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Factors associated with patient delay among new tuberculosis patients in Anqing, China.

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Abstract

Tuberculosis remains a serious global public health problem. Delays in diagnosis and treatment of tuberculosis patients not only increases transmission of tuberculosis in the community but may also lead to more serious complications and higher mortality. The objective of this study was to assess factors associated with patient delay among new pulmonary tuberculosis patients in Anqing, China. From June 2013 to December 2014, a cross-sectional study was carried out among 1083 new pulmonary tuberculosis patients. Data were collected using a structured questionnaire (interviewer-administered questionnaire for illiterate patients and self-administered questionnaire for literate patients) and tuberculosis management system. All participants were divided into longer patient delay and shorter patient delay groups and non-conditional logistic regression was applied to determine the factors associated with longer patient delay. The median patient delay was 11 days (interquartile range: 1-34). The logistic regression showed that factors associated with longer patient delay included having expectoration when first consulted the healthcare system (OR: 1.520; 95 % CI: 1.020-2.266; P=0.040), having blood-tinged sputum when first consulted the healthcare system (OR: 0.490; 95% CI: 0.278-0.864; P=0.014) and unknown whether there were tuberculosis patients around (OR: 1.903; 95 % CI: 1.229-2.947; P=0.004). Tuberculosis patients with different symptoms seem to have different behaviors of patient delay. A combination of interventions is needed to encourage tuberculosis patients to seek appropriate health-care as early as possible.

Keywords: Patient delay, Tuberculosis, New tuberculosis patients, Factors.

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Introduction

Tuberculosis (TB) is a major public health burden throughout the world. Globally, about 9.6 million TB cases were diagnosed and 1.5 million died of TB in 2014 [1]. Early detection, diagnosis, and prompt initiation of effective chemotherapy are essential for an effective TB control program. However, delays in diagnosis and treatment are inevitable.

The Fifth National Sampling Survey of TB Epidemiology showed that only 47% Chinese patients with TB symptoms sought medical care timely [2]. In other developing countries, for example, in Northwest Ethiopia, 62% TB patients sought medical care after WHO recommended period (21 days) [3]; in Uganda, 58% TB patients had unacceptable patient delay and 88% had health service delay [4]. Delays in diagnosis and treatment of TB patients not only increases disease transmission within the community [5] but may also lead to more serious complications, higher mortality [6] and multi-drug resistant tuberculosis (MDR-TB) [7].

Patient delay, an important type of the delays, was studied frequently across countries. The median of patient delay varies significantly from 14 days in Malawi [8] to 30 days in South Brazil [9] and Angola [10] and up to 59 days in Ghana [11], 61 days in Mozambique [12]. The situation of patient delay is so serious; therefore, it is necessary to know the situation of patient delay in our country and then take measures to improve the situation.

Factors contributing to patient delay in diagnosis and treatment are likely to vary depending on the population's local settings. The study among Chinese TB patients found that living in rural areas, female patients, and low educational attainment were risk factors for patient delay [13]. The previous report focusing on Asia emphasized that male, unemployed, low income, hemoptysis, positive sputum smear and long travel time/ distance to the first healthcare provider were significantly

correlated with patient delay [14]. Another research in sub-Saharan Africa showed that consulting traditional healers first consistently led to patient delay [15]. In addition, multiple care-seeking [16], no medical insurance, perceived stigma [11], farming, low TB knowledge and coexistence of a chronic disease [12] were associated with prolonged patient delay. Therefore, discussing the problems of TB diagnosis and treatment in different regions, and finding the main factors associated with patient delay are crucial to TB control.

China has the world's second largest tuberculosis epidemic. Anqing area, with high proportion population of farming in Anhui Province, has high TB prevalence. Studies on the delays in TB diagnosis and treatment in this area are absent. In this regard, it is necessary to explore the duration of patient delay and factors related to it among new TB patients in Anqing, Anhui Province.

Material and Methods

Study setting

Anqing area, situated at Southwest Anhui Province, has high TB prevalence. In 2013, the number of rural population was 3.16 million (59.04%) and the per capita gross domestic product (GDP) was 26657.89 RMB. Anqing area was selected not only due to its high proportion population of farming and high TB prevalence but also because it is a typical rural area in the central of China, and can represent the Central China in some extent.

Study population

This study was conducted from June 2013 to December 2014 in Anqing area. All the new pulmonary tuberculosis patients among eight counties and three municipal districts would be asked to fill in the questionnaire (interviewer-administered questionnaire for illiterate patients and self-administered questionnaire for literate patients) when they were registered in the TB management system of local Centers for Disease Control and Prevention (CDCs). 1118 TB patients who had lived in their current residence over six months before the survey were recruited. Among them 35 were excluded due to lack of information about patient delay.

The investigators in local TB dispensaries and CDCs had been trained before the survey. All TB patients were informed about the objectives of this study and provided verbal informed consent before the survey. Patients who refused to participate or worked in the city temporarily (seasonal workers) were dropped.

Questionnaire and data collection

The questionnaire was designed based on the standardized questionnaire on major issues of national infectious diseases [17]. It was pre-tested among 100 TB patients and modified as necessary. The first section of the questionnaire was information on socio-demographic characteristics (age, sex, ethnicity, residence, education level, family members and family income in the past year, smoking and drinking habits), medical insurance, TB patients around, history of bacillus Calmette-Guérin (BCG) vaccination, health education accessibility of TB.

The second section of the questionnaire was patients' core knowledge on TB. It contained 11 items and was divided into several sections: TB pathogen (1 question), symptoms (3 questions), detection methods (2 questions), transmission (2 questions) and treatment (3 questions). Answers were established as yes, no and unknown and each question was awarded 1 mark for the correct answer, while each incorrect or unknown answer was given 0 mark. Then the score was dichotomized into two categories (good or poor knowledge) using the median score as the cut-off.

The third section of the questionnaire was about patient delay. Patients were asked to estimate the time in days from the onset of first TB symptoms to the first presented to the healthcare system (either public or private). Then we classified patient delay into two categories: shorter patient delay and longer patient delay using median as the cut-off. The symptoms when they first contacted with healthcare system and the institution where they first consulted were inquired as well.

Operational definition of terms

- Patient delay was defined as the time interval between the onset of any tuberculosis symptom (e.g., cough, expectoration, blood-tinged sputum, or night sweats) and first contact with the healthcare system (i.e., health centers, hospitals or TB treatment centers) [8,10,12,18].
- New tuberculosis patient refers to a patient who has never treated for tuberculosis or who has taken anti-tuberculosis drugs for less than one month or who has taken anti-tuberculosis drugs regularly for more than one month but has not completed the standard treatment regimen.
- Smoking included patients who were smoking presently or smoked previously.
- In term of education level, "elementary" was referred to elementary school; "secondary" was referred to junior high school, senior high school and secondary specialized school; "higher" was referred to junior college and above.
- "TB patients around" was referred to TB patients who were in the household, neighborhood, work place or school.
- Income was referred to per capita annual income (RMB).
- Body mass index (BMI) was calculated as weight in kilogram divided by height in meter squared, and then BMI was classified into three groups (<18.5 kg/m^2, 18.5-23.9 kg/m^2, >23.9 kg/m^2).

Statistical analysis

EpiData software Version 3.1 was used for data entry and SPSS Version 18.0 was used for data analysis. The descriptive statistics (including median, interquartile range, frequencies and percentages) were used to show the distribution of the personal socio-demographic characteristics, core knowledge of TB, symptoms and institutions when first presented to the

healthcare system, duration of patient delay. The median patient delay was used to dichotomize patient delay into acceptable (shorter) or longer delay [10,11,18,19]. Comparisons between groups were made using the Chi-square test for qualitative/categorical variables. The multivariate logistic regression analysis was used to evaluate associated factors of longer patient delay. Variables showed marginal association with longer patient delay in univariate analysis ($P \leq 0.20$) [4,10,11,18,19] were included in the multivariate logistic model. $P < 0.05$ was considered to indicate a statistically significant difference.

Ethics statement

The study is carried out in compliance with the Declaration of Helsinki of the World Medical Association. According to a protocol approved by Medical Ethics Committee of Wannan Medical College, all participants were informed about the objectives of this study and provided verbal informed consent before the survey.

Results

Socio-demographic characteristics of patients

Among the 1083 new TB patients, 72.3% were males, and the median age was 55 years (Interquartile Range (IQR): 38-65). A majority of patients had medical insurance (96.73%). There were 38.84% and 36.13% patients had elementary and secondary educational level, respectively. Most patients were from rural areas (87.87%) and had 3 or more family members (86.51%). Only 37.55% patients had BCG vaccination and 33.00% indicated having access to health education of TB. In addition, smear negative and smear positive patients accounted for 51.71% and 33.70%, respectively.

Table 1. *Socio-demographic characteristics of new Tuberculosis (TB) patients and the comparison with shorter and longer patient delay.*

Characteristics		Total (n, %)	Patient delay		χ^2	P
			Longer (n, %)	Shorter (n, %)		
Gender	Male	783 (72.30)	372 (70.71)	404 (73.86)	1.34	0.247
	Female	300 (27.70)	154 (29.29)	143 (26.14)		
Age group	<25	133 (12.33)	56 (10.49)	77 (14.13)	4.321	0.229
	25-45	214 (19.83)	103 (19.29)	111 (20.37)		
	45-65	443 (41.06)	231 (43.26)	212 (38.90)		
	≥ 65	289 (26.78)	144 (26.97)	145 (26.61)		
	Missing	4	-	-		
Residence	Town	116 (12.13)	58 (12.11)	58 (12.16)	0.001	0.981
	Rural area	840 (87.87)	421 (87.89)	419 (87.84)		
	Missing	127	-	-		
Ethnicity	Han	1073 (99.54)	533 (99.81)	540 (99.26)	0.767	0.381
	Others	5 (0.46)	1 (0.19)	4 (0.74)		
	Missing	5	-	-		
Education	Illiterated	220 (20.54)	118 (22.26)	102 (18.85)	5.93	0.115
	Elementary	416 (38.84)	216 (40.75)	200 (36.97)		
	Secondary	387 (36.13)	174 (32.83)	213 (39.37)		
	Higher	48 (4.48)	22 (4.15)	26 (4.81)		
	Missing	12	-	-		
Medical insurance	Yes	1035 (96.73)	513 (96.61)	522 (96.85)	0.047	0.828
	No	35 (3.27)	18 (3.39)	17 (3.15)		
	Missing	13	-	-		
Income	<5000	255 (29.31)	141 (32.12)	114 (26.45)		
	5000~15000	506 (58.16)	239 (54.44)	267 (61.95)	5.078	0.079

	≥ 15000	109 (12.53)	59 (13.44)	50 (11.60)		
	Missing	213	-	-		
Family members	<3	142 (13.49)	64 (12.38)	78 (14.55)	1.461	0.482
	3~5	458 (43.49)	223 (43.13)	235 (43.84)		
	≥ 5	453 (43.02)	230 (44.49)	223 (41.60)		
	Missing	30	-	-		
Smoking	Yes	475 (44.43)	243 (45.68)	232 (43.20)	0.662	0.416
	No	594 (55.57)	289 (54.32)	305 (56.80)		
	Missing	14	-	-		
Drinking	Yes	294 (27.55)	135 (25.71)	159 (29.34)	1.752	0.186
	No	773 (72.45)	390 (74.29)	383 (70.66)		
	Missing	16	-	-		
BCG	Yes	383 (37.55)	171 (33.14)	212 (42.06)	8.659	0.003
	No	637 (62.45)	345 (66.86)	292 (57.94)		
	Missing	63	-	-		
TB patients around	Yes	136 (12.87)	223 (42.72)	245 (45.79)	3.484	0.175
	No	453 (42.86)	61 (11.69)	75 (14.02)		
	Unknown	468 (44.28)	238 (45.59)	215 (40.19)		
	Missing	26	-	-		
Had health education of TB	Yes	327 (33.00)	175 (35.21)	152 (30.77)	2.211	0.137
	No	664 (67.00)	322 (64.79)	342 (69.23)		
	Missing	92	-	-		
BMI	<18.5	289 (28.76)	138 (27.11)	151 (30.44)	1.412	0.494
	18.5~23.9	610 (60.70)	315 (61.89)	295 (59.48)		
	≥ 24	106 (10.55)	56 (11.00)	50 (10.08)		
	Missing	78	-	-		
Sputum smear status	Negative	560 (51.71)	269 (50.19)	291 (53.20)	1.141	0.538
	Positive	365 (33.70)	183 (35.26)	176 (32.18)		
	Unknown	158 (14.59)	78 (14.55)	80 (14.63)		
Knowledge of TB	Good	569 (52.54)	278 (51.87)	291 (53.20)	0.193	0.66
	Poor	514 (47.46)	258 (48.13)	256 (46.80)		

BCG: Bacillus Calmette-Guérin; BMI, Body Mass Index

About 40% patients did not know whether there were TB patients around (Table 1).

Patient delay

The median patient delay was 11 days (IQR: 1-34). Among the socio-demographic characteristics, only BCG vaccination had significant difference between two groups (P=0.003) (Table 1).

Core knowledge of TB

41.92% patients knew the pathogen of TB and 54.66% patients had knowledge that cough and expectoration for 2 or more weeks was the symptom of TB. Most patients (78.95%) realized that TB was an infectious disease and 55.22% knew that TB could transmit by cough/sneezing. Furthermore, 70.91% patients had heard about the national TB policy of free detection/treatment, and 58.91% knew the institutions to implement the policy. Only TB symptom of blood-tinged

sputum had difference between the shorter and longer patient delay groups (P=0.045) (Table 2).

The median score of core TB knowledge was 7 (IQR: 3-9).

Table 2. Core TB knowledge among new TB patients and the comparison with shorter and longer patient delay.

Core knowledge of TB	Total n (%)	Patient delay		χ^2	P
		Longer (n, %)	Shorter (n, %)		
Had knowledge of the pathogen of TB	454 (41.92)	240 (44.78)	214 (39.12)	3.554	0.059
Had knowledge of TB symptoms					
Cough and expectoration for 2 or more weeks	592 (54.66)	284 (52.99)	308 (56.31)	1.206	0.272
Hemoptysis	456 (42.11)	212 (39.55)	244 (44.61)	2.838	0.092
Blood-tinged sputum	336 (31.02)	151 (28.17)	185 (33.82)	4.037	0.045
All above TB symptoms	291 (26.87)	132 (24.63)	159 (29.07)	2.717	0.099
Had knowledge of TB transmission					
TB is an infectious disease	855 (78.95)	426 (79.48)	429 (78.43)	0.18	0.672
Transmitted by cough/sneezing	598 (55.22)	304 (56.72)	294 (53.75)	0.965	0.326
Had knowledge of TB detection method					
Sputum smear examination	497 (45.89)	242 (45.15)	255 (46.62)	0.235	0.628
X-ray	479 (44.23)	235 (43.84)	244 (44.61)	0.064	0.8
Had knowledge of TB treatment					
TB is a curable disease	768 (70.91)	391 (72.95)	377 (68.92)	2.128	0.145
Aware of free detection/treatment policy	770 (71.10)	387 (72.20)	383 (70.02)	0.628	0.428
Aware of institutions to implement the free detection/treatment policy	638 (58.91)	325 (60.63)	313 (57.22)	1.303	0.254

Table 3. TB symptoms when patients first presented to the healthcare system and the comparison with shorter and longer patient delay.

Symptoms	Total(n,%)	Patient delay		χ^2	P
		Longer(n,%)	Shorter(n, %)		
Cough	719 (66.39)	392 (73.13)	327 (59.78)	21.635	<0.0001
Expectoration	393 (36.29)	229 (42.72)	164 (29.98)	19.012	<0.0001
Chest tightness and shortness of breath	219 (20.22)	116 (21.64)	103 (18.83)	1.327	0.249
Blood-tinged sputum	182 (16.81)	69 (12.87)	113 (20.66)	11.736	0.0006
Low-grade fever	184 (16.99)	84 (15.67)	100 (18.28)	1.308	0.253
Night sweat	145 (13.39)	82 (15.30)	63 (11.52)	3.338	0.068
Fatigue	217 (20.24)	127 (23.69)	90 (16.45)	8.859	0.003
Lack of appetite	84 (7.76)	51 (9.51)	33 (6.03)	4.588	0.032
Other	99 (9.14)	49 (9.14)	50 (9.14)	0.000	0.999

There was no difference of level of TB knowledge between shorter and longer patient delay groups (Table 1).

TB symptoms when patients first presented to the healthcare system

The results indicated that the common symptoms were cough (66.39%), expectoration (36.29%), fatigue (20.24%) and chest tightness and shortness of breath (20.22%) when patients first presented to the healthcare system. There were significant differences of cough, expectoration, blood-tinged sputum, fatigue and lack of appetite between shorter and longer patient delay groups (all P <0.05) (Table 3).

Healthcare system TB patients first consulted

Most TB patients (57.62%) first contacted with comprehensive county hospital, only 18.84% first presented to TB prevention and control institutions (Table 4). But TB patients in shorter and longer patient delay groups had no difference of the healthcare system they consulted first (P=0.056).

Factors associated with longer patient delay

The multivariate logistic analysis showed that expectoration when first consulted the healthcare system (OR: 1.520; 95 % CI: 1.020-2.266; P=0.040), blood-tinged sputum when first consulted the healthcare system (OR: 0.490; 95 % CI: 0.278-0.864; P=0.014) and unknown whether there were TB

patients around (OR: 1.903; 95 % CI: 1.229-2.947; P=0.004) were associated factors of longer patient delay (Table 5).

Table 4. *Healthcare system TB patients first consulted.*

Healthcare system TB patients first consulted	Total n (%)	Patient delay		χ^2	P
		Longer (n, %)	Shorter (n, %)		
TB prevention and control institutions (e.g. TB dispensaries, CDC, epidemic prevention station)	204 (18.84)	117 (21.83)	87 (15.90)	3.653	0.056
Comprehensive County Hospital	624 (57.62)	299 (55.78)	325 (59.41)	-	-
Township Health Center	119 (10.99)	60 (11.19)	59 (10.79)	-	-
Tuberculosis Specialist Hospital	33 (3.05)	14 (2.61)	19 (3.47)	-	-
Others	103 (9.51)	46 (8.58)	57 (10.42)	-	-

CDC: Center for Disease Control and Prevention

Table 5. *Multivariate logistic regression analysis on factors related to longer patient delay.*

Factors	B	S.E.	Wald χ^2	OR	95%CI	P
Expectoration when first consulted the healthcare system	0.419	0.204	5.241	1.520	1.020-2.266	0.040
Blood-tinged sputum when first consulted the healthcare system	-0.714	0.290	6.079	0.490	0.278-0.864	0.014
Unknown whether there were TB patients around	0.644	0.223	8.316	1.903	1.229-2.947	0.004

B, regression coefficient; S.E.: Standard Error; OR: Odds Ratios; 95% CI, 95% Confidence Interval

Discussion

Tuberculosis (TB) is preventable if people can access to health care for prompt diagnosis and treatment. Analysis of factors associated with patient delay is an important starting point to identify how to improve the quality of TB care and control. This study assessed patient delay and associated factors in the diagnosis of TB in Anqing, China.

Differing from the previous reports in Shandong, China [20] and southern Taiwan [21] where the median initial health care-seeking delay time were 6 and 7 days, respectively, this study showed that 49.49 % of patients delayed their first visit to healthcare system following symptoms for more than 11 days. And this result was similar to the studies in Shenzhen, China [22] and Malawi [8] where the median healthcare-seeking delay time was 10 and 14 days, respectively. However, a majority of researches reported that the median patient delay was 30 days in low and high prevalence countries [9,10,23,24], and even longer to 59 days in Ghana [11] and 61 days in Mozambique [12]. These differences might be linked to the fact that the majority of the patient delay studies carried out elsewhere were conducted in referral hospitals, where longer patient delay was expected [12]. In addition, TB patients had only vague symptoms and could not clearly recognize symptoms at the onset of the disease were an aspect of reasons [10]. On the other hand, a majority of patients had medical insurance, suggesting that patients in this study setting had better access to healthcare, so they were less likely to delay. And besides, TB patients included retreatment cases or not might also result in the differences.

Factors associated patient delay like patients' characteristics were studied frequently, but other enabling factors were studied infrequently, although they were most often associated with delay [15]. Our study included not only patients' socio-demographic characteristics but also patients' core knowledge of TB, TB symptoms when first presented to the healthcare system and other enabling factors. We found that expectoration when first consulted the healthcare system was associated with longer patient delay, which was more or less similar to the studies in the state of Rio de Janeiro, Brazil [23] and in France [24] that cough and initial fever were independently associated with patient delay, respectively. The reasons might be ascribed to the fact that expectoration, cough, fever etc. were common symptoms for both tuberculosis and other diseases. When patients had these symptoms, they might not care about these symptoms or make their first visit to a drug store and take self-medication, and thus delayed. Self-medication, on the other hand, was also a risk factor for patient delay [18,25].

TB patients neglected the symptoms was the most common reason for patient delay [26]. However, Storla et al. demonstrated that although patients had classical TB symptoms, medical staff they consulted first often did not ask about previous TB, perform an X-ray, or obtain a sputum smear [27]. Because TB symptoms, especially chronic cough with sputum, were prevalent in most people, they often neglected the suspicion of TB [27]. While patients had blood-tinged sputum or hemoptysis [14] were less likely to had longer patient delay. The reasons might be attributed to the fact that hemoptysis and blood-tinged sputum were more serious than cough, expectoration etc. So patients with these symptoms were more likely to seek medical care immediately and medical staff was also less likely to neglect them.

It is important for people to know whether there are TB patients around. We can imagine that if people have symptoms like cough, expectoration but do not know whether there are TB patients around, they will not consult healthcare system for TB timely. Furthermore, according to the study in San Francisco, a smear-negative TB patient contributed to 17% (95% CI: 12-24%) of TB transmission [28]. So people should know whether there are TB patients around and TB patients should seek medical help immediately in order to reduce the period of transmission, reduce the risk of exposure of other people.

Unlike other studies [8,12,16], we could not find associations between lacking TB knowledge and patient delay. The reasons might be linked to the fact that in our study most patients first consulted comprehensive county hospital, where medical personnel would tell them some basic knowledge of TB. So there were no significant differences in TB knowledge. In addition, other factors such as age, sex, educational level, sputum smear status, first contact rural primary healthcare vs. district/mission facilities or the health centre differing from the DOTS centre, which had been identified to be significantly associated with patient delay [8,10,13,14,22,25] could not be established in this study as well. This might be due to different sample sizes and study settings.

Feasible and effective measures should be taken to improve the situation of delays in diagnosis and treatment of TB patients. One is the “care manager” nurses in the primary health care system [29]. They serve as a bridge between physicians and patients. They understand the diagnosis and treatment goals of physicians’ and can explain to their patients to help them understand their illness. They also pass patients’ needs to physicians to help establish more suitable treatment regimes. In addition, they help patients to change their lifestyle, monitor their physical condition, increase their health knowledge, enhance self-management skills, and achieve better compliance with care recommendations.

Our study has several limitations. Firstly, because of this design and limited study area, the patient delay of new TB patients may not be representative of those at the national level. Secondly, the questionnaire we used did not contain information on occupation, HIV status, self-medication and multiple care-seeking behaviors, which probably had associations with patient delay. Thirdly, patients’ attitude and practice of TB (e.g., perceived severity of stigma when had TB), which were likely to associated with the patient delay, were not included in our study. Further studies on other regions are needed and more enabling factors should be included. Forth, use questionnaire may cause deficiency of some important information, especially self-administered questionnaire. Although we referred to TB management system, we could not add the whole missing information. Interviewer-administered questionnaire should be adopted no matter illiterate patients and literate patients.

Conclusion

In summary, about half of TB patients in our study had longer patient delay, and TB patients with different symptoms seem to have different behaviors of patient delay. Measures must be taken to encourage TB patients to seek medical help as early as possible. In addition, people were encouraged to know whether there were TB patients around and take suitable action when contact with TB patients.

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