

A CASE CONTROL STUDY OF RISK FACTORS ASSOCIATED WITH PULMONARY TUBERCULOSIS IN ROMANIA: EXPERIENCE AT A CLINICAL HOSPITAL OF PNEUMOLOGY

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Abstract

Background and aim. Tuberculosis (TB) remains a major public health issue in Romania. The aim of the present study was to evaluate the potential demographic, socioeconomic and behavioral risk factors for TB among hospitalized patients in Romania.

Methods. This is a case-control study conducted between March 1st 2014 and March 30th 2015 at Leon Daniello Clinical Hospital of Pneumology, Cluj Napoca. A total of 150 TB patients defined as “cases” were matched for age, sex and county of residence to 150 controls selected from patients attending the same hospital with respiratory diseases other than TB. Data collection was obtained through patient interviews using a structured questionnaire. Factors potentially associated with TB infection were analyzed using univariate and multivariate logistic regression.

Results. Factors independently associated with TB were illiteracy (OR=2.42, 95% CI 1.09-5.37), unemployment (OR=2.08, 95% CI 1.23-3.53), low household income (OR=4.12, 95% CI 2.53-6.71), smoking (more than 20 cigarettes per day) (OR=2.12, 95% CI 1.20-3.74), poor knowledge of TB (OR=3.46, 95% CI 1.97-6.07), presence of TB patient in household (OR=4.35, 95% CI 1.42-13.36), prior TB treatment (OR=2.2, 95% CI 1.93-2.5) and diabetes (OR=3.32, 95% CI 1.36-8.08).

Conclusion. This study provided useful information that might help to develop and adapt effective policies for TB control in Romania.

Keywords: tuberculosis, risk factors, prevention, odds ratio, Romania

Introduction

Tuberculosis (TB) remains a public health concern worldwide. Efforts to control this disease have been largely

focused on improving treatment and diagnosis of patients with active disease. However, in spite of those intensive efforts, high per capita rates of TB are still common, particularly in developing countries in Asia, Africa, Eastern Europe and the former Soviet Union [1].

With an estimated annual TB incidence of 94 new

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cases and a prevalence of 144 per 100,000 population, Romania has the highest incidence and prevalence in the European Union [2]. It accounts for 27% of the EU's total cases [3]. WHO has identified Romania as one of the eighteen high-priority countries in the European region [2]. However, few studies have been performed in Romania to clarify how different factors interact in the development of active TB. Studies that address risk groups help to prioritize TB research and intervention among the most vulnerable in the community, enabling effective and efficient TB control.

The aim of the present study was to evaluate the potential demographic, socioeconomic and behavioral risk factors for tuberculosis among hospitalized patients in Romania.

Methods

Study setting and Data collection

We conducted a case-control study at Leon Daniello center, a clinical hospital of pneumology serving predominantly patients from Cluj County and its surroundings. Cases were patients aged >15 years with confirmed pulmonary TB according to the World Health Organization (WHO) and Romania's National Tuberculosis Control Program guidelines. Controls were patients matched for sex, age and county of residence attending the same hospital with respiratory diseases other than TB.

A structured questionnaire prepared in local language was administered to both cases and controls through face-to-face interviews. Studied factors included demographic, socioeconomic, behavioral and biological indicators. Exclusion criteria were refusal to participate, serious illness (Human Immuno-Deficiency Virus and mental disorders), death and respondents with missing major data.

Data analysis

Data were recorded in Excel worksheet and the analysis was conducted using cases and controls. Odds ratios (OR) and their 95% confidence intervals (CI) were estimated using conditional logistic regression, with TB as an outcome. The likelihood ratio test used to assess the association between the explanatory variables and the risk of TB, and to test for interaction and trend. Univariate analyses were performed to examine the effect of each variable on the risk of TB. Multivariable models were then constructed, including variables that showed an effect in the prediction of TB in the univariable analyses at the $p=0.05$ level of significance. The analyses were performed using SPSS version 20 (Chicago, IL, USA).

Ethical consideration

The study was approved by the Ethics Committee of the Iuliu Hatieganu University of Medicine and Pharmacy. The objective of the study was explained in detail to study participants and an informed consent form was signed by each individual before conducting the interview.

Results

Baseline characteristics of the study participants

A total of 300 participants were enrolled in the study between 01st March 2014 and 30th March 2015. Of the 300 participants, 150 were diagnosed positive for *M. tuberculosis* and 150 were negative for *M. tuberculosis*. The average age was 42.92 years with a range of 17 to 84 years. Clinical symptoms mainly included weight loss (68.6%), cough (55.4%), fever (45.3%), expectoration (43.3%) and hemoptysis in 12% cases. Seventy-six (25.3%) and 94 (31.3%) participants had cavities and nodular lesions respectively on their chest X-ray (Table I).

Table I. Baseline characteristics of the study participants.

Variable	Cases (n)=150	Controls (n)=150
Age (mean, SD)	43.9 (7.8)	42.5 (9.3)
Gender (n, %)		
Male	118 (78.6)	118 (78.6)
Female	32 (21.3)	32 (21.3)
White Blood Cells (*103/ μ l), Mean (range)	8.24 (2.4-15.9)	8.36 (4.1-15.8)
Lymphocytes (*103/ μ l), Mean (range)	1.78 (0.05-3.1)	1.91 (0.05-3.2)
% Lymphocytes, Mean (range)	21.09 (6.4-41.9)	22.52 (6.4-39)
Erythrocyte Sedimentation Rate (mm), Mean (range)	64.29 (7-132)	52.56 (2-125)
Weight loss (n)	114	92
Persistent cough (n)	116	49
Cavitation on chest X-ray (n)	64	12
Nodular lesion on chest X-ray (n)	95	9

Factors associated with pulmonary tuberculosis

The relationship between studied risk factors and TB infection as evaluated by univariate analysis is presented in

Tables II and III. The final multivariate model identified several risk factors independently associated with TB (Table IV).

Table II. Univariate analysis of demographic, socioeconomic and behavioral factors associated with pulmonary tuberculosis in a case-control study, Cluj-Napoca, Romania.

Variable	Cases n (%) (N=150)	Controls n (%) (N=150)	OR (95% CI)	P-value
Marital status				
Single	67 (44.6)	62 (41.3)	1.17 (0.86-1.60)	0.324
Married	63 (42)	62 (41.3)	-	
Other (widowed, divorced)	20 (13.3)	26 (17.3)	0.83 (0.57-1.21)	
Education (Schooling)				
No	25 (16.6)	11 (7.3)	1.43 (1.08-1.91)	0.026
1-5 years	58 (38.6)	62 (41.3)	0.59 (0.35-0.99)	
>5 years	67 (44.6)	77 (51.3)	-	
Household monthly income				
≥ 800 lei/month	60 (40)	110 (73.3)	-	0.001
< 800 lei/month	90 (60)	40 (26.6)	1.96 (1.55-2.47)	
Occupation				
Employed	29 (19.3)	50 (33.3)	-	0.006
Unemployed	121 (80.6)	100 (66.6)	1.49 (1.09-2.04)	
Residential area				
Large city / urban	73 (48.6)	82 (54.6)	-	0.298
Small city / rural	77 (51.3)	68 (45.3)	1.27 (0.80-2.00)	
Persons per room				
1-2	125 (83.3)	20 (13.3)	-	0.419
>2	25 (16.6)	130 (86.6)	1.30 (0.68-2.45)	
Smoking history				
Never	53 (35.3)	105 (70)	-	0.325
Past/Current	97 (64.6)	45 (30)	0.78 (0.48-1.27)	
Frequency of smoking				
< 1 pack/day	46 (30.6)	69 (46)	-	0.009
> 1 pack/day	51 (34)	36 (24)	1.46 (1.10-1.94)	
Alcohol history				
Never	66 (44)	59 (39.3)	-	0.412
Past/Current	84 (56)	91 (60.6)	0.82 (0.52-1.30)	
Frequency of drinking				
Less than once a week	30 (20)	43 (28.6)	-	0.122
Several times a week	54 (36)	48 (32)	1.61 (0.87-2.95)	
Drug user				
No	143 (95.3)	140 (93.3)	-	0.45
Yes	7 (4.6)	10 (6.6)	0.81 (0.45-1.4)	

OR = odds ratio; CI = confidence interval.

* P ≤ 0.05 (significance level).

Table III. Univariate analysis of clinical and disease-related factors associated with pulmonary tuberculosis in a case-control study, Cluj-Napoca, Romania.

Variable	Cases n (%) (N=150)	Controls n (%) (N=150)	OR (95% CI)	P-value
Diabetes				
Yes	21 (14)	7 (4.6)	1.58 (1.23-2.02)	0.005
No	129 (86)	143 (95.3)	-	
BCG vaccination status				
Un-vaccinated	9 (6)	12 (8)	0.84 (0.3-1.79)	0.49
Vaccinated	141(94)	138 (92)	-	
Knowledge of TB				
Poor	56 (37.3)	22 (14.6)	1.69 (1.37-2.08)	0.001
Well	94 (62.6)	128 (85.3)	-	
Presence of TB patient in household				
Yes	16 (10.6)	4 (2.6)	1.67 (1.30-2.14)	0.005
No	134 (89.3)	146 (97.3)	-	
History of prior TB treatment				
Yes	25 (16.6)	0	-	-
No	125 (83.3)	150 (100)	-	
Satisfaction with health services				
Yes	137 (91.3)	129 (86)	-	
No	13 (8.6)	21 (14)	0.58 (0.28-1.21)	0.145

OR = odds ratio; CI = confidence interval.

* P ≤ 0.05 (significance level).

Table IV. Multivariable logistic regression model showing risk factors associated with pulmonary tuberculosis in a case-control study, Cluj-Napoca, Romania.

Variable	OR (95% CI)	P-value
Education (Schooling)		
No	2.42 (1.09-5.37)	0.026
1-5 years	-	
Household monthly income		
< 800 (lei/month)	4.12 (2.53-6.71)	0.001
≥ 800 (lei/month)	-	
Occupation		
Unemployed	2.08 (1.23-3.53)	0.006
Employed	-	
Frequency of smoking		
> 1 pack/day	2.12 (1.20-3.74)	0.009
< 1 pack/day	-	
Diabetes		
Yes	3.32 (1.36-8.08)	0.005
No	-	
Knowledge of TB		
Poor	3.46 (1.97-6.07)	0.001
Well	-	
Presence of TB patient in household		
Yes	4.35 (1.42-13.36)	0.005
No	-	
History of prior TB treatment		
Yes	2.2 (1.93-2.5)	0.001
No	-	

Discussion

This study aimed at reassessing the main risk factors that influence the development of TB in Romania in order to collect information which might help adjust and adapt effective policies for TB control in this country.

The results showed that smoking more than a pack (20 cigarettes) per day was associated with TB infection. Previous studies both in developed and developing countries have shown an increased vulnerability of smokers to the infection and development of TB, most probably owing to patho-physiological changes in the lungs induced by chronic smoking [4,5,6]. Bronchoalveolar macrophages among smokers contain high levels of iron implicated in promoting the growth of *M. tuberculosis* [7,8]. Smoking 1 pack of cigarettes is equivalent to inhaling 1.1 µg of iron [9]. In this study, patients smoking more than one pack per day were twice as likely to have TB as those who smoke less than one pack per day. Smoking is great public health issue in Romania, even in hospitalized patients. Our results might reinforce the need to devise effective strategies for counseling TB patients and their relatives about quitting smoking. Anti-smoking campaigns also need to be strengthened to have considerable effects on the health of all population, following the recommendations contained in the WHO Framework Convention on Tobacco Control [10]. This is an especially important finding for Romania, where free smoking cessation services are unavailable to most Romanian TB patients.

The present study found no association between alcohol consumption and TB, which differs from other studies which concluded that alcohol had a stronger association with tuberculosis [11]. Ruffino-Neto, several decades ago, investigated the role of alcohol consumption and smoking in the risk of developing tuberculosis and found that smoking was associated with tuberculosis only in the group of drinkers [12,13]. However, alcoholics should also be counseled effectively to wean them away from these unhealthy behaviors and minimize the risk of developing the disease.

The low household income (<800 lei per month, approximately 230 US Dollars) appears to be a risk factor for developing TB in our study. Measures of poor living conditions like low family income, poor household equipment and malnutrition have been found to be associated with an increased risk of developing tuberculosis [14,15]. Poverty undoubtedly contributes to the incidence of tuberculosis through increased progression from infection to disease due to poor diet or stress, and greater difficulties in using health services [16]. In Romania, Stillo has also observed that poverty is not only a risk factor for TB, but also the single greatest barrier that prevents people under treatment from becoming cured. This is especially true when one's household responsibilities do not allow them to submit to the long hospitalization periods that are standard in Romanian TB treatment, particularly for drug-

resistant TB [2,17,18].

Lower level of education and poor knowledge about TB appeared to favor the development of the disease. TB more strongly affects disadvantaged population groups [18,19]. However, illiterate individuals need to be focused on a priority basis for educational interventions regarding the disease. WHO also recognizes the importance of tuberculosis-related knowledge, attitude and practice surveys in advocacy, communication and social mobilization strategy planning [20]. Romania's most recent KAP survey took place in 2012 and, like previous ones, revealed serious deficits in knowledge about TB in the population [21].

Consistent with the previous studies, this study found a strong association between a reported presence of TB patient in the family and the development of TB [22]. This risk increases with the number of persons in the household having had TB in the past, due to a higher chance of getting the TB bacillus via their respiratory tract. This result supports the recommendation of the Tuberculosis Control Cluster, which recommends the special care of persons who have had close contact with a TB patient. Our results also suggest that prior TB history is the predominant risk factor for developing TB. We defined patients with prior TB history as those who had a history of anti-tuberculosis treatment for active TB infection based on medical record review. Those patients were more likely to develop the disease than patients without a history of TB.

We found a strong association of diabetes with pulmonary TB, which agree with the findings of other studies [15,23,24]. It is known that diabetes mellitus could affect chemotaxis, phagocytosis, and antigen presentation by macrophages in response to *M. tuberculosis*. Production of interferon γ , growth, function, and proliferation of T lymphocytes might be adversely affected by diabetes [25,26].

Our study has some limitations. First, the study was conducted at a referral hospital, which usually manages patients with more severe and extensive disease. Some of our results, particularly concerning X-ray data, may not be representative of patients with less severe disease. Second, diabetes status collected by self-report and types I vs. II could not be differentiated.

Conclusion

This study confirmed the multifactorial aspect of TB and showed that interventions for this disease need to be appropriate for those most at risk. Our findings may help to plan and implement country-specific prevention strategies aiming at reducing the morbidity and transmission of this burden.

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