



Journal of Medical Sciences

ISSN 1682-4474

science
alert

ANSI*net*
an open access publisher
<http://ansinet.com>



Research Article

Diagnosis of a Spectrum of Pulmonary Tuberculosis at Islam Hospital Sukapura, Jakarta, Indonesia: A Retrospective Study of 317 Cases

¹Tri Ariguntar Wikanningtyas, ²Mochammad Hatta, ²Muhammad Nasrum Massi, ¹Indah Pratiwi, ³Muhammad Fachri, ⁴Slamet Sudi Santoso, ⁴Amir Syarifuddin, ^{2,5}Ressy Dwiyanthi and ²Rizki Amelia Noviyanthi

¹Department of Clinical Pathology, Faculty of Medicine and Health, University of Muhammadiyah Jakarta, Indonesia

²Molecular Biology and Immunology Laboratory, Faculty of Medicine, Hasanuddin University Makassar, Indonesia

³Department of Pulmonology and Respiratory Medicine, Faculty of Medicine and Health, University of Muhammadiyah Jakarta, Indonesia

⁴Department of Medical Education, Faculty of Medicine and Health, University of Muhammadiyah Jakarta, Indonesia

⁵Department of Medical Microbiology, Faculty of Medicine, Tadulako University, Palu, Indonesia

Abstract

Background and Objective: In 2015, Indonesia ranked as the second highest tuberculosis-infected country in the world, after India. The accuracy of diagnosis determines the success of treatment and control and reduction of incidence of tuberculosis. Therefore, this study aimed to describe the diagnosis spectrum of pulmonary tuberculosis. **Materials and Methods:** This was a retrospective study with a cross-sectional design. The study subjects were 317 patients diagnosed with tuberculosis from 1st January, 2015 to 30th June, 2017 at Islam Hospital Sukapura Jakarta, Indonesia. **Results:** Most tuberculosis patients were 18-49 years old (55.5%) and male (63.4%), at senior high school (56.2%) and worked as seller/farmer/fisher/labor/entrepreneur (36.6%). Most patients had a productive cough (96.2%) with duration of cough ≥ 2 weeks (70.3%), shortness of breath (80.1%), loss weight (85.8%), night sweating (77.6%) were smear-negative (68.8%) and had duplex pulmonary tuberculosis (54.6%). The most common diagnoses were category I spectrum tuberculosis, prescribed anti-tuberculosis drugs (91.8%), pulmonary tuberculosis (94.3%), smear-negative tuberculosis (68.8%) and new case tuberculosis (85.5%). Smear-negative new case tuberculosis was the most frequent diagnosis (71.6%). Association between tuberculosis recurrence and the result of sputum microscopy was statistically significant ($p = 0.009$). **Conclusion:** The accuracy of tuberculosis diagnosis greatly determines the success of treatment and control of tuberculosis infection. In this study, the most frequent diagnoses were spectrum pulmonary tuberculosis, pulmonary tuberculosis, smear-negative tuberculosis, new case tuberculosis and smear-negative new case tuberculosis.

Key word: Infection, smear-negative tuberculosis, pulmonary tuberculosis, diagnosis spectrum, anti-tuberculosis drugs

Citation: Tri Ariguntar Wikanningtyas, Mochammad Hatta, Muhammad Nasrum Massi, Indah Pratiwi, Muhammad Fachri, Slamet Sudi Santoso, Amir Syarifuddin, Ressy Dwiyanthi and Rizki Amelia Noviyanthi, 2018. The diagnosis of a spectrum of pulmonary tuberculosis at Islam Hospital Sukapura, Jakarta, Indonesia : A retrospective study of 317 cases. J. Med. Sci., 18: 143-148.

Corresponding Author: Mochammad Hatta, Laboratory of Molecular Biology and Immunology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

Copyright: © 2018 Tri Ariguntar Wikanningtyas *et al.* This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Tuberculosis (TB) infection is a leading cause of mortality. Over 95% of TB mortality cases occur in poor and developing countries¹. The number of newly diagnosed pulmonary tuberculosis cases in Indonesia increased from 324,539 in 2014 to 330,910 in 2015. Indonesia is ranked as the second highest TB-infected country in the world, after India^{2,3}.

The fundamental issues for the diagnosis and management of TB are the accuracy of the diagnosis, appropriate and standardized treatment, monitoring and treatment evaluation and public health responsibility. An improved accuracy of diagnosis would increase the success of TB treatment and control and thus reduce the incidence of tuberculosis⁴.

Indonesia has the opportunity to half the rates of morbidity and mortality due to TB infection recorder for 2015. The Millennium Development Goals (MDGs) indicator for TB control has achieved its target. Diagnosis of pulmonary tuberculosis in an adult should be mainly based on bacteriology examination, such as direct microscopy examination and rapid testing. Previous study revealed that AFB smear positive found more in adult pulmonary TB patients with type 2 DM compared to TB patient without type 2 DM. It also found statistically significant between type 2 DM with the AFB smear results on adult pulmonary TB patient⁵.

If the bacteriology examination result is negative, the diagnosis of pulmonary tuberculosis could be based on appropriate clinical findings and supportive examinations (at least chest X-ray) conducted by a trained doctor. Extrapulmonary tuberculosis is diagnosed based on clinical findings and the affected organ(s). The definite diagnosis of extra pulmonary tuberculosis is based on the clinical findings, bacteriology examination and histopathology examination from the sample of the affected organ⁶.

Based on the above, this study aimed to describe the diagnosis spectrum of pulmonary tuberculosis based on clinical findings, bacteriology, laboratory and radiology examination at Islam Hospital Sukapura Jakarta, Indonesia from 2015 to the first semester of 2017.

MATERIALS AND METHODS

Study design: This was a retrospective study with a cross-sectional design. The study subject was all patients diagnosed was tuberculosis at Islam Hospital Sukapura Jakarta, Indonesia, from 1st January, 2015 to 30th June, 2017. This study used the secondary data from patient medical records and had been approved by the Research Ethics Committee of Islam Hospital Sukapura Jakarta, Indonesia. The

sample was collected consecutively. The inclusion criteria were: (1) Patients who had been diagnosed as tuberculosis, (2) Adult tuberculosis patients >18 years old, (3) Having bacteriology examination, laboratory examination, radiology examination, the status of TB drug and the type of TB data available. The exclusion criterion was that the suspected tuberculosis patient had not yet been treated as a TB patient.

Study data: The data collected from medical records included patient profile (name, number of medical record, age, weight, birth date, gender, address, marital status, educational background), clinical findings, physical examination results, radiology examination results, bacteriology examination results (Spot/Morning/Spot sputum examination or GeneXpert), TB diagnosis and TB drug status.

Diagnosis of tuberculosis: Tuberculosis diagnosis was classified based on anatomy, history of TB drug and sputum microscopic examination. Based on the anatomy, TB diagnosis was classified as pulmonary or extra pulmonary tuberculosis. Pulmonary tuberculosis is a TB infection involving the lung parenchyma or tracheobronchial and extra pulmonary tuberculosis involving the organs outside of the lung parenchyma, such as the pleura, lymph node, abdomen, genitourinary tract, skin, joint, bone and meninges. Based on the history of TB drugs, TB diagnosis was classified as new or relapse cases. New case TB includes TB patients with no prior history of TB treatment or history of anti-tuberculosis drugs treatment in the past 1 month and relapse-case TB includes TB patients with a history of TB treatment and declared to have been cured or completed the treatment and recently diagnosed as recurrent TB. Based on sputum microscopy examination, TB diagnosis was classified as smear-positive TB or smear-negative TB.

Statistical analysis: Data were expressed as the percentage of the group for categorical and continuous variables. Appropriate descriptive statistics, such as proportion and percentage were used to analyze the findings and to draw the inferences. A database was created in Microsoft Excel and after appropriate cleaning, statistical analyses were performed using SPSS software (version 20.0 SPSS, Inc., Chicago, IL, USA). The Chi-square test was used to detect an association between the recurrence and sputum AFB results. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Based on the TB patient medical record at Islam Hospital Sukapura Jakarta, Indonesia, from 2015 to June 2017, 317 TB patients were included in the study.

Table 1: Characteristics of adult TB patient at Islam Hospital Sukapura Jakarta, Indonesia, from January, 2015-June, 2017

Characteristics	Frequency (Hz)	Percentage
Age		
18-49 years old	176	55.5
50-79 years old	141	44.5
>80 years old	0	0
Gender		
Male	201	63.4
Female	116	36.6
Bloody cough		
Yes	76	24
No	241	76
Shortness of breath		
Yes	254	80.1
No	63	19.9
Productive cough		
Yes	305	96.2
No	12	3.8
Cough duration		
≥2 weeks	223	70.3
<2 weeks	94	29.7
Loss weight		
Yes	272	85.8
No	45	14.2
Fever		
Yes	272	85.8
No	45	14.2
Night sweating		
Yes	246	77.6
No	71	22.4
AFB		
Negative	218	68.8
1+	40	12.6
2+	37	11.7
3+	22	6.9
Chest X-ray		
Duplex pulmonary TB	173	54.6
Sinistra pulmonary TB	35	11
Dextra pulmonary TB	63	19.9
Pleuritis TB	17	5.4
Other	29	9.1
Level of education		
No educational background	3	0.9
Primary school	63	19.9
Junior high school	57	18.0
Senior high school	178	56.2
D3/S1/S2/S3	16	5.0
Working status		
Unemployed/retired	42	13.2
Housewife	83	26.2
Government employee/police/military	5	1.6
Private employee	70	22.1
Seller/farmer/fisher/labor/entrepreneur	116	36.6
Professional worker	1	0.3
Anti-tuberculosis drugs		
Category I	291	91.8
Category II	26	8.2

AFB: Acid fast bacilli

Most TB patients are 18-49 years old (55.5%) and male (63.4%) (Table 1). Based on clinical symptoms, most of the

Table 2: Diagnosis Spectrum Pulmonary Tuberculosis Patient at Islam Hospital Sukapura Jakarta, Indonesia from 2015-2017

Diagnosis spectrum	Number	Percentage
Based on anatomy		
Pulmonary TB	299	94.3
Extra pulmonary TB	18	5.7
Based on AFB		
Smear-positive TB	99	31.2
Smear-negative TB	218	68.8
Based on history of TB drugs		
New case TB	271	85.5
Relapse case TB	46	14.5
Based on history of TB drugs and microscopy examination		
Smear-positive new case TB	77	28.4
Smear-negative new case TB	194	71.6
Smear-positive relapse case TB	22	47.8
Smear-negative relapse case TB	24	52.2

AFB: Acid fast bacilli

patients have a productive cough (96.2%) with duration of cough ≥2 weeks (70.3%), shortness of breath (80.1%), weight loss (85.8%) and night sweating (77.6%). Based on chest X-ray, most of the patients had duplex pulmonary TB (54.6%). Based on the level of education, most of the patients were in senior high school (56.2%), with the most frequent working status being seller/farmer/fisher/labor/entrepreneur group (36.6%). Based on anti-tuberculosis drugs category, most of the patients were receiving category I anti-tuberculosis drugs (91.8%).

The classifications of the diagnosis spectrum of pulmonary tuberculosis at Islam Hospital Sukapura Jakarta, Indonesia, from 2015-2017 are shown in Table 2. Based on anatomy, most of the subjects were diagnosed with pulmonary tuberculosis (94.3%). Based on AFB, most of the TB case were smear-negative TB (68.8%) and based on TB drug history, new case TB (85.5%) was more frequent than cases of relapse TB. Overall, smear-negative new case TB was the most frequent classification (71.6%).

The result of bivariate analysis based on the classification of TB diagnosis and the result of sputum microscopy from Table 3 showed that there is a significant association between TB recurrence and the result of sputum microscopy ($p = 0.009$).

DISCUSSION

In this study, most TB patients were male. The higher rate of TB in males might be attributed to their high-risk behaviors, such as alcohol, substance and tobacco abuse and also their typical work type. Smoking habit, type of job, lifestyle, environmental interactions and working outdoor might put people at higher risk of *Mycobacterium tuberculosis* infection^{7,8}. Compared with females, earlier studies also reported a direct association between male gender and risk of

Table 3: Comparisons between TB recurrence and the results of microscopy examinations of pulmonary tuberculosis patients at Islam Hospital Sukapura, Indonesia, from 2015-2017

	Chi-Square test	Microscopy examination		p-value	OR	CI 95%
		Smear-negative (%)	Smear-positive (%)			
Classification	New case	194 (71.6%)	77 (28.4%)	0.009	0.011	0.009-0.013
	Relapse case	24 (52.2%)	22 (47.8%)			

TB infection, as well as unsuccessful TB treatment outcome. A clear association between TB incidence and gender has also been reported⁸. Similar to previous studies conducted by Riello *et al.*⁷, Atif *et al.*⁸, Lin *et al.*⁹, Marais *et al.*¹⁰, Sunnetcioglu *et al.*¹¹ and WHO¹², pulmonary TB patients were more likely to be males than females. The Indonesia Health profile, in 2013, 2014 and 2015, released by the Health Government Indonesian Republic, also reported that pulmonary TB was more frequent in males than females (prevalence = 0.4%)^{3,4}.

Most of the patients were 18-49 years old. The higher rate of TB in those of productive age might be attributed to the high risk of TB droplet transmission in their environment or workplace. Similar results were reported by Lin *et al.*⁹ and Marais *et al.*¹⁰, where TB mostly occurred in those of productive age. Based on the WHO Tuberculosis Report 2017 in the Asian Region, TB cases were more frequent in those of productive age (ranged 25-48 years old)¹². A similar result was reported by Riello *et al.*⁷, where the mean age of TB patients was 46 years. A previous study including 310 TB patients who underwent sputum microscopy examination found that 58.7% of patients were 16-40 years old¹³. In Indonesia, it is estimated that 75% of pulmonary TB patients are 15-50 years old¹⁴. Similar results have shown that tuberculosis cases in Southeast Asia are mostly found in those of productive age (15-44 years old)¹².

Most of the patients were in senior high school (56.2%). A possible justification for this finding is that poorly educated patients fail to protect and prevent themselves from airborne infection and might have lower compliance to TB treatments. A Malaysian study found a positive relationship between TB-related knowledge and education level of the patients⁸. In a study conducted by Esmael *et al.*¹⁵ and Javed *et al.*¹⁶, the majority of pulmonary TB patients were illiterate and uneducated (58.1 and 51.7%). Similarly, Jethani *et al.*¹⁷ also reported that 95% of patients had a family history of the disease and were uneducated. Most patients were members of the seller/farmer/fisher/labor/entrepreneur group (36.6%). This could be explained by working outdoors, which might put people at a higher risk of TB droplet transmission. Similarly, Gupta *et al.*¹⁸ also reported a higher prevalence of TB infection among laborers (44%).

Most of the patients had pulmonary TB infection (94.3%). Lung parenchyma was the main predilection of aerobic bacteria, including *Mycobacterium tuberculosis*. Also, TB infection was easier to transmit via droplet than other transmission routes¹². Another possible justification for this finding is the limited availability of diagnostic tools for extra pulmonary TB relative to pulmonary TB. Similar results were reported in the studies by Gomes *et al.*¹⁹ in Brazil and Memish *et al.*²⁰ in Saudi Arabia. The WHO¹² Tuberculosis Report also stated that pulmonary TB was more frequent (85%) than extra pulmonary TB.

Based on the WHO and The International Union Against Tuberculosis and Lung Disease (IUATLD) guidelines, sputum microscopy examination should be conducted at least three times²¹. The majority of the patients in our study had smear-negative TB (68.8%). A possible explanation for this finding was the low sensitivity value of sputum microscopy examination. This could be due to the limitation of Ziehl-Neelsen staining ability in detecting AFB<10⁴-10⁵ basil per mL under optimal conditions. It has been shown that the sensitivity of AFB microscopy examination^{22,23} is 22-43%. Ziehl-Neelsen staining could only reach its maximum sensitivity of up to 60% under optimal conditions²⁴. Similarly, the WHO¹² Report also showed that smear-negative TB is more frequent than smear-positive TB in the Philippines (63 vs. 37%). Geleta *et al.*²⁵ also found that the sensitivity value of the sputum microscopy examination is lower than other diagnostic tools, such as GeneXpert MTB/RIF (9.3 vs. 16.7%) in high prevalence TB infection. Reechaipichitkul *et al.*²⁶ also showed that the sensitivity and specificity of sputum AFB smears are lower than the GeneXpert MTB/RIF assay test (48 vs. 94% and 84 vs. 92%). Therefore, the low sensitivity and high specificity value of the sputum microscopy examination could explain the higher incidence of smear-negative TB in this study.

In this study, new cases of TB were more frequent than relapse cases. However, there were a greater proportion of smear-positive cases among the relapse TB cases (from 28.4-47.8%). This was supported by our finding of a significant association between sputum microscopy examination and TB recurrence (p = 0.009). High defaulter rate and the irrational use of second-line drugs by some public and private providers

might contribute to the increase of relapse-cases²⁷. Also, low levels of TB-related knowledge might contribute to low compliance with TB treatment⁸. Therefore, it could be assumed that this subgroup of people might stop taking anti-TB drugs and then develop relapses. A similar result was also reported by Cross *et al.*²⁸.

Relapse cases were defined as patients who had a history of TB drugs and were declared as cured or had completed treatment and then recently diagnosed as having suffered a recurrent TB episode⁶. Resistance would develop if patients had a poor response to adequate therapy²⁷. Rohmawaty *et al.*²⁹ stated that inadequate exposure to anti-tuberculosis drugs could be a reasonable factor of suboptimal response to therapy. This is supported by the findings of Burhan *et al.*³⁰, which showed an association between low concentration of anti-tuberculosis drugs and poor response to therapy. Rohmawaty *et al.*²⁹ also showed a significant difference in *Mycobacterium tuberculosis* load between the conversion group and non-conversion group after first-line TB drug treatment ($p = 0.04$). This could explain the significant association between TB recurrence and the result of sputum microscopy examination in this study.

This study describes the spectrum of pulmonary tuberculosis and emphasizes its importance in establishing the diagnosis of tuberculosis infection. Establishing proper diagnosis by general practitioners is crucial in determining appropriate therapy selection and preventing recurrence of tuberculosis.

CONCLUSION

The accuracy of TB diagnosis will greatly determine the success of treatment and control of tuberculosis infection. Classification of TB diagnosis also varied depending on the anatomy, the result of microscopy examination, history of treatment and both history of treatment and result of microscopy examination. In this study, the diagnosis spectrum of pulmonary tuberculosis is most frequent in pulmonary tuberculosis, smear-negative tuberculosis, new case tuberculosis and smear-negative new case TB.

SIGNIFICANCE STATEMENT

Although, there has been considerable previous research on tuberculosis, the novelty of this research was to describe the spectrum of diagnosis of pulmonary tuberculosis based on anatomy, microscopic examination, medical history and the combination of medical history and microscopic examination.

This study also addressed the relationship between microscopic examination and relapse case, which had been only briefly discussed in previous studies.

ACKNOWLEDGMENT

Authors would like to thank the Director of the Islam Hospital Sukapura Jakarta, Indonesia, the Dean of the Faculty of Medicine and Health, University of Muhammadiyah Jakarta and all who participated in this study.

REFERENCES

1. Falzon, D., H.J. Schunemann, E. Harausz, L. Gonzalez-Angulo, C. Lienhardt, E. Jaramillo and K. Weyer, 2017. World Health Organization treatment guidelines for drug-resistant tuberculosis, 2016 update. Eur. Respir. J., Vol. 49. 10.1183/13993003.02308-2016.
2. Reviono, R., W. Setianingsih, K.E. Damayanti and R. Ekasari, 2017. The dynamic of Tuberculosis case finding in the era of the public-private mix strategy for Tuberculosis control in Central Java, Indonesia. Global Health Action, Vol. 10. 10.1080/16549716.2017.1353777.
3. Kementerian Kesehatan Republik Indonesia, 2015. Profil kesehatan Indonesia 2015. Kementerian Kesehatan Republik Indonesia.
4. PerhimpunanDokterParu Indonesia, 2011. Tuberkulosis pedoman diagnosis dan penatalaksanaan di Indonesia. <http://klikdpi.com/konsensus/Xsip/tb.pdf>.
5. Fachri, M., M. Hatta, S. Abadi, S.S. Santoso and T.A. Wikanningtyas *et al.*, 2018. Comparison of Acid Fast Bacilli (AFB) smear for *Mycobacterium tuberculosis* on adult Pulmonary tuberculosis (TB) patients with type 2 Diabetes Mellitus (DM) and without type 2 DM. Respir. Med. Case Rep., 23: 158-162.
6. Kementrian Kesehatan Republik Indonesia, 2014. Pedoman nasional pengendalian tuberkulosis. Direktorat Jendral Pengendalian Penyakit Dan Penyehatan Lingkungan. http://www.tbindonesia.or.id/opendir/Buku/bpn_p-tb_2014.pdf
7. Riello, F.N., R.T.S. Brigido, S. Araujo, T.A. Moreira, L.R. Goulart and I.M.B. Goulart, 2016. Diagnosis of mycobacterial infections based on acid-fast bacilli test and bacterial growth time and implications on treatment and disease outcome. BMC Infect. Dis., Vol. 16. 10.1186/s12879-016-1474-6.
8. Atif, M., S.A.S. Sulaiman, A.A. Shafie, I. Ali, M. Asif and Z.U. Babar, 2014. Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia. BMC Infect. Dis., Vol. 14. 10.1186/1471-2334-14-399.

9. Lin, C.H., C.J. Lin, Y.W. Kuo, J.Y. Wang and C.L. Hsu *et al*, 2014. Tuberculosis mortality: Patient characteristics and causes. *BMC Infect. Dis.*, Vol. 14. 10.1186/1471-2334-14-5
10. Marais, E., C.K. Mlambo, J.J. Lewis, N. Rastogi and T. Zozio *et al*, 2014. Treatment outcomes of multidrug-resistant tuberculosis patients in Gauteng, South Africa. *Infection*, 42: 405-413.
11. Sunnetcioglu, A., M. Sunnetcioglu, I. Binici, A.I. Baran, M.K. Karahocagil and M.R. Saydan, 2015. Comparative analysis of pulmonary and extrapulmonary tuberculosis of 411 cases. *Ann. Clin. Microbiol. Antimicrob.*, Vol. 14. 10.1186/s12941-015-0092-2.
12. WHO., 2017. Global tuberculosis report, 2017. World Health Organization, Geneva, Switzerland. http://www.who.int/tb/publications/global_report/gtbr2017_main_text.pdf
13. Guernier, V., T. Diefenbach-Elstob, D. Pelowa, S. Pollard, G. Burgess, E.S. McBryde and J. Warner, 2018. Molecular diagnosis of suspected tuberculosis from archived smear slides from the Balimo region, Papua New Guinea. *Int. J. Infect. Dis.*, 67: 77-81.
14. Hatta, M., A.R. Sultan, N. Tandirogang, Masjudi and Yadi, 2010. Detection and identification of mycobacteria in sputum from suspected tuberculosis patients. *BMC Res. Notes*, Vol. 3. 10.1186/1756-0500-3-72.
15. Esmael, A., I. Ali, M. Agonafir, A. Desale, Z. Yaregal and K. Desta, 2013. Assessment of patients' knowledge, attitude and practice regarding pulmonary tuberculosis in eastern Amhara regional state, Ethiopia: Cross-sectional study. *Am. J. Trop. Med. Hyg.*, 88: 785-788.
16. Javed, I., M.T. Javed, Z. Mahmood, M. Riaz, R. Iqbal, N. Rafiq and S. Rafiq, 2017. Socio-demographic and co-morbidity study of TB patients from selected areas of Punjab Pakistan. *Res. J. Life Sci. Bioinform. Pharm. Chem. Sci.*, 3: 109-121.
17. Jethani, S., J. Semwal, R. Kakkar and J. Rawat, 2012. Study of epidemiological correlates of tuberculosis. *Indian J. Community Med.*, 24: 304-309.
18. Gupta, S., V. Shenoy, C. Mukhopadhyay, I. Bairy and S. Muralidharan, 2011. Role of risk factors and socio economic status in pulmonary tuberculosis: A search for the root cause in patients in a tertiary care hospital, South India. *Trop. Med. Int. Health*, 16: 74-78.
19. Gomes, T., B. Reis-Santos, A. Bertolde, J.L. Johnson, L.W. Riley and E.L. Maciel, 2014. Epidemiology of extra pulmonary tuberculosis in Brazil: A hierarchical model. *BMC Infect. Dis.*, Vol. 14. 10.1186/1471-2334-14-9
20. Memish, Z.A., E.A. Bamgboye, N. Abuljadayel, H. Smadi, M.S. Abouzeid and R.F. Al Hakeem, 2014. Incidence of and risk factors associated with pulmonary and extra-pulmonary tuberculosis in Saudi Arabia (2010-2011). *PLoS One*, Vol. 9. 10.1371/journal.pone.0095654.
21. Tuberculosis Division International Union against Tuberculosis and Lung Disease, 2005. Tuberculosis bacteriology-priorities and indications in high prevalence countries: Position of the technical staff of the tuberculosis division of the international union against tuberculosis and lung disease. *Int. J. Tuberc. Lung Dis.*, 9: 355-361.
22. Bansal, R., P.K. Sharma, S.C. Jaryal, P.K. Gupta and D. Kumar, 2017. Comparison of sensitivity and specificity of ZN and fluorescent stain microscopy with culture as gold standard. *J. Tuberculosis Res.*, 5: 118-128.
23. Singhal, R. and P.M. Vithal, 2015. Microscopy as a diagnostic tool in pulmonary tuberculosis. *Int. J. Mycobacteriol.*, 4: 1-6.
24. Agrawal, M., A. Bajaj, V. Bhatia and S. Dutt, 2016. Comparative study of GeneXpert with ZN stain and culture in samples of suspected pulmonary tuberculosis. *J. Clin. Diagn. Res.*, 10: 9-11.
25. Geleta, D.A., Y.C. Megerssa, A.N. Gudeta, G.T. Akalu, M.T. Debela and K.D. Tulu, 2015. Xpert MTB/RIF assay for diagnosis of pulmonary tuberculosis in sputum specimens in remote health care facility. *BMC Microbiol.*, Vol. 15. 10.1186/s12866-015-0566-6.
26. Reechaipichitkul, W., T. Suleesathira and T. Chaimanee, 2017. Comparison of GeneXpert MTB/RIF assay with conventional AFB smear for diagnosis of pulmonary tuberculosis in Northeastern Thailand. *Southeast Asian J. Trop. Med. Public Health*, 48: 313-321.
27. Collins, D., F. Hafidz and D. Mustikawati, 2017. The economic burden of tuberculosis in Indonesia. *Int. J. Tuberculosis Lung Dis.*, 21: 1041-1048.
28. Cross, G.B., K. Coles, M. Nikpour, O.A. Moore and J. Denholm *et al*, 2014. TB incidence and characteristics in the remote gulf province of Papua New Guinea: A prospective study. *BMC Infect. Dis.*, Vol. 14. 10.1186/1471-2334-14-93.
29. Rohmawaty, E., H.S. Sastramihardja, R. Ruslami and M.N. Shahib, 2017. Mycobacterium Tuberculosis Load and Rifampicin Concentration as Risk Factors of Sputum Conversion Failure. In: *Advances in Biomolecular Medicine*, Hofstra, R., N. Koibuchi and S. Fucharoen (Eds.). CRC Press, London, ISBN: 9781351804189, pp: 75-78.
30. Burhan, E., C. Ruesen, R. Ruslami, A. Ginanjar and H. Mangunnegoro *et al*, 2013. Isoniazid, rifampin and pyrazinamide plasma concentrations in relation to treatment response in Indonesian pulmonary tuberculosis patients. *Antimicrob. Agents Chemother.*, 57: 3614-3619.