Prevalence of and Factors Influencing Anti-Tuberculosis Treatment Non-Adherence Among Patients with Pulmonary Tuberculosis: A Cross-Sectional Study in Anhui Province, Eastern China

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCE 1 Xue-Hui Fang*
E 2 Hui-Hui Shen*
F 3 Wan-Qian Hu
D 2 Qi-Qi Xu
F 1 Lei Jun
B 4 Zhi-Ping Zhang
C 1 Xiao-Hong Kan
ABE 1 Dong-Chun Ma
A 5 Guo-Cui Wu

1 Anhui Provincial TB (Tuberculosis) Institute, Hefei, Anhui, P.R. China
2 Department of Clinical Medicine, The Second School of Clinical Medicine, Anhui Medical University, Hefei, Anhui, P.R. China
3 Department of Clinical Medicine, College of Medicine, Yangzhou University, Yangzhou, Jiangsu, P.R. China
4 Anqing Center for Disease Control and Prevention, Anqing, Anhui, P.R. China
5 School of Nursing, Anhui Medical University, Hefei, Anhui, P.R. China

Corresponding Authors:
Source of support:

* Xue-Hui Fang and Hui-Hui Shen contributed equally to this work and should be considered co-first authors
Dong-Chun Ma, e-mail: madongchun126@126.com, Guo-Cui Wu, e-mail: gcwu82@126.com
Departmental sources

Background: To assess the non-adherence rate among pulmonary tuberculosis (TB) patients in Anhui Province, eastern China and to explore the influential factors, so as to identify targets for intervention.

Matreial/Methods: A total of 339 TB patients were recruited from TB dispensaries in 8 counties of Anhui Province, eastern China using a stratified sampling method. All study subjects were surveyed using a structured questionnaire. Differences between groups involving categorical data were analyzed using the chi-square test.

Results: Overall, of the 339 patients, 33.63% missed medication. Divorced and widowed patients were more likely to miss medication compared with those who were married or unmarried ($P<0.01$). Regarding the knowledge related to topics such as transmission route, preventive measures, and suspicious symptoms, the awareness rate in the group with good medication compliance was higher than in the group with poor compliance ($P<0.05$). We found that compliance was not significantly associated with seeking medical treatment in professional institutions, the national free TB treatment policy, or discrimination ($P>0.05$). The rate of non-compliance under supervision (26.10%) was lower than that without supervision (64.18%) ($P<0.001$).

Conclusions: The anti-TB treatment non-adherence rate in TB patients is relatively high in Anhui Province, eastern China, and is associated with marital status, annual income, TB knowledge, and medical staff visits.

MeSH Keywords: Factor Analysis, Statistical • Patient Compliance • Tuberculosis

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/913510

📄 2613   ▦ 5   📊 —   📑 28

Background

Tuberculosis (TB) remains a major public health problem globally despite the fact that the causative organism has been known for more than 100 years, and highly effective drugs and vaccines have been available for decades [1]. China has one of the highest burdens of TB worldwide and it ranks second among the 22 high-burden countries in the world [2]. In order to control the TB epidemic, China has implemented the Directly Observed Treatment Short Course (DOTS) strategy, which has been promoted vigorously by the World Health Organization (WHO) since 1991 and has provided universal coverage for patients with TB. Furthermore, all diagnosed TB cases (including new and relapsed patients) are required to be registered at the local TB dispensaries (LTD) and reported to upper-level health authorities in China. As a result, the cure rate of active TB cases has reached over 90% [3].

However, with the emergence of pulmonary TB multidrug-resistant (MDR) or extensively drug-resistant strains (XDR), treatment outcome of the disease is getting increasingly worse, contributing to prolonged duration of infectiousness and continued transmission [4–7]. Hence, it is of great importance to determine the risk factors leading to the emergence of MDR-TB strains to improve its overall management. As a consequence of global concerns about this problem, many studies have found that poor patient adherence to anti-TB treatment is the main risk factor [8]. Many TB patients do not complete their 6-month course of anti-TB medications and are not aware of the importance of sputum re-examinations, thereby putting themselves at risk of developing multidrug-resistant and extensively drug-resistant forms of tuberculosis and relapse [9]. According to the WHO, adherence to TB treatment is the extent to which a patient's medication-taking coincides with the prescribed treatment. Those who have completed treatment (directly observed therapy strategy, DOTS) or are cured correspond to adherents, and the patients who do not complete treatment correspond to non-adherents [10]. Non-adherence to TB treatment threatens the success of treatment, increases the risk of TB spread, causes drug resistance, and increases morbidity and mortality [4,11–13]. Many quantitative studies have investigated risk factors associated with poor adherence to anti-TB treatment [9,14,15]. However, few studies have examined the relationship between socio-economic determinants and treatment adherence. Thus, the aim of this study was to assess the adherence rate among pulmonary TB patients in Anhui Province, eastern China and to explore the factors affecting adherence to anti-TB treatment.

Material and Methods

Sample size and sampling technique

The study used the stratified cluster sampling method. Data on pulmonary TB patients were collected from LTDs, and all patients were diagnosed and registered between January 1, 2015 and December 30, 2015. With DOTS treatment management, patients get their medicine at the outpatient clinic and are regularly checked. Community doctors or family supervisors are responsible for overseeing patients. After stochastically selecting 8 counties from the whole province, 45 eligible pulmonary TB patients over 15 years old were randomly selected from each county. In this study, the diagnosis of pulmonary TB was established according to the Tuberculosis Diagnosis Standard issued by the Ministries of Health of the People's Republic of China. The diagnosis of active TB was confirmed by experienced clinicians according to sputum smear examination, chest X-ray examination for exudative lesions, cavities, and lesion size, and anti-tuberculosis treatment. Second, Smear-positive or smear-negative patients who were newly treated were included and the treatment regimens were all 2HRZ/4HR. We distributed 360 copies of the questionnaire, and 339 copies of the valid questionnaire were returned, with an effective rate of 94.17%.

Study design

This study was conducted in Anhui province, which consists of 106 counties (districts) with a total population of 62.548 million at the end of 2015. A total of 8 counties/districts (including Yuexi county, Taihu county, Jinzhai country, Shou county, Feixi county, Huoqiu county, Shushan district, and Tongcheng city) were selected as study sites. Based on relevant literature and expert consultation, the questionnaire was developed and administered by trained doctors and health workers. The questionnaire is composed of 4 parts: general information, status of treatment, knowledge on TB prevention and treatment, and access to information on TB. The first section includes 13 questions involving demographic and economic characteristics (such as gender, occupation, educational level, marital status, annual income, annual income, medication adherence, and presence of chronic diseases). The second section consists of 23 questions, including questions on missed medication and reasons why, completion of treatment course, whether visited by the medical staff and levels of the staff, and distance from residence to the nearest clinic or hospital. The section on TB knowledge is composed of 12 questions covering items such as tuberculosis transmission, suspicious symptoms of tuberculosis, and BCG. The access to information on TB section is made up of 5 clear multiple-choice questions. For the respondents who were unable to response themselves, the questionnaire was completed with the help of trained LTD nurses.

Table 1. The Socio-demographic and clinical characteristics of the study participants.

Variables		Frequency	Percent (%)
Gender	Male	259	76.4
	Female	80	23.6
Occupation	Farmer	261	77.0
	Worker	40	11.8
	Others	38	11.2
Educational level	Primary and illiterate	170	50.2
	Junior and senior high schools or technical secondary schools	142	41.9
	Junior college or above	27	7.9
Marital status	Unmarried	74	21.8
	Married	234	69.0
	Divorced or widowed	31	9.2
Annual income	<5000	124	36.6
	5000–9999	78	23.0
	10000–19999	60	17.7
	≥20000	77	22.7
Sputum smear status	Positive	81	23.9
	Negative	258	76.1
Suffering from chronic diseases	Yes	85	25.1
	No	254	74.9
Medication adherence	Adherent	114	33.6
	Non-adherent	225	66.4

Definition

We used the frequency of missing taking medication to define adherence to TB treatment. In the course of treatment, if the patient had not missed any dose of medication or if the frequency of missing taking medication is 0, it was judged as adherent. If the frequency of missing taking medication is greater than or equal to 1, it was judged as non-adherent.

Statistical analysis

Statistical analysis was conducted with SPSS version 23.0 and Epi Info version 7.0. All data are presented as mean ±SD if normally distributed. The chi-square test or Fisher's exact test was used to assess differences in categorical data between 2 groups. Two-tailed $P \leq 0.05$ was considered statistically significant.

Ethical approval

All participants were fully informed before written consents were taken. Then, written informed consent was obtained from each participant who was willing to take part in this study. The participants were assured about the confidentiality of the data.

Results

Characteristics of the Study Participants

A total of 339 pulmonary TB patients were included in the study, with a mean age of 49.17±15.55 years; 259 (76.4%) were males and 80 (23.6%) were females. Most of them were farmers (77.0%). In terms of education level, 50.15% were primary level and illiterate, 41.89% were junior and senior high school or technical secondary school level, and only 7.96% were junior

Table 2. Patients' knowledge of TB.

Variables		Number	Proportion (%)
Do you think TB is serious	Very serious	107	31.6
	Serious	179	52.8
	Not too serious	53	15.6
Tuberculosis is spread by droplets	Know	312	92.0
	Unknow	27	8.0
Hand washing, ventilation, and exercise can prevent TB	Know	304	89.7
	Unknow	35	10.3
Cough sputum more than two weeks or sputum with blood, suspected TB	Know	285	84.1
	Unknow	54	15.9
Patients should go to professional TB treatment institutions	Know	328	96.8
	Unknow	11	3.2
TB can be cured by sticking to regular treatment	Know	324	95.6
	Unknow	15	4.4
The free policy	Know	325	95.9
	Unknow	14	4.1
Can BCG prevent TB	Yes	170	50.1
	Uncertain	69	20.4
	No	55	16.2
	Unknown	45	13.3
TB patients should be given enough care instead of discrimination	Yes	289	85.3
	No	14	4.1
	Unknown	36	10.6

college level or above. More than half of the patients (234; 69%) were married. Most patients had a low annual income (less than 10 000 yuan). Furthermore, smear-positive adult PTB patients accounted for 23.9% and smear-negative 76.1%. Overall, 25.1% had chronic diseases and 33.6% of patients missed doses of medication. The results are shown in Table 1.

Knowledge of TB

We found that 92.0% of patients knew that pulmonary TB was transmitted through droplets. Regarding prevention, 89.7% believed that frequent hand washing, good ventilation, and physical exercise could effectively prevent pulmonary TB. Results showed that 84.1% of patients were aware that TB should be suspected when coughing and spitting last for more than 2 weeks or when there is blood in the sputum. As for treatment, 96.8% of the patients understood that TB patients should be treated by professional prevention and treatment institutions; 95.6% believed that TB could be cured through formal treatment, while 95.9% knew that the country had free TB medication policies. About half of the patients believed that Bacillus Calmette Guerin (BCG) vaccination can prevent TB. Most of them

thought TB patients should be given adequate care and should not be discriminated against. The results are displayed in Table 2.

The relationship between patient adherence and demographic factors

Most demographic factors, including gender, occupation, and educational level, were not related with TB patient's adherence to treatment ($P>0.05$). Notably, the ordinal logistic regression model showed that marital status ($\chi^2=36.32$, $P<0.001$) and annual income ($\chi^2=25.08$, $P<0.001$) were independent influencing factors. With regard to annual income, patients whose annual income was less than 5000 yuan had the highest frequency of missing doses of medication (54.65%), while patients whose annual income was greater than or equal to 20 000 yuan had the lowest rate of non-compliance (22.97%) (Table 3).

The relationship between patient adherence and knowledge of TB

Those patients who understood the symptoms of tuberculosis ($\chi^2=13.84$, $P<0.001$), who knew how to prevent TB

Table 3. Socio-demographic factors for medication adherence.

Variables		Adherent		Non-adherent		χ^2	P
		N	%	N	%		
Sex	Male	168	64.86	91	35.14	1.12	0.291
	Female	57	71.25	23	28.75		
Occupation	Farmer	170	65.13	91	34.87	1.90	0.387
	Worker	26	65.00	14	35.00		
	Others	29	76.32	9	23.68		
Educational status	Primary and illiterate	105	61.76	65	38.24	3.25	0.197
	Junior and senior high schools or technical secondary schools	101	71.13	41	28.87		
	Junior college or above	19	70.37	8	29.63		
Marital status	Unmarried	43	58.11	31	41.89	36.32	<0.001
	Married	175	74.79	59	25.21		
	Divorced or widowed	7	22.58	24	77.42		
Annual income	<5000	39	45.35	47	54.65	25.08	<0.001
	5000–9999	50	66.67	25	33.33		
	10000–19999	79	75.96	25	24.04		
	≥20000	57	77.03	17	22.97		

(χ^2=14.94, P<0.001), who had knowledge of BCG (χ^2=31.96, P<0.001), and who were not worried that they would miss work (χ^2=30.33, P<0.001) were more likely to adhere to TB treatment. Among TB patients who were adherent, 79.44% considered TB to be a very serious problem. However, only 20.56% of patients who missed doses of medication thought that TB was very serious, revealing that the understanding of these people needs to be improved. As for related knowledge about TB, the awareness rate of the group who had not missed doses of medication was clearly higher than that of the non-adherent treatment group (P<0.05). On the other hand, as far as whether TB patients should be given professional diagnosis and treatment in formal medical institutions, the national policy and stigma, no significant differences were found between the 2 groups (P>0.05). The results are shown in Table 4.

The relationship between treatment adherence and other related factors

Having medical staff visits (χ^2=34.92, P<0.001) and the level of the visiting personnel (χ^2=23.93, P<0.001) were confirmed to be associated factors. The proportion of non-adherent patients who were visited by medical staff was only 26.10%, while the group who were not visited by medical staff was 64.18%, and this difference was significant (P<0.001). In addition, when visiting personnel were at the county level and above, the proportion of non-adherent patients was only 10.34%, while when the visiting personnel was a village doctor, the rate was 40.00% Also, there was no significant difference between the distance from residence to the nearest clinic or hospital and treatment adherence (P=0.096). The results are displayed in Table 5.

Association between adherence to treatment and the rate of successful treatment

This study included both smear-positive and smear-negative TB patients. The treatment outcome of smear-positive patients is indicated by cure rate, while the treatment outcome of smear-negative patients is described as the completion rate of treatment rather than cure rate. Therefore, in our study, we combined these together as the rate of successful treatment. We found that the rate of successful treatment among the adherent group and the non-adherent group was 96.00% and 83.33%, respectively (χ^2=16.02, P<0.001), demonstrating a link between adherence to treatment and the rate of successful treatment.

Table 4. Comparison of medication adherence in patients with different knowledge of TB.

Variables		Adherent N (%)		Non-adherent N (%)		χ^2	P
Do you think TB is serious	Very serious	85	(79.44)	22	(20.56)	13.73	0.001
	Serious	104	(58.10)	75	(41.90)		
	Not too serious	36	(67.92)	17	(32.08)		
Tuberculosis is spread by droplets	Know	215	(68.91)	97	(31.09)	11.31	0.001
	Unknow	10	(37.04)	17	(62.96)		
Cough sputum more than two weeks or sputum with blood, suspected TB	Know	201	(70.53)	84	(29.47)	13.84	<0.001
	Unknow	24	(44.44)	30	(55.56)		
Hand washing, ventilation, and exercise can prevent TB	Know	212	(69.74)	92	(30.26)	14.94	<0.001
	Unknow	13	(37.14)	22	(62.86)		
Patients should go to professional TB prevention and treatment institutions	Know	219	(66.77)	109	(33.23)	–	0.518*
	Unknow	6	(54.55)	5	(45.45)		
TB can be cured by sticking to regular treatment	Know	219	(67.59)	105	(32.41)	–	0.046*
	Unknow	6	(40.00)	9	(60.00)		
The free policy	Know	216	(66.46)	109	(33.54)	–	0.536*
	Unknow	9	(64.29)	5	(35.71)		
Can BCG prevent TB	Yes	130	(76.47)	40	(23.53)	31.96	<0.001
	Uncertain	51	(73.91)	18	(26.09)		
	No	24	(43.64)	31	(56.36)		
	Unknown	20	(44.44)	25	(55.56)		
TB patients should be given enough care instead of discrimination	Yes	195	(67.47)	94	(32.53)	4.07	0.131
	No	11	(78.57)	3	(21.43)		
	Unknown	19	(52.78)	17	(47.22)		
If Leaders knew whether it affected your work	Yes	39	(51.32)	37	(48.68)	30.33	<0.001
	No	128	(81.53)	29	(22.67)		
	Unknown	58	(54.72)	48	(45.28)		
If symptoms disappear, whether continue taking the medication	Yes	219	(70.65)	91	(29.35)	0.14	0.712
	No	6	(20.69)	23	(79.31)		

* Means that the theoretical number is too small and adopt the exact probability method.

Discussion

Overall, the treatment adherence among pulmonary TB patients in Anhui province was not good. Only 66.4% of the patients were considered adherent. The proportion of patients who had missed one or more doses of medication during treatment was 33.6%. In our study, a total of 114 people had missed taking medication. Among them, 101 people missed <10 doses of medication (88.6%) and 74 people missed <5 doses of medication (64.9%). Although the proportion of patients who missed taking medication was high, those who missed <5 doses accounted for the majority; therefore, the rate of successful treatment was relatively high. However, compared with the adherent group (96.00%), the rate of successful treatment was significantly lower in the non-adherent group (P<0.001). Some previous studies in China also indicated low treatment adherence among TB patients [16,17]. Zhou et al. reported that 16% of migrant TB patients were not adherent to TB therapy [16]. The proportion of non-adherence in our study was higher than those reported in previous studies, and the difference may be due to differences in study design and definition of non-adherence to anti-TB treatment. No criterion standard definition of adherence to anti-TB treatment is currently available, although consideration of quantity and timing of missed medication or

Table 5. The relationship between treatment adherence and other related factors.

Variables		Adherent		Non-adherent		χ^2	P
		N (%)		N (%)			
The distance from residence to the nearest clinic or hospital	0–10 Km	190	(65.52)	100	(34.48)	4.69	0.096
	11–20 Km	28	(80.00)	7	(20.00)		
	>21 Km	7	(50.00)	7	(50.00)		
Have medical staff visited	Yes	201	(73.90)	71	(26.10)	34.92	<0.001
	No	24	(35.82)	43	(64.18)		
Visiting personnel	Village doctor	75	(60.00)	50	(40.00)	23.93	<0.001
	Rural doctor	74	(83.15)	15	(16.85)		
	Doctors at county level and above	52	(89.66)	6	(10.34)		

hospital appointments was recommended by the WHO [18]. For example, a frequently used definition of non-adherence is the WHO-recommended measure, which defines a TB treatment defaulter as a patient who interrupted treatment for 2 consecutive months or more, but some studies considered a patient who had missed 10% or more of the total prescribed doses of TB drugs as non-adherent [16,19].

Adherence to long-term treatment is a complex phenomenon, influenced by various factors. Our study showed that TB knowledge in our subjects was fairly good: 92.0% of the patients knew that pulmonary TB was transmitted by droplets, 95.6% believed that TB could be cured through formal treatment, and 95.9% knew that the country had a free TB treatment policy. The relationship between presence of social support and cooperation with the treatment procedure was confirmed. Previous studies in India indicated that social support was important in treatment supervision [20]. We found that married patients had better treatment adherence than unmarried and divorced patients, which is consistent with studies that indicated family members played a positive role in treatment supervision [16,21].

Additionally, in accordance with the findings of other studies, this study also illustrated that the socio-economic status of TB patients was an important factor influencing TB treatment adherence [22–24]. In a study in Ghana, default from treatment was significantly associated with income, ability to afford supplementary drugs, availability of social support, and problems relating with others while on treatment [25]. Our study found that patients whose annual income was well below the average for the country had the highest frequency of missing doses of medication. China has implemented the DOTS at the county level from 2005, which provides free and standard short-course chemotherapy, but patients still have

other costs, such as transportation and opportunity cost during treatment. Hence, when a strong economic guarantee is provided, patients are more likely to receive regular treatment and to have good treatment adherence.

Our study also indicated that TB disease knowledge is a vital factor associated with TB treatment adherence, showing that greater TB knowledge is associated with better adherence to treatment, which agrees with previous studies [2,16,20,26]. Moreover, supervision by medical staff during the treatment was an important indicator affecting patient compliance. Interestingly, there was a positive effect of medical personnel visiting on improving treatment adherence, which was similar to findings in Nepal and India [27,28], in which visits from higher-level visiting personnel were associated with better patient adherence. During the process of visiting patients, the medical staff teach patients about TB knowledge and made them more aware of the importance of treatment adherence. Undoubtedly, the higher the level of medical staff, the higher the level of health education. On the other hand, patients also thought that medical staff paid more attention to them and had more confidence to be cured. Furthermore, our study revealed an association between adherence to treatment and the rate of successful treatment, suggesting that patients with good adherence have a better prognosis.

Several limitations of this study need to be considered. Firstly, the treatment adherence levels were based on self-reported information from patients, so recall bias was unavoidable. Secondly, the occurrence of adverse drug reactions of taking anti-TB medications, which was a determinant of non-adherence, was not taken into consideration in our analysis. Despite these limitations, the present study has several merits. First, the questionnaire was developed using a range of scientific methodologies including literature reviews, focus groups, and pilot testing. Second, some key variables were measured in

this study setting, such as individual or household income and marital status. Finally, we found that social support from family members or medical staff visiting could improve adherence.

Conclusions

Our study indicates that treatment adherence among pulmonary TB patients in Anhui province is not high. Moreover, marital status, annual income, medical personnel supervision, and patient

knowledge about anti-TB treatment is crucial to improving pulmonary TB patients' treatment adherence. Understanding the risk factors affecting adherence to anti-tuberculosis treatment may help make more effective policies targeting the most at-risk patients and provide a scientific basis for making effective policies and measures in the future.

Conflict of interests

None.

References:

1. Das R, Baidya S, Das JC, Kumar S: A study of adherence to DOTS regimen among pulmonary tuberculosis patients in West Tripura District. Indian J Tuberc, 2015; 62(2): 74–79

2. Zhou C, Chu J, Geng H et al: Pulmonary tuberculosis among migrants in Shandong, China: Factors associated with treatment delay. BMJ Open, 2014; 4(12): e005805

3. Xianyi C, Fengzeng Z, Hongjin D et al: The DOTS strategy in China: Results and lessons after 10 years. Bull World Health Organ, 2002; 80(6): 430–36

4. Centers for Disease Control (CDC): Patients with recurrent tuberculosis. MMWR Morb Mortal Wkly Rep, 1982; 30(52): 645–47

5. Espinal M, Laserson K, Camacho M et al: Determinants of drug-resistant tuberculosis: Analysis of 11 countries. Int J Tuberc Lung Dis, 2001; 5(10): 887–93

6. Lönnroth K, Castro K, Chakaya J et al: Tuberculosis control and elimination 2010–50: Cure, care, and social development. Lancet, 2010; 375(9728): 1814–29

7. Zager E, McNerney R: Multidrug-resistant tuberculosis. BMC Infect Dis, 2008; 8: 10

8. Abarca Tomás B, Pell C, Bueno Cavanillas A, Guillén Solvas J et al: Tuberculosis in migrant populations. A systematic review of the qualitative literature. PLoS One, 2013; 8(12): e82440

9. El Sahly H, Wright J, Soini H et al: Recurrent tuberculosis in Houston, Texas: A population-based study. Int J Tuberc Lung Dis, 2004; 8(3): 333–40

10. Putera I, Pakasi TA, Karyadi E: Knowledge and perception of tuberculosis and the risk to become treatment default among newly diagnosed pulmonary tuberculosis patients treated in primary health care, East Nusa Tenggara: A retrospective study. BMC Res Notes, 2015; 8: 238

11. Maartens G, Wilkinson R: Tuberculosis. Lancet, 2007; 370(9604): 2030–43

12. Kilpatrick G: Compliance in relation to tuberculosis. Tubercle, 1987; 68(2 Suppl.): 31–32

13. Chaulk C, Kazandjian V: Directly observed therapy for treatment completion of pulmonary tuberculosis: Consensus Statement of the Public Health Tuberculosis Guidelines Panel. JAMA, 1998; 279(12): 943–48

14. Munro S, Lewin S, Smith H et al: Patient adherence to tuberculosis treatment: A systematic review of qualitative research. PLoS Med, 2007; 4(7): e238

15. Shargie E, Lindtjørn B: Determinants of treatment adherence among smear-positive pulmonary tuberculosis patients in Southern Ethiopia. PLoS Med, 2007; 4(2): e37

16. Zhou C, Chu J, Liu J et al: Adherence to tuberculosis treatment among migrant pulmonary tuberculosis patients in Shandong, China: A quantitative survey study. PLoS One,. 2012; 7(12): e52334

17. Hu D, Liu X, Chen J et al: Direct observation and adherence to tuberculosis treatment in Chongqing, China: A descriptive study. Health Policy Plan, 2008; 23(1): 43–55

18. Woimo TT, Yimer WK, Bati T, Gesesew HA: The prevalence and factors associated for anti-tuberculosis treatment non-adherence among pulmonary tuberculosis patients in public health care facilities in South Ethiopia: A cross-sectional study. BMC Public Health, 2017; 17(1): 269

19. Yao S, Huang W, van den Hof S et al: Treatment adherence among sputum smear-positive pulmonary tuberculosis patients in mountainous areas in China. BMC Health Serv Res, 2011; 11: 341

20. Barnhoorn F, Adriaanse H: In search of factors responsible for noncompliance among tuberculosis patients in Wardha District, India. Soc Sci Med, 1992; 34(3): 291–306

21. Tekle B, Mariam D, Ali A: Defaulting from DOTS and its determinants in three districts of Arsi Zone in Ethiopia. Int J Tuberc Lung Dis, 2002; 6(7): 573–79

22. Zhou C, Tobe RG, Chu J et al: Detection delay of pulmonary tuberculosis patients among migrants in China: A cross-sectional study. Int J Tuberc Lung Dis, 2012; 16(12): 1630–36

23. Wang W, Jiang Q, Abdullah A, Xu B: Barriers in accessing to tuberculosis care among non-residents in Shanghai: A descriptive study of delays in diagnosis. Eur J Public Health, 2007; 17(5): 419–23

24. Cheng G, Tolhurst R, Li R et al: Factors affecting delays in tuberculosis diagnosis in rural China: A case study in four counties in Shandong Province. Trans R Soc Trop Med Hyg, 2005; 99(5): 355–62

25. Wanyonyi AW, Wanjala PM, Githuku J et al: Factors associated with interruption of tuberculosis treatment among patients in Nandi County, Kenya 2015. Pan Afr Med J, 2017; 28(Suppl. 1): 11

26. Liam C, Lim K, Wong C, Tang B: Attitudes and knowledge of newly diagnosed tuberculosis patients regarding the disease, and factors affecting treatment compliance. Int J Tuberc Lung Dis, 1999; 3(4): 300–9

27. Wares D, Singh S, Acharya A, Dangi R: Non-adherence to tuberculosis treatment in the eastern Tarai of Nepal. Int J Tuberc Lung Dis, 2003; 7(4): 327–35

28. Jaiswal A, Singh V, Ogden J et al: Adherence to tuberculosis treatment: Lessons from the urban setting of Delhi, India. Trop Med Int Health, 2003; 8(7): 625–33