	No (%)	p value	Patient's delay > 30 days	p value
Age <40 ≥40	20 (32.26) 42 (67.74)	0.0223 *	8 (12.9) 22 (35.48)	0.0259*
Sex Male Female	34 (54.84) 28 (45.16)	0.4461	18 (29) 15 (24.2)	0.3613
Smoking Smokers Non smokers	26 (41.93) 36 (58.07)	0.1346	14 (22.58) 16 (25.8)	0.4862
Residence Urban Rural	28 (45.16) 34 (54.84)	0.44	15 (24.2) 14 (22.58)	0.8551
Alcoholism Yes No	8 (12.9) 54 (49.1)	< 0.01 **	5 (8) 25 (40.32)	< 0.01**
TB in family Yes No	11 (17.74) 51 (82.26)	< 0.01 **	4 (6.45) 26 (41.93)	< 0.01**
Diabetes mellitus Yes No	7 (11.29) 55 (88.71)	< 0.01 **	4 (6.45) 26 (41.93)	< 0.01**
TB relapse Yes No	10 (16.13) 52 (83.87)	< 0.01 **	5 (8) 25(40.32)	< 0.01 **
Cough Yes No	53 (85.48) 9 (14.52)	< 0.01 **	27 (43.54) 3 (4.83)	< 0.01 **
Productive cough Yes No	32 (51.61) 30 (48.38)	0.7995	19 (30.65) 19 (30.65)	1
Hemoptysis Yes No	12 (19.35) 50 (80.64)	< 0.01 **	7 (11.29) 22 (35.48)	< 0.01 **
Dyspnea Yes No	19 (30.65) 43 (69.35)	< 0.01 **	4 (6.45) 27 (43.54)	< 0.01 **
Chest pain Yes No	41 (66.13) 21 (33.87)	0.0111 *	12 (19.35) 9 (14.52)	0.1698
Night sweating Yes No	34 (54.84) 28 (45.16)	0.4461	15 (24.2) 14 (22.58)	0.6892
Weight loss Yes No	27 (43.54) 35 (53.45)	0.3096	22 (35.48) 6 (9.68)	0.3320
Fever Yes No	29 (46.77) 33 (53.22)	0.6115	18 (29) 11 (17.74)	0.6892
Anaemia Yes No	15 (24.2) 47 (75.8)	< 0.01 **	6 (9.68) 24 (38.7)	< 0.01 **
Tachycardia Yes No	16 (25.8) 46 (74.19)	< 0.01 **	10 (16.13) 23 (37)	< 0.01 **
Auscultation + Yes No	46 (74.19) 16 (25.81)	< 0.01 **	22 (35.48) 8 (12.9)	< 0.017 *
Sputum smear Positive Negative	48 (77.42) 14 (22.58)	< 0.01 **	23 (37) 7 (11.29)	0.0209*
Excavation Yes No	37 (59.68) 25 (40.32)	0.1275	16 14	0.8551

*significant ($p < 0.05$) **highly significant ($p < 0.01$)

Table II. Pulmonary TB patients' characteristics and total delay in diagnosis in South Banat County, Serbia, 2006-2010

Parametre	No (%)	p value	Total delay > 103 days	p value
Age <40 ≥40	20 (32.26) 42 (67.74)	0.0223 *	10 6	< 0.01 **
Sex Male Female	34 (54.84) 28 (45.16)	0.4461	8 8	0.0376*
Smoking Smokers Non smokers	26 (41.93) 36 (58.07)	0.1346	7 9	0.3
Residence Urban Rural	28 (45.16) 33 (54.84)	0.44	9 6	0.05*
Alcoholism Yes No	8 (12.9) 54 (49.1)	< 0.01 **	1 15	0.08
TB in family Yes No	11 (17.74) 51 (82.26)	< 0.01 **	3 15	0.26
TB relapse Yes No	10 (16.13) 52 (83.87)	< 0.01 **	2 14	0.07
Cough Yes No	53 (85.48) 9 (14.52)	< 0.01 **	15 1	< 0.01 **
Productive cough Yes No	32 (51.61) 30 (48.38)	0.7995	11 4	< 0.01 **
Night sweating Yes No	34 (54.84) 28 (45.16)	0.4461	10 6	0.037*
Weight loss Yes No	27 (43.54) 35 (53.45)	0.3096	11 5	< 0.01 **
Fever Yes No	29 (46.77) 33 (53.22)	0.6115	10 6	< 0.01 **
Anaemia Yes No	15 (24.2) 47 (75.8)	< 0.01 **	4 12	0.05
Tachycardia Yes No	16 (25.8) 46 (74.19)	< 0.01 **	7 9	0.6
Auscultation + Yes No	46 (74.19) 16 (25.81)	< 0.01 **	13 (21) 3 (4.84)	< 0.01 *
Sputum smear Positive Negative	48 (77.42) 14 (22.58)	< 0.01 **	14 2	< 0.01 **
Excavation Yes No	37 (59.68) 25 (40.32)	0.1275	8 7	< 0.01 **

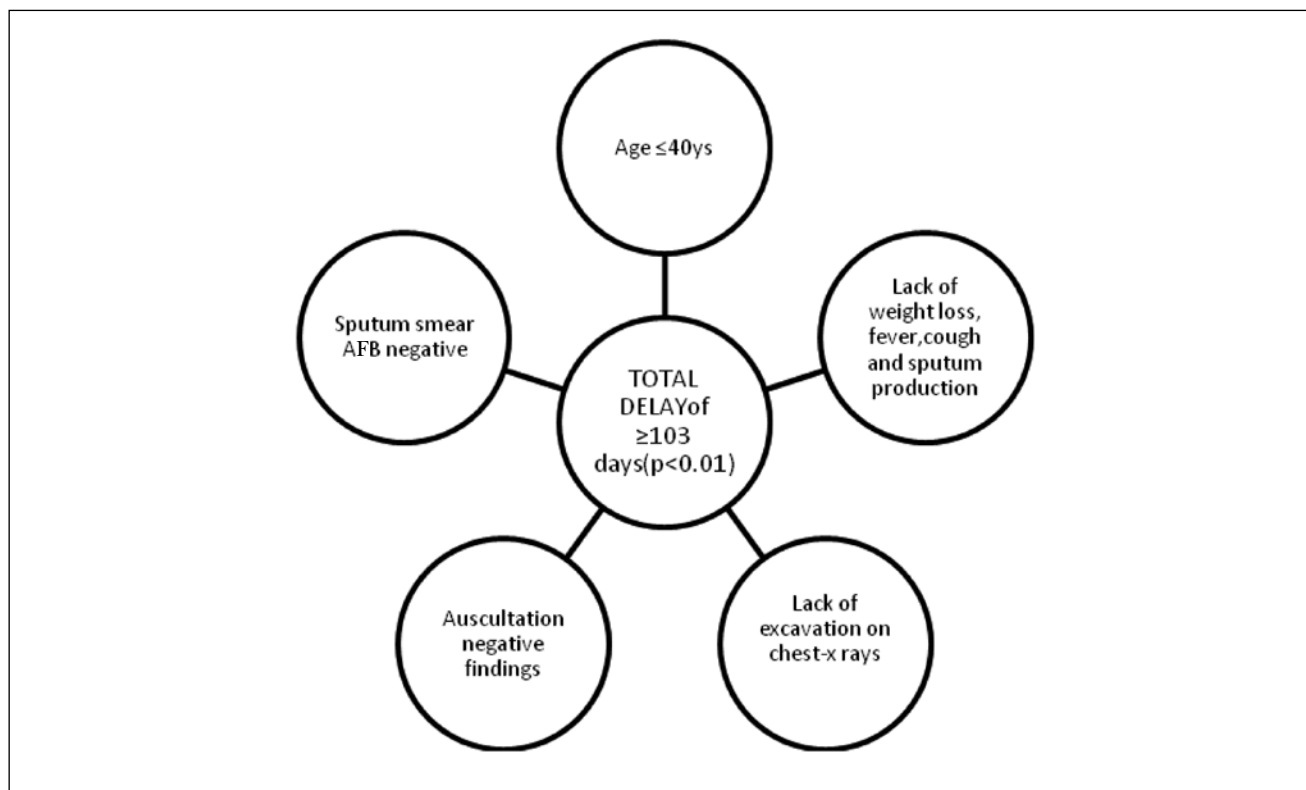
*significant ($p < 0.05$) **highly significant ($p < 0.01$)

population of Serbia and that one of the strongest predictors of misconceptions was older age¹⁵. Thus, population education on TB may greatly contribute to the prevention of TB spreading within community, starting from activities of advocacy, communication and social mobilisation. A useful tool which follows StopTB strategy in a step manner that can assist countries in evaluating the efficiency of their surveillance system in detecting cases has been developed

and already used to evaluate the efficiency of the case-finding process in 22 countries of the Eastern Mediterranean Region¹⁶.

Many studies reported higher estimates of TB disease among health care workers than in the general population, and this was suggestive of nosocomial transmission. Increasing health care workers' consciousness on epidemiological situation in the local settings and in the world, together with their

Figure 2. The most significant associations with total delay of ≥ 103 days ($p < 0.01$)



continual education on risk factors for TB, may be of crucial importance in early detection of the disease in symptomatic patients. A step more – active case finding of TB in risk groups may contribute to global plan to stop TB^{1,3}.

Conclusion

Further population awareness and education on TB is warranted. Proceeding of continual medical education, especially with primary health care workers would improve the services and increase awareness and knowledge on TB. To achieve the goals in TB control, apart from clinical examination of symptomatic subjects who

come to seek for care, an active approach in case detection should be also applied. As the best contribution to the global plan to stop TB, these could diminish delay in TB diagnosis, allow earlier start of treatment and decrease dissemination of *M. tuberculosis* within community. The results of our study are potentially important for guiding the National TB Programme to further improve performances.

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References

1. StopTB Partnership and World Health Organization. The global plan to stop TB, 2006-2015. Available from: <http://www.stoptb.org/globalplan/assets/documents/GlobalPlanFinal.pdf>. Accessed: March 14, 2011.
2. Bothamley G.H., Ditiu L., Migliori G.B., Lange C. and TBNET contributors. Active case-finding of tuberculosis in Europe. A TBNET (Tuberculosis Network European Trials Group) survey. *Eur Respir J* 2008; 32(4):1023-1030.
3. Pešut D., Active case detection for tuberculosis in risk groups in Serbia, *Med Pregl* 2004; LVII (Suppl. 1): 75-80. [In Serbian].
4. Maciel E.L.N., Golub J.E., Peres R.L., Hadad D.J., Fávero J.L., Molino L.P. et al., Delay in diagnosis of pulmonary tuberculosis at a primary health clinic in Vitoria, Brazil. *Int J Tuberc Lung Dis* 2010; 14(11):1403-1410.
5. Golub J.E., Bur S., Cronin W.A., Gange S., Baruch N., Comstock G.W. et al., Delayed tuberculosis diagnosis and tuberculosis transmission. *Int J Tuberc Lung Dis* 2006;10(1):24-30.
6. Greenaway C., Menzies D., Fanning A., Grewal R., Yuan L., Fitzgerald J.M., Delay in diagnosis among hospitalized patients with active tuberculosis – predictors and outcomes. *Am J Resp Crit Care Med* 2002;165(7):927-33.
7. Rodger A., Jaffar S., Paynter S., Hayward A., Carless J., Maguire H., Delay in the diagnosis of pulmonary tuberculosis, London, 1998-2000: analysis of surveillance data. *BMJ* 2003;326(7395):909-10.
8. Sreeramareddy C.T., Kishore P.V., Menten J., Van den Ende J., Time delays

- in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infectious Diseases*. 2009;9(1):91.
9. Storla D.G., Yimer S., Bjune G.A., A systematic review of delay in the diagnosis and treatment of tuberculosis. *BMC Public Health*. 2008;8(1):15.
10. Nnoaham K.E., Pool R., Bothamley G., Grant A.D., Perceptions and experiences of tuberculosis among African patients attending a tuberculosis clinic in London. *Int J Tuberc Lung Dis* 2006; 10(9):1013-1017.
11. Chang C.T., Esteman A., Diagnostic Delay among Pulmonary Tuberculosis Patients in Sarawak, Malaysia: A Cross-sectional Study. *Rural and Remote Health* 2007; 7(2): 667.
12. Pesut D.P., Gledovic Z.B., Grgurević A., Nagorni-Obradović Lj., Adžić T., Tuberculosis Incidence in Elderly in Serbia: Key Trends in Socioeconomic Transition. *Croat Med J* 2008; 49:807-12.
13. Veen J., Microepidemics of tuberculosis: the stone-in-the-pond principle. *Tuber Lung Dis*. 1992;73:73-6.
14. Creswell J., Raviglione M., Ottmani S., Migliori G.B., Uplekar M., Blanc L. et al., Tuberculosis and noncommunicable diseases: neglected links and missed opportunities. *Eur Respir J* May 1, 2011; 37 (5):1269-1282.
15. Vukovic D., Nagorni-Obradovic L., Bjegovic V., Knowledge and misconceptions of tuberculosis in the general population in Serbia. *Eur J Clin Microbiol Infect Dis* 2008;27:761-7.
16. Bassili A., Seita A., Baghdadi S., Enarson D., Tuberculosis case finding in twenty-two countries of the Eastern Mediterranean Region. *Int J Tuberc Lung Dis* 2011 Apr;15(4):556-61.