Delayed inpatient diagnosis and isolation of active pulmonary tuberculosis patients, a large tertiary care academic hospital experience in Riyadh, Saudi Arabia

What are we missing?

Abdulellah M. Almohaya, MBBS, Naif H. Alotaibi, MBBS, Muath A. Alotaibi, MBBS, Ali M. Somily, MBBS, FRCP.

ABSTRACT

Objectives: To identify pulmonary tuberculosis (PTB) delayed inpatient diagnosis duration and contributing factors in an academic center in Saudi Arabia (SA).

Methods: Retrospective review of all culture-confirmed PTB cases between May 2015 and April 2019. The outcomes were the timing between admission and suspicion of PTB or isolation to either: early group (within 24 hours of admission) and late group (24 hours after admission).

Results: Forty-nine cases were included with a median age of 49 years; a third of them were above 65 years of age. Most patients were of Saudi nationality and male. Approximately 38% of the cases were in the delayed group, half of them were smear-positive, with an average delay of 5.5 days. This was significant with: age above 65 years (odds ratio [OR]=8.93, 95% confidence interval [CI]=2.22-35.95) presence of non-respiratory symptoms (OR=5.6, 95% CI=1.46-122.71), chronic medical problems (OR=4.90, 95% CI=1.31-18.32), missed chest x-ray findings (OR=48, 95% CI=8.63-266.88) or procalcitonin level above 0.5 ng/mL (OR=12, 95% CI=1.58-91.08).

Conclusion: Physicians in SA need to have a low threshold for PTB consideration in elderly patients or those with a history of malignancy. A careful review of the initial chest x-ray might help to overcome missing cases of PTB.

Keywords: pulmonary tuberculosis, early diagnosis, infection control

Saudi Med J 2020; Vol. 41 (2): 183-188
doi: 10.15537/smj.2020.2.24883

From the Department of Medicine, Infectious Diseases Unit (Almohaya, Alotaibi N, Alotaibi M), from the Department of Pathology and Laboratory Medicine, Microbiology Units (Somily), King Saud University Medical City, King Saud University, Riyadh, Kingdom of Saudi Arabia

Received 20th September 2019. Accepted 26th December 2019.

Address correspondence and reprint request to: Dr. Abdulellah M. Almohaya, Department of Medicine, King Saud University Medical City, Riyadh, Kingdom of Saudi Arabia. E-mail: almohayaam@gmail.com. ORCID ID: https://orcid.org/0000-0003-4532-4626
Tuberculosis (TB) is among the 10 reasons for death worldwide. Approximately 13% of 10 million human immunodeficiency virus-negative people who were diagnosed with TB in 2017 eventually died.\(^1\) In the Kingdom of Saudi Arabia (KSA), in all age groups, 3.2 per 100,000 population were estimated to die from TB in 2017.\(^1\) Although recent studies have found TB is becoming a disease of young people; older age is still associated with a 20% fatality rate.\(^2\)\(^,\)\(^4\)

Early detection and treatment are the main pathways to eliminate TB. These help to implement the appropriate infection control measures promptly and initiate appropriate treatment. Therefore, the World Health Organization goal is to reach TB diagnosis within 2 to 3 weeks of symptom onset.\(^1\) Once pulmonary TB is suspected, a prompt isolation to an airborne-infection isolation (AlI) room is recommended by the Centers for Disease Control.\(^5\) Failure to achieve these goals could facilitate the transmission of the disease, lead to more severe illness, and result in worse outcomes.\(^6\) Tuberculosis was diagnosed late in many previous reports, including studies from Arab countries, with a median delay of 2 months.\(^7\)\^-\(^10\) In addition to the delay in patient presentation, the diagnosis of pulmonary TB (PTB) was delayed in two-thirds of the cases until more than 3 days after admission in one report.\(^11\) Moreover, a longer delay (5 days) was reported among patients in the intensive care unit (ICU) from a study in KSA.

However, there is lack of studies in the region that have previously investigated stable, non-ICU patients, who are expected to be misdiagnosed or missed. This study aimed to identify the interval time between the initial patient assessment in the emergency room and inpatient diagnosis of PTB and to explore the risk factors that might be linked to this delay in the diagnosis.

**Methods.** This study was performed at King Saud University Medical City, Riyadh, KSA. As per the hospital policy, cases of typically presenting respiratory infections have to be admitted under the general medicine team. Once a special diagnosis (example, PTB) is made, the transfer of care to the appropriate specialty is made. All clinical specimens were processed in the mycobacteriology level III laboratory of King Khalid University Hospital, Riyadh, KSA. In this laboratory, a positive culture was reported approximately 111 times annually. The study was approved in December 2018 from the University’s Institutional Review Board (IRB) [18/0843/IRB].

This study is a retrospective review of all cases of culture-confirmed PTB between May 2015 and April 2019. All patients who were diagnosed with non-tuberculous Mycobacterium, who were not admitted through the emergency department, or patients known to have PTB who were already on anti-tuberculous treatment (ATT) were not included. Patient data were collected from the Hospital Information System (HIS). All data were collected from the progress notes of the initial medical assessment. The time interval was calculated from the date of hospital admission until a physician had documented suspicion of PTB, or if not clearly documented, the date of collection of respiratory samples or the date of initiation of ATT. Cases were categorized based on the timing of isolation in an airborne-infection negative pressure isolation room, into early isolation (within 24 hours of presentation) and late isolation (after 24 hours of presentation). All recruited patients have signed consent and agreed to be part of any study undertaken in the hospital.

All demographic and clinical data were collected, including past medical history, clinical presentation including duration of symptoms (3 weeks or more), diagnosis of physician on admission, interval until diagnosis, interval until ATT initiation, length of hospital stay, and outcome. Physicians who first suspected of PTB were classified, based on their qualifications and according to their job level in the hospital, (resident doctor, fellow/registrar, or consultant).

Laboratory investigations (including procalcitonin, [PCT]) and radiological findings were recorded. Microbiological data, including the type of sample and result of acid-fast bacilli (AFB) smear classified into negative, +1 (1-9/100 fields), and +2 or more, in addition to culture identification, were also included. PubMed search and Mesh databases were performed with the terms “delayed diagnosis” and “pulmonary tuberculosis” to review previous studies in the literature.

**Statistical analysis.** Data are presented as frequency, mean, median, and standard deviation. Data analysis was performed by the Statistical Package for Social Sciences for Mac, version 23 (IBM Corp, Armonk, NY, USA) using the Chi-square test with p-value of <0.05 of statistical significance. The odds ratio (OR) for the study outcome was also calculated.

All sputum samples were collected, transferred, and processed on the same day by the microbiology
Department. Samples were stained by the Ziehl-Neelsen and auramine-rhodamine stains in which smear results were reported based on the Centers for Disease Control and Prevention classification. Then it was cultured in mycobacterial growth indicator tube (MGIT) Bactec 960 liquid medium, Lowenstein-Jensen solid pyruvate, and glycerol media. Xpert MTB/RIF molecular testing (Cepheid Inc, Sunnyvale, California, USA) was directly performed on all samples. Incubation at 37°C in the aerobic atmosphere was carried out for the solid media until mycobacterial growth. Identification was based on colony morphology, pigmentation, rate of growth, and biochemical tests, including niacin test, nitrate reductase test, and heat-stable catalase and pyrazinamidase tests.

Results. During the 4-year study period, 444 positive TB cultures were identified. Of them, 49 cases of culture-proven PTB were included. The median age was 49 years (range 16-91), a third of them (30.6%) were above 65 years of age. The majority of cases were male (65.3%), of Saudi nationality (83.7%), and were treated in non-ICU settings (81.6%), further details on patients’ characteristics, presentation, investigations and hospital course is presented in Tables 1 & 2. Processed respiratory samples were obtained from expectorated sputum in 38 cases (77.6%), induced sputum in 9 cases (18.4%), or deep sample (bronchioalveolar lavage or tracheal aspirate) in 2 cases (4%). Two-thirds of the cases’ respiratory samples were positive for acid-fast bacilli smear (35 cases, 71.4%), 26 cases were considered +2 or more. Xpert MTB/RIF was performed in 95.9% of cases; only 5 cases were negative. In addition to pulmonary TB, disseminated TB was also diagnosed in 9 cases (18.4%); TB meningitis in 4 cases (8.2%); vertebral TB in 2 cases (4.1%), and lymphadenitis in 2 cases (4.1%). Overall time interval from admission to suspicion was 2.6 days (±5.3), to isolation was 3.4 days (±6.1), to respiratory sample collection was 4.5 days (±5.9), to anti-TB initiation was 7.6 days (±10.8), to discharge was 40.8 days (±29.7), and to death was 43.4 days (±28.3).

Pulmonary TB was not suspected upon admission in 38.8% of the cases (delayed group); therefore, they were not transferred to an AII room within 24 hours of admission, while the rest (30 patients, 61.2%) were in the early group. Compared to the early group, the delayed isolation group had a longer average interval until transfer to AII room (0 versus [vs.] 5.5 days), interval until the physician order to collect the respiratory specimen (2 vs. 6.4 days).

As shown in Table 3, late decision for admission to an AII room (delayed group) was significantly associated with age above 65 years (p=0.001), presence of non-respiratory system symptoms (p=0.006), malignancy (p=0.006), chronic medical problems (p=0.014), missed chest x-ray findings (p=0.001), or PCT level above 0.5 ng/mL (p=0.01). In contrast, factors that prevented late diagnosis were the presence of cough, presence of cough in addition to at least one symptom of weight loss, night sweats or loss of appetite (p=0.018), differential diagnosis of pneumonia (p=0.001), previous hospital

### Table 1 - Overall characteristics of patients with pulmonary tuberculosis included in the study.

| Variable             | n   | (%) |
|----------------------|-----|-----|
| **Age**              |     |     |
| Above 65 years       | 15  | (30.6) |
| Below 65 years       | 34  | (69.4) |
| **Gender**           |     |     |
| Male                 | 32  | (65.3) |
| Female               | 17  | (34.7) |
| **Nationality**      |     |     |
| Saudi                | 41  | (83.7) |
| Other nationality    | 8   | (16.3) |
| **Prior medical history** |   |     |
| No known history (medically free) | 21 | (42.9) |
| Malignancy           | 7   | (14.3) |
| Diabetes             | 17  | (34.7) |
| **Tuberculosis history** |   |     |
| Previous TB disease  | 2   | (4.1) |
| Previous TB exposure | 7   | (14.3) |
| **Body mass index, kg/m²** |  |     |
| Below 18             | 21  | (42.9) |
| 18-25                | 18  | (36.7) |
| Above 25             | 10  | (20.4) |
| **Smoker**           |     |     |
| Yes                  | 18  | (36.7) |
| No                   | 31  | (63.3) |
| **Previous hospital visit** | |     |
| At least 1 previous hospital visit | 29 | (59.2) |
| 2 or more visits     | 6   | (12.2) |
| **Symptoms**         |     |     |
| Cough                |     |     |
| Cough + any B symptoms* | 40 | (81.6) |
| Fever                | 31  | (63.4) |
| Appetite loss        | 28  | (57.1) |
| Sputum               | 24  | (49.0) |
| Night sweats         | 24  | (49.0) |
| Weight loss          | 23  | (46.0) |
| Dyspnea              | 23  | (46.0) |
| Fatigue              | 20  | (40.8) |
| Pleuritic chest pain | 15  | (30.6) |
| Hemoptysis           | 8   | (16.3) |
| **Duration of suffering (since first symptom)** | |     |
| More than 3 weeks    | 14  | (28.6) |
| Less than 3 weeks    | 34  | (69.4) |

Values are presented as numbers and percentages (%).

TB: tuberculosis, *B symptoms (excluding fever): weight loss, loss of appetite, or night sweats
Delayed inpatient tuberculosis diagnosis ...

Almohaya et al

Table 2 - Hospital course and laboratory and radiological investigations of cases with pulmonary tuberculosis included in the study.

| Variable | n (%) |
|----------|-------|
| Interval until suspicion | After first 24 hours (delayed group) 19 (38.8) Smear positive 11 Within first 24 hours (early group) 30 (61.2) | |
| Doctor who first suspected PTB | Resident 30 (61.2) Fellow/registrar 13 (26.5) Consultant 6 (12.2) |
| Hospital course and outcome | Required ICU (average= 4.22 days) 9 (18.4) Discharged home 38 (77.6) Died 11 (22.4) |
| White-blood-cell counts (x 10^9/L) | Above 11 30 (61.2) Below 11 19 (38.8) |
| Procalcitonin (ng/mL) | Above 0.5 12 (24.5) Below 0.5 10 (20.4) Not done 27 (55.1) |
| C-reactive protein (mg/L) | Above 10 33 (67.3) Not done 16 (32.7) |
| Erythrocyte sedimentation rate (mm/hr) | Above 25 33 (67.3) Below 25 7 (14.3) Not done 9 (18.4) |
| ATT initiation | Within 7 days of admission 34 (69.4) After 7 days of admission 12 (24.5) |
| Chest x-ray first impression | Normal 3 (6.1) Did not comment on CXR 12 (24.5) Abnormal 34 (69.4) Location upper 15 Infiltration 13 Cavity 13 Miliary 3 Effusion 3 Pneumothorax 1 |
| Physician impression on CXR compared to CT (total 19) | Missed infiltration 7 Missed cavity 6 Missed miliary 3 |

PTB: pulmonary tuberculosis, LRT: lower respiratory tract, TB: tuberculosis, CXR: chest x-ray, CT: computed tomography, ICU: intensive care unit, ATT: anti-tuberculous therapy

visit \((p=0.011)\), and active smoking status \((p=0.012)\). Non-significant variables are presented in Table 4.

Discussion. Leading to potential infection transmission in hospital settings, more than a third (38%) of the PTB cases were missed upon admission. In particular, elderly patients and those with a history of malignancy, which could be due to co-existing confounding or misleading symptoms or atypical presentation in these patient groups. Previous studies have shown a higher proportion of failed cases upon admission, ranging from 45-67% of PTB cases.\(^7\,^{12}\) Smear-positive cases constitute approximately half of these failed cases, which is in accordance with the proportion of smear positivity in our cases (57%).\(^13\) In the late isolation group, the median interval from date of admission until isolation date was shorter in our study compared to the study by Greenaway et al\(^13\) (5.5 vs. 12.5 days); and, similar to ICU patients in KSA previously reported by Mahmoud et al\(^14\) (5.5 vs. 5 days). Older age was significantly related to delay in diagnosis or isolation of PTB (OR=8.93, 95%CI= 2.22-35.95), in agreement with previous reports.\(^7\,^{11}\) This might be explained by the unusual presentation that is usually encountered in those patients.\(^15\)

A delay in PTB diagnosis was previously linked to the absence of cough (30-day delay) or to the presence of non-respiratory symptoms (15-day delay) on presentation.\(^16,17\) Similarly, in our data, the OR of late PTB diagnosis was 8.16 (95% CI= 1.47-45.18) for the absence of cough (OR=5.60; 95% CI=1.56-19.98) for the presence of non-respiratory symptoms. The majority of these symptoms were gastrointestinal in origin (41.61%).

A previous hospital visit was reported in the literature to be associated with outpatient late diagnosis of PTB in Egypt, Somalia, and Pakistan.\(^10\) We found that those patients reported with at least one previous hospital visit were more likely to have an earlier inpatient diagnosis of PTB.

The presence of comorbid medical condition is known to influence later diagnosis of PTB. For example, Han et al\(^11\) reported the late diagnosis of PTB in patients with malignancy.\(^11\) Although patients with malignancy represent a small proportion in our study population, they were more likely to have a late diagnosis of PTB (OR=13.38, 95% CI=1.46-122.71).

Normal chest x-ray upon admission was one of the causes that might lead to delay in diagnosis of PTB, according to a meta-analysis.\(^7\) However, in our study, having normal (n=3) or abnormal (n=34) chest x-ray did not influence the time of diagnosis \((p=0.86)\). However, we identified 19 cases in which the initial assessment did not include chest x-ray interpretation. Despite being ordered and conducted, missing (or lack of documented interpretation of) chest x-ray findings were associated with late PTB diagnosis (OR=48, 95% CI: 8.63-266.88). Out of the 19 cases, we were able to assess 16 cases’ chest x-rays, and compared them to CT scans if available. Infiltration (n=7), cavity (n=6), and
Delayed inpatient tuberculosis diagnosis ...

Table 3 - Significant variables in relation to timing of suspicion and isolation of patients with pulmonary tuberculosis included in the study.

| Variables                                | Late isolation | Early isolation | P-value | OR for late isolation (95% CI) |
|------------------------------------------|----------------|-----------------|---------|-------------------------------|
| Age above 65 years                       | 11             | 4               | 0.001   | 8.93 (2.22-35.95)*            |
| Previous hospital visit                  | 7              | 22              | 0.011   | 0.21 (0.06-0.72)              |
| Smoker                                   | 3              | 15              | 0.012   | 0.17 (0.04-0.73)              |
| Had at least 1 comorbid condition        | 15             | 13              | 0.014   | 4.90 (1.31-18.32)             |
| Medically free                           | 4              | 17              | 0.014   | 0.20 (0.05-0.76)              |
| Malignancy                               | 6              | 1               | 0.006   | 13.38 (1.46-122.71)*          |
| Absence of cough                         | 7              | 2               | 0.012   | 8.16 (1.47-45.18)             |
| Cough + any B symptoms                   | 9              | 24              | 0.018   | 0.22 (0.06-0.80)              |
| Initial diagnosis of LRT infection       | 5              | 29              | <0.001  | 0.012 (0.001-0.116)           |
| Missed CXR finding                       | 16             | 3               | <0.001  | 48 (8.63-266.88)*             |
| Procalcitonin above 0.5 (ng/mL)          | 9              | 3               | 0.01    | 12 (1.58-91.08)*              |

*Positive significant result. †After 24 hours of presentation. ‡B symptoms (excluding fever): Weight loss, loss of appetite, or night sweats.

Table 4 - Non-significant variables in relation to timing of suspicion and isolation of patients with pulmonary tuberculosis included in the study.

| Variables                                | Late isolation (after 24hrs) | Early isolation | P-value |
|------------------------------------------|------------------------------|-----------------|---------|
| Female gender                            | 7                            | 10              | 0.801   |
| Fever                                    | 11                           | 20              | 0.535   |
| Sputum                                   | 6                            | 18              | 0.309   |
| Dyspnea                                  | 7                            | 16              | 0.260   |
| Pleuritic chest pain                     | 3                            | 12              | 0.073   |
| Hemoptysis                               | 2                            | 6               | 0.324   |
| Weight loss                              | 6                            | 17              | 0.086   |
| Night sweats                             | 7                            | 17              | 0.176   |
| Appetite loss                            | 9                            | 19              | 0.271   |
| Fatigue                                  | 10                           | 10              | 0.181   |
| Duration of suffering >3 weeks           | 13                           | 21              | 0.766   |
| Any finding in respiratory examination   | 10                           | 17              | 0.782   |
| Admitted under other than general medicine| 6                            | 18              | 0.052   |

Level of physician who first suspected PTB

| Resident                                 | 11                           | 19              |         |
| Fellow/Registrar                         | 7                            | 6               | 0.281   |
| Consultant                               | 1                            | 5               |         |
| Smear negative                           | 8                            | 16              | 0.09    |
| WBC above 11 (x 10^9/L)                  | 6                            | 13              | 0.411   |
| Discharged home                          | 12                           | 26              | 0.059   |
| Death at 30 days                         | 7                            | 4               | 0.059   |

WBC: white blood cells, CXR: chest x-ray.

miliary (n=3) findings were missed by the first medical assessment. Leung et al18 found that smoking history is more likely to be associated with TB (OR >12.09). Therefore, previous meta-analysis has shown that history of smoking might influence physicians early PTB suspicion. Similarly, our data reproduced this finding with early suspicion and isolation (OR=5.71, 95% CI: 1.36-23.93).

Procalcitonin level is a good deferential tool between lower respiratory tract infections due to TB versus common bacterial pathogens. A meta-analysis reviewed the use of PCT to distinguish TB from non-TB causes of pulmonary infections and found that negative likelihood ratio (LR [-] 0.67, 95%CI 0.50-0.90) for PCT above 0.25 ng/ml.12 Although we used higher cut-off for PCT, patients who were eventually diagnosed with PTB and had PCT above 0.5 were more likely to have delayed isolation (OR=12, 95%CI: 1.58-91.08), increasing the possibility of bacterial superinfection.12

The specialty of the admitting team might lead to a short time between admission to isolation. Han et al11 reported delayed diagnosis among patients who were admitted under other than infectious diseases or pulmonology teams. No significant association was found in our study in relation to admitting team specialty (p=0.052).11

Study limitations. The study was retrospective and included a relatively small number of patients. Also, it was based on a single center experience, which may limit the strength of the study and subsequently the ability to generalize the conclusion. However, addressing this issue in this study should draw researchers’ attention to preform larger studies to explore more predictors compared to control cases and to build a scoring tool for early detection of PTB in low-incidence countries.

In conclusion, despite being in a country with a low prevalence of TB, physicians should have a low threshold to consider early isolation in patients who...
are elderly or those who present with a history of malignancy. A careful review of the initial chest x-ray might help to overcome missing cases of PTB. Lastly, a physician should not be deterred from suspecting PTB by the presence of non-respiratory symptoms or high PCT levels.

Acknowledgment. The authors gratefully acknowledge Editage (www.editage.com) for the English language editing.

References

1. World Health Organization. Global Tuberculosis Report 2018. Geneva (S2): WHO; 2018. Available from URL: https://www.who.int/tb/publications/global_report/en/
2. Memish ZA, Bamgboye EA, Abuljadayel N, Smadi H, Abouzeid MS, Hakeem RF et al. Incidence of and risk factors associated with pulmonary and extra-pulmonary tuberculosis in Saudi Arabia (2010-2011). PLoS One 2014; 9: e95654.
3. Aljohaney A. Mortality of patients hospitalized for active tuberculosis in King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Saudi Med J 2018; 39: 267-272.
4. Abouzeid MS, Al Hakeem RF, Memish ZA. Mortality among tuberculosis patients in Saudi Arabia (2001-2010). Ann Saudi Med 2013; 33: 247-252.
5. Jensen PA, Lambert LA, Iademarco MF, Ridzon R. Guidelines for preventing the transmission of mycobacterium tuberculosis in health-care settings, 2005. Morb Mortal Wkly Rep (MMWR) 2005; 54: 1-141.
6. Shah NS, Yuen CM, Heo M, Tolman AW, Becerra MC. Yield of contact investigations in households of patients with drug-resistant tuberculosis: systematic review and meta-analysis. Clin Infect Dis 2014; 58: 381-391.
7. Getnet F, Demissie M, Assefa N, Mengistie B, Worku A. Delay in diagnosis of pulmonary tuberculosis in low-and middle-income settings: systematic review and meta-analysis. BMC Pulm Med 2017; 17: 202.
8. Sreeramareddy CT, Panduru KV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. BMC Infect Dis 2009; 9: 91.
9. Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC Public Health 2008; 8: 15.
10. Bassili A, Seita A, Baghdadi S, AlAbsi A, Abdilai I, Agboarwalla M, et al. Diagnostic and treatment delay in tuberculosis in 7 countries of the Eastern Mediterranean Region. Infect Dis Clin Pract 2008; 16: 23-35.
11. Han J, Nam BD, Park SY, Park J, Lee E, Lee EJ, et al. Risk factors for delayed isolation of patients with active pulmonary tuberculosis in an acute-care hospital. Sci Rep 2019; 9: 4849.
12. Huang SL, Lee HC, Yu CW, Chen HC, Wang CC, Wu JY, et al. Value of procalcitonin in differentiating pulmonary tuberculosis from other pulmonary infections: a meta-analysis. Int J Tuberc Lung Dis 2014; 18: 470-477.
13. Greenaway C, Menzies D, Fanning A, Grewal R, Yuan L, Mark FitzGerald J, et al. Delay in diagnosis among hospitalized patients with active tuberculosis—predictors and outcomes. Am J Respir Crit Care Med 2002; 165: 927-933.
14. Mahmoud ES, Baharoon SA, Alsafi E, Al-Jahdaly H. Acute respiratory distress syndrome complicating community-acquired pneumonia secondary to mycobacterium tuberculosis in a tertiary care center in Saudi Arabia. Saudi Med J 2016; 37: 973-978.
15. Smith PW, Rajagopalan S, Yoshikawa TT. Tuberculosis in long-term-care facilities. Infect Control Hosp Epidemiol 2000; 21: 611-615.
16. Maciel EL, Golub JE, Peres RL, Hadad DJ, Fávero JL, Molino LP, et al. Delay in diagnosis of pulmonary tuberculosis at a primary health clinic in Vitoria, Brazil. Int J Tubere Lung Dis 2010; 14: 1403-1410.
17. Jurcev-Savicevic A, Mulic R, Kozul K, Ban B, Valic J, Bacun-Ivcek L, et al. Health system delay in pulmonary tuberculosis treatment in a country with an intermediate burden of tuberculosis: a cross-sectional study. BMC Public Health 2013; 13: 250.
18. Leung CC, Yew WW, Chan CK, Tam CM, Lam CW, Chang KC, et al. Smoking and tuberculosis in Hong Kong. Int J Tuberc Lung Dis 2003; 7: 980-986.