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Relationship between Diagnosis Period and Internal and External Air Quality in Patients with Tuberculosis

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ABSTRACT

Objective: The aim of this study was to investigate the relationship between bacteriological case definitions and indoor and outdoor air quality parameters in tuberculosis (TB).

Materials and Methods: A total of 200 patients with TB diagnosed and treated in our hospital during 2012-2018 were included to this study. The air monitoring measurement parameters of the National Air Quality Network [particulate matter 10 (PM10), sulfur dioxide (SO2), air temperature, air pressure, and relative humidity] for the same time period were obtained from the web page http://laboratory.cevre.gov.tr/Default.ltr.aspx.

Results: Of the 200 patients, 62.5% (125) were males and 37.5% (75) were females. The rate of diagnosis based on culture and smear positivity was 48.4% (31), which was significantly higher than that in the clinic [10.9% (7)] among patients who used stove for warming. The rate of diagnosis based on culture and smear positivity [52.1% (25)] was significantly higher than that in the clinic [8.3% (4)] among patients who were exposed to biomass. The univariate analysis revealed no significant independent effect of warming and biomass use on case definition. According to the case definitions, the mean values of PM_{10}, SO_2, and temperature in the diagnosed month showed no statistically significant difference. The humidity level in the month was significantly higher, during which cases diagnosed using smear and culture positivity were compared with cases diagnosed using only culture positivity (p=0.023).

Conclusion: This study indicates that biomass used as a cooking fuel is a risk factor for pulmonary TB, implying that TB occurrence can be reduced significantly by lowering or preventing the exposure to cooking smoke emitted from biomass fuel.

Keywords: Air quality, biomass, stove, tuberculosis

Introduction

Air pollution is still the most important environmental factor that has adverse effects on human health. Extensive research has demonstrated an increase in the rates of morbidity and mortality due to diseases with an increase in air pollution (1). In 2015, air pollution affected more than one billion people, and it has been estimated that this number will increase to four billion in 2050 (2, 3).

Tuberculosis (TB) is an airborne disease caused by *Mycobacterium tuberculosis*, and one-third of people in the world are known to be infected with this disease (4).

TB generally affects the lungs, but it can also affect all other organs. TB still remains one of the major causes for mortality and morbidity worldwide (5).

The most contagious patients are those with laryngeal TB and those with pulmonary TB showing smear positivity to Ehrlich–Ziehl–Neelsen (EZN) staining and presenting cavitary lesions. Smear-negative TB patients are less contagious (6, 7).

TB is still one of the 10 most common infectious diseases that affects millions of people causing deaths each year. According to the World Health Organization (WHO) 2018 report, approximately 1.3 million people had died from TB in 2017 (8). In Turkey as well, TB continues to be an important public health problem as in the world. As of 2016, the incidence of TB was estimated

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at 18% and the mortality rate was estimated at 0.62 per 100,000 population (9).

Studies show that TB frequency increases with exposure to cigarette smoke and the use of biomass that degrade indoor air quality (4, 10-13). These studies were also responsible for the initiation of the discussion about the relationship between outdoor air quality and TB.

In the present study, we investigated the relationship between bacteriological case definitions and indoor and outdoor air quality parameters in the context of TB.

Material and Methods

Study group

A total of 200 patients with TB diagnosed and treated in our hospital during 2012-2018 were included in this study. Approval for conducting this study was obtained from the ethics committee. The diagnostic criteria of the patients with TB included in this study are summarized below.

Pulmonary TB and extrapulmonary TB

Pulmonary TB

This type of TB infects the lung parenchyma or the tracheal bronchial tree. When there is no involvement of the lung parenchyma, TB with pleural effusion or lymph node enlargement in the thorax (hilum, mediastinum) is considered as extrapulmonary TB.

Extrapulmonary TB

Patients with histological and clinical findings consistent with TB or patients who have smear-positive samples obtained from organs other than the lung parenchyma are included in this group.

Pulmonary TB with extrapulmonary TB

Patients who have both pulmonary and extrapulmonary involvement are included in this group.

Smear-positive, culture-positive, and clinical TB

Smear-positive pulmonary TB

Patients who exhibit smear positivity in at least two sputum samples

- Patients who show smear positivity in one sputum sample and radiological findings compatible with pulmonary TB
- Patients who show smear positivity in one sputum sample and culture positivity are included in this group.

Culture-positive pulmonary TB

Patients with sputum smear-negative but culture-positive.

Clinical TB

Patients who demonstrate clinically and radiologically compatible TB findings with three sputum smear-negative samples and who do not respond despite the use of broad-spectrum antibiotics (quinolone-free) for at least 1 week and who decide to undergo treatment for TB in a hospital with adequate facilities for differential diagnosis.

New and relapse cases

New cases

Patients who have not previously received TB treatment or who have received treatment for less than 1 month.

Relapse cases

Patients who are diagnosed again with TB after they have been diagnosed earlier and had successfully completed the treatment, i.e., smear positivity is detected again in the patient sputum, are considered as relapse cases.

Data collection

TB record forms were reviewed. The contact information, diagnosis-treatment follow-up process reached from hospital information processing system. Information about the indoor air pollution during the period when they were diagnosed was obtained by telephone calls (85 patients were contacted).

The air monitoring measurement parameters of the National Air Quality Network [particulate matter 10 (PM_{10}), sulfur dioxide (SO_2), air temperature, air pressure, and relative humidity] for the same time period were obtained from the web page (http://laboratory.cevre.gov.tr/Default.ltr.aspx).

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Corp.; Armonk, NY, USA). Comparisons were made using Student's *t*-test and analysis of variance (ANOVA). Spearman's analysis was used to determine the correlations between smear-positive TB, culture-positive TB, clinical TB, and the levels of PM_{10}, SO_2, relative humidity, and air temperature and pressure. $p<.05$ was considered to be statistically significant.

Results

Of the 200 patients, 62.5% (125) were males and 37.5% (75) were females. The mean age was 56.2±20.6 (min: 20, max: 94) years, and 91% (182) of the patients were newly diagnosed, 76.5% (153) had pulmonary TB, and 20% (40) had extrapulmonary TB (Table 1).

The seasons during which the patients were diagnosed were spring (31%), autumn (25.5%),

Table 1. Demographic and clinical characteristics of reported tuberculosis cases from 2012 to 2018

Characteristics (n=200)		No (%) mean±SD (range)
Gender	Male	125 (62.5)
	Female	75 (37.5)
Age		56.2±20.6 (20-94)
Method of diagnosis	smear+	80 (40)
(case type)	culture+	86 (43)
	clinic+	34 (17)
Location of TB	Pulmonary	153 (76.5)
	Extrapulmonary	40 (20)
	Pulmonary+ Extrapulmonary	7 (3.5)
Past history of TB	New	182 (91)
	Relapse	18 (9)
Radiological findings	Normal	25 (12.5)
	Cavity	13 (6.5)
	Infiltration	113 (56.5)
	Cavity+Infiltration	32 (16)
	Pleural effusion	15 (7.5)
	Hilar fullness	2 (1)

TB: tuberculosis

summer (22%), and winter (21.5%). Table 2 shows the diagnosis rates of the cases according to the years and seasons.

Details such as warming, income level, biomass exposure, smoking, and farming activities of the patients were collected via phone calls or using records obtained by examining the hospital information system, which are shown in Table 3.

Table 2. Diagnosis of patients with tuberculosis according to seasons and years

Diagnosis Time		No (%)
Season	Spring	62(31.0)
	Summer	44(22.0)
	Autumn	51(25.5)
	Winter	43(21.5)
Years	2012	14(7.0)
	2013	30(15.0)
	2014	36(18.0)
	2015	30(15.0)
	2016	47(23,5)
	2017	20(10.0)
	2018	23(11.5)

The rate of diagnosis based on culture and smear positivity [48.4% (31)] was significantly higher than that in the clinic [10.9% (7)] among patients who used stove for warming (Fisher's exact test p=0.019; Bonferroni subgroup analysis was used). The rate of diagnosis based on culture and smear positivity [52.1% (25)] was significantly higher than that in the clinic [8.3% (4)] among patients who were exposed to biomass. Smoking, passive exposure, alcohol consumption, and farming were not associated with the case definitions.

The univariate analysis revealed no significant independent effect of warming (F=2.656, p=0.107, mean square=1.344) and biomass use (F=3.824, p=0.054, mean square=1.934) on case definitions. The mean values of air pollution parameters in the case types are presented in Table 4.

According to the case definitions, the mean values of PM_{10}, SO_2, and temperature in the diagnosed month showed no statistically significant difference. The humidity level in the month was significantly higher, during which the cases diagnosed using smear and culture positivity were compared with cases diagnosed using only culture positivity (p=0.023).

Table 3. Warming, income level, biomass exposure, smoking, and farming activities of patients who were contacted via phone or the hospital information system

		n*	%	% for all group
Warming#	Natural gas	20,00	23,8	10
	Stove	64,00	76,2	32
Biomass	No	36,00	42,9	18
exposure$	Yes	48,00	57,1	24
Smoking	No	40,00	38,5	20
	Yes	64,00	61,5	32
Passive exposure	No	23,00	31,1	11,5
to cigarette smoke	Yes	51,00	68,9	25,5
Alcohol consumption	No	69,00	79,3	34,5
	Yes	18,00	20,7	9

*: Number of patients accessible from hospital information and telephone
#: Used only for heating purposes questioned
$: Used only for cooking purposes questioned

Table 4. Mean values of air pollution parameters in case types

Mean±SD	Smear(+) cases	Culture(+)cases	Clinical diagnosis	p One-Way
	n=78*	n=82*	n=34	ANOVA
PM_{10} (µg/m^3)	94.2±51.4	84.3±43.4	90.6±52.2	0.425
SO2 (ppb)	8.0±4.6	8.2±4.3	6.3±3.6	0.103
Temperature (°C)	14.6±8.5	16.4±7.7	16.2±8.1	0.350
Pressure (g/m3)	77.3±14.5 *	71.9±16.4	77.0±12.9	0.051

*: Relative humidity level in smear-positive and culture-positive cases was significantly different from that of culture-positive cases, with LSD (one-way ANOVA with LSD) (p=0.023)
*: Smear-positive 2 cases, culture-positive 4 cases did not measure the station during the diagnosis period

Discussion

In the present study, we found that among patients who used biomass for warming and cooking, the rate of diagnosis based on smear and culture positivity was significantly higher than that of clinically diagnosed patients. Moreover, the number of smear-positive cases was significantly higher than the culture-positive cases in the months during which the relative humidity levels were high (p=0.023).

Previous studies have shown that smoke impairs the function of pulmonary alveolar macrophages (AMs). AMs comprise an important early defense mechanism against bacteria and the target cells for *M. tuberculosis* infection. AMs have been isolated from smokers' lungs (13). Öztürk et al. (4) compared 362 newly diagnosed TB patients and 409 control group subjects and reported that smoking and indoor air pollution increased the risk of TB. In the present study, 61.5% of patients were smokers and 69% were passively exposed to cigarette smoke. However, smoking and passive exposure to smoking had no effect on the case definitions.

Previous studies have also shown a significant relationship between TB prevalence and indoor air pollution from combustion of solid fuels (14, 15). Jassal et al. (16) examined smear-positive (n=111) and smear-negative (n=85) patients and found that smear-positive patients had more exposure to $PM_{2.5}$ (p=0.0044). They further indicated that exposure to ambient pollution is a risk factor for TB. $PM_{2.5}$ may play a potential role in affecting the TB lung pathology. In our study, we divided the patients into three groups according to the method of diagnosis (smear- and culture-positive, culture-positive smear-negative, and clinical diagnosis), and we found that there was no relationship between air pollution parameters (SO_2, PM_{10}).

One of the air pollutants is PM_{10}; these particles are found suspended in the atmosphere. PM_{10} penetrates into the lungs and can cause inflammation and other respiratory diseases such as asthma, chronic bronchitis, and respiratory tract obstruction. PMs >10 mm that enter the respiratory tract are caught in the nose and the nasopharynx, those <10 mm get accumulated in the bronchi, PMs with diameters of 1-2 mm are collected in the alveoli, and those measuring 0.5 mm in size are diffused into the intracapillary space from the alveoli (3). We did not find a significant result, which might be because the PM_1 and $PM_{2.5}$ values were not evaluated in our study.

Biomass fuel can be any material derived from plants or animal wastes, which is burnt by human beings. Households often continue to use simple biomass fuels even where more sophisticated fuels are available in developing countries (17). Kolappan et al. (14) conducted a case-control study and investigated the relationship between TB and biomass and found that biomass has a stronger association (OR 1.7) with pulmonary TB than smoking (OR 1.4). However, this association was found to be weaker than that of medium SLI (OR 2.0) and low SLI (OR 3.0). In this study, based on the method of diagnosis, we found that in patients who used biomass fuel and stove, the rate of diagnosis using smear and culture positivity was significantly higher than that of clinically diagnosed patients (for stove p=0.019; for biomass p=0.027).

Chen et al. (18) investigated 389 patients with TB retrospectively and observed that the number of smear-positive cases increased in the period when PM_{10} levels increased. They also found that patient smears that became negative have a lower diagnosis rate during the periods of increased PM_{10}. In our study, we did not find a relationship between PM_{10} and smear positivity and negativity.

Studies have investigated the efficacy, virulence, and effects of virus (19-21) and bacteria (22, 23) under relative humidity (RH) conditions. For instance, in a study investigating the effect of high RH on BCG (bacillus Calmette–Guerin) aerosols, it was found that when RH increased, the BCG aerosols increased more or less in a stepwise manner. The authors of that study also stated that TB contamination can be reduced by reducing the humidity levels (23). We found that as RH increases, the rate of smear positivity, which is important in infectiousness, increases.

The major limitation of our study is that the exposure of our cases to air pollution was based on estimation. Home-specific exposure assessments could not be performed due to the lack of exact geographical addresses. The monitoring was limited by the number of observations made by the National Air Quality Monitoring Network stations. Moreover, important air pollutants such as $PM_{2.5}$ and ozone measurements were not monitored in our region; therefore, the effects of these pollutants could not be investigated.

In conclusion, in our study wherein we investigated the relationship between bacteriological case definitions and indoor and outdoor air quality parameters in the context of TB, we observed that biomass exposure and warming using a stove resulted in a greater number of TB cases with smear and culture positivity. Moreover, the humidity level in the months was significantly higher, during which cases diagnosed using smear and culture positivity were compared with cases diagnosed using only culture positivity.

The major conclusion of this study is that biomass used as a cooking fuel is a risk factor for pulmonary TB, implying that TB occurrence can be reduced significantly by lowering or preventing the exposure to cooking smoke emitted from biomass fuel.

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