The effects of family, society and national policy support on treatment adherence among newly diagnosed tuberculosis patients: a cross-sectional study

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Abstract

Background: Non-adherence to tuberculosis (TB) treatment is the most important cause of poor TB treatment, and improving support for TB patients is a primary priority for governments, but there has been little research on the effects of family, social and national policy support factors on TB treatment adherence. The current study evaluated the treatment adherence of newly diagnosed TB patients in Dalian, northeast of China, and determined the effects of family, society, national policy support factors on treatment adherence.

Methods: A cross-sectional survey was conducted among newly diagnosed TB patients treated at the outpatient department of Dalian Tuberculosis Hospital from September 2019 and January 2020. Data were collected using questionnaire that measured medication adherence, family support, social support, and national policy support and so on. Differences between groups were assessed using the chi-square test and Fisher’s exact tests. Ordinal logistic regression analysis was used to determine the predictors of adherence.

Results: A total of 481 newly diagnosed TB patients were recruited, of whom 45.7% had good adherence, and 27.4% and 26.8% had moderate and low adherence, respectively. Patients with family members’ frequent supervision of medication (OR: 0.34, 95% CI: 0.16-0.71), family members’ often spiritual encouragement (OR: 0.14, 95% CI: 0.03-0.80), good doctor-patient relationship (OR: 0.58, 95% CI: 0.38-0.88), more TB-related knowledge (OR: 0.49, 95% CI: 0.33-0.72) and high need for TB treatment policy support (OR: 0.39, 95% CI: 0.22-0.67) performed satisfactory medication adherence. However, patients with a college degree or higher (OR: 1.78, 95% CI: 1.10-2.88) were more likely to have a lower adherence.

Conclusions: Our findings suggested that non-adherence was high in newly diagnosed TB patients. Family members’ frequent supervision of medication and spiritual encouragement, good doctor-patient relationship and TB-related knowledge, high need for policy support contributed to high adherence. It is recommended to strengthen the training of medical staff and the health education of patients and their families, increase the financial support for improve adherence.

Introduction

Tuberculosis (TB), a chronic respiratory infectious disease caused by the Mycobacterium tuberculosis complex (MTBC), has affected humans for thousands of years, and it is one of the top ten causes of death in the world[1]. In 2018, there were an estimated 10 million new cases of TB and 1.5 million deaths in the world[2]. About 1.7 billion people worldwide were infected with the Mycobacterium tuberculosis, all of whom were at risk of developing TB[3]. China, one of the most heavily burdened countries in the world, is also still suffering from a severe TB epidemic. In 2018, there were 866,000 new TB patients, or 61 per 100,000 people[2], and the incidence has been maintaining at a high level. Why is the TB epidemic so difficult to control? The national government has always attached great importance to the prevention and control of TB, raised funding and implemented partial relief policies for TB. But TB is currently treated
with anti-TB medications, and the treatment cycle of the disease is long, and the adverse drug reactions are serious[4]. The symptoms of patients in the continuation phase are not significantly improved, and many patients also suffer considerable psychological, social and economic costs[5]. These lead to decreased patient adherence and irregular medication. Several previous studies have shown that irregular treatment, i.e. poor patient adherence, is the most important reason for poor TB treatment[6-8]. Low adherence will lead to treatment failure or even relapse into drug-resistant TB in patients with smear-negative smear, which also will lead to prolonged infectious period in patients with smear-positive smear and increase the number of drug-resistant and relapse cases[4, 9]. Other studies have also shown that non-adherence is the most common cause of relapse, and the relapse rate of patients with poor adherence is as high as 50.5%, while the relapse rate of patients with good adherence is only 1.1%[10]. Therefore, the study on the influencing factors of the adherence of newly treated TB patients and the discovery of new ways to improve adherence not only contribute to the improvement of TB cure rates, but also prevent the relapse of TB and the emergence of drug-resistant TB, which is crucial to the global goal of ending TB. In order to gain a thorough understanding of the barriers and enablers that affect adherence, many countries have studied the factors that influence adherence. A study from Sri Lanka identified barriers to adherence related to patient and health service delivery[11]. Studies in northwestern Ethiopia had shown that knowledge of disease and treatment, complications, alcohol abuse, forgetfulness and busy work schedules were significantly associated with non-adherence[12]. A cross-sectional study conducted in four regions of Russia confirmed that psychosocial factors were also influencing low adherence[13]. China is a country with a high TB burden that accounts for 9 percent of the world's cases[2]. Studies on influencing factors of adherence have been conducted in Anhui, Shenzhen, Hubei and so on. Studies have identified the relationship between medication adherence and socio-demographic characteristics, socio-economic factors, health systems and drug adherence[9, 14]. In addition, some studies have shown that psychological factors such as stigma and depressive symptoms significantly affect patient adherence[15]. Improving support for TB patients is a major priority for governments[16]. However, few studies have examined the impact of family, society and national policy support factors on TB treatment adherence. In recent years, more and more studies have been conducted on the adherence of TB patients in China. However, most studies have focused on the adherence of migrant population, patients from impoverished mountainous area, relapsed TB patients and multidrug-resistant TB patients. Few studies have been conducted only among newly diagnosed TB patients. Liaoning province is a more prosperity than other provinces in the northeast of China. The morbidity and mortality of the whole province TB report all occupied the first two places of infectious disease. In 2018, the statutory reported incidence of TB was 55.81/100,000 and the mortality rate was 0.49/ 100,000 in Liaoning province[17]. TB seriously endangers the health of people and affects the development of economy and society in this province. Dalian is the best economically developed area in Liaoning province. In 2016, the incidence rate of TB was 64.66/100,000 in the general population of Dalian[18]. In recent years, although the incidence rate of TB has been declining slowly, it is still the main killer health among of infectious diseases. 1.1 Aim The aim of this study was to evaluate the level of adherence to anti-TB treatment among newly treated TB patients in Dalian, Liaoning province, northeastern China, and
we would further identify the potential effects of family, society and national policy support factors on adherence.

**Methods**

2.1 Study design and setting

A cross-sectional, questionnaire-based survey was conducted at the Dalian Tuberculosis Hospital in Liaoning province, northeastern China from September 2019 and January 2020. Dalian Tuberculosis Hospital is the only TB control hospital in Dalian, divided into two parts: the northern branch and the southern one. The hospital occupies an area of 45,000 square meters. It is responsible for the diagnosis, treatment, prevention, training and scientific research of TB and pulmonary diseases in Dalian. In order to enhance the treatment adherence, reduce the interruption of treatment and improve the completion rate of treatment of newly registered TB patients, Dalian municipal government has introduced a policy to benefit the people. Since January 1, 2011, transportation and nutrition subsidies have been provided to newly registered pulmonary TB patients (excluding tuberculous pleurisy and other extrapulmonary TB) and chronic prolonged pulmonary TB with positive sputum smear tests during the current year who were treated on time in our hospital. The subsidy standard is 45 yuan for transportation allowance and 200 yuan for nutrition allowance per month. The newly diagnosed patients were given for 6 months and the patients with relapse for 8 months.

2.2 Participants

The study participants were made up of TB patients who met the inclusion criteria and had outpatient visits at the Dalian Tuberculosis Hospital from September 2019 to January 2020. The inclusion criteria included: (1) newly diagnosed TB patients, that is, the patient’s medical records indicate that the patient has denied any prior anti-TB treatment or any history of anti-TB treatment beyond 30 days[19]; (2) age greater than or equal to 18 years; (3) patients who have begun to take anti-TB drugs and have no mental disorder; (4) patients who are easy to communicate and can understand the contents of the questionnaire; (5) patients who voluntarily and agree to participate in this study and can truly express their views on the problem. A total of 485 patients were interviewed in this study, of which 4 did not complete the interview, and response rate was 99.2%. In the end, the study included 481 patients.

2.3 Data Collection

Structured questionnaires were used for data collection. The questionnaire was designed after we had consulted a large number of relevant literatures at home and abroad and consulted experts in related fields. In addition, a preliminary survey was conducted on the survey site, and the questionnaire was supplemented and modified according to the situation of the preliminary survey to ensure the validity of the questionnaire. The questionnaire was composed of medication adherence, socio-demographic characteristics, family support, social support and national policy support factors. The data were collected by a team of trained and qualified graduate students.
The adherence of TB patients was investigated using the eight-item Morisky Medication Adherence Scale of Chinese version (C-MMAS-8). The revised Chinese edition was based on the grade-by-grade translation and reverse translation of the MMAS-8 according to international guidelines[20]. This scale is one of the simplest ways to measure a patient’s medication adherence. The scale consists of eight items that measure a specific medication behavior. The highest score on this scale was 8, indicating a high adherence. A score less than 8 but not less than 6 was considered to have a moderate adherence, while a score less than 6 was classified as having a low adherence. This scale was of good reliability and sensitivity, and Cronbach's $\alpha$ was 0.81 in this study.

The sociodemographic characteristics of the study included 6 questions involving gender, age, marital status, education level, self-reported average monthly income, and the time required to arrive at a health facility. The family support section consisted of 4 questions, including the supervision of medication, spiritual encouragement, the relationship between family members, and the help to solve the problems in daily life. Social support was made up of 12 questions covering care, support and help from friends, neighbors, colleagues and doctors, as well as objective condition of inhabiting situation, and the patient's participation in group activities and acquired knowledge of TB. Patients' access to TB knowledge was assessed by asking 6 questions, such as how TB is transmitted and how to treat it. Patients get one point for each correct answer, and higher scores indicate better understanding. In this study, 2 points and 4 points are used as segmentation points to divide knowledge level into three parts. The national policy support module was composed of 4 issues, such as policy understanding, policy satisfaction and the need for increased national TB treatment policies. The last question in the module was an open question on what policy support was still needed.

2.4 Data Analysis

On the day the questionnaires were returned, researchers checked the completeness of questionnaires and eliminated the illogical data. After ensuring that the questionnaire was complete and correct, the questionnaire was coded. Data were entered into the database established by software EpiData3.1 (EpiData Association, Odense, Denmark) by double-entry method. The results were tested for consistency, and the original questionnaires were searched for inconsistencies. Excel database was established and SPSS 21.0 (IBM Corporation, Armonk, State of New York) was used for statistical analysis. Quantitative data were described by mean and standard deviation. The classified data were described by frequency and percentage. Chi-square test was used to evaluate the differences in the classified data between different groups. For scarce data, we used the Fisher's exact tests. All the statistically significant variables in the univariate analysis entered into ordinal logistic regression analysis to determine the predictors of adherence. Odds ratio ($OR$) and its 95% confidence interval ($CI$) were calculated. If $P<0.05$, the difference was statistically significant.

Results

3.1 The level of non-adherence to anti-TB treatment
A total of 481 newly diagnosed TB patients were included in this study. The mean score of the medication adherence scale was 6.53±1.85. The 220 (45.7%) patients included in our study were classified as having good adherence, and 132 (27.4%) and 129 (26.8%) had moderate and low adherence, respectively.

3.2 Socio-demographic characteristics

In our study, patients ranged in age from 18 to 88 years, with an average age of 44.10±17.85 years. More than half of TB patients (62.0%) entering the study were male, whereas only 183 (38%) were female. Nearly three-quarters of TB patients (71.5%) were married, compared with 18 (3.7%) who were divorced or widowed. TB patients with an education level of secondary school or below (41.0%) accounted for the most percentage. Most TB patients have low monthly incomes, with only 84 (17.5%) of TB patients earning more than 5,000 yuan a month. Nearly one third of TB patients (32.0%) arrived at the facility more than an hour and 136 (28.3%) less than 30 minutes. The results of the univariate analysis showed that education level and the time required to reach the medical institution were significantly correlated with the medication adherence of TB patients ($P<0.05$), and the adherence of TB patients of different genders, ages, marital status, and monthly income in our study could not be considered to be different ($P>0.05$). (Table 1).

Table 1. Medication adherence level by sociodemographic factors
| Variables                        | Total n (%) | Adherence Level n (%) | P       |
|---------------------------------|-------------|-----------------------|---------|
|                                 |             | Low       | Medium  | High    |         |
| Sex                             |             |           |         |         |         |
| Male                            | 298(62.0)   | 78(26.2)  | 84(28.2) | 136(45.6) | 0.869   |
| Female                          | 183(38.0)   | 51(27.9)  | 48(26.2) | 84(45.9)  |         |
| Age (years)                     |             |           |         |         |         |
| <30                             | 128(26.6)   | 36(28.1)  | 37(28.9) | 55(43.0)  | 0.942   |
| 30-60                           | 244(50.7)   | 65(26.6)  | 67(27.5) | 112(45.9) |         |
| >60                             | 109(22.7)   | 28(25.7)  | 28(25.7) | 53(48.6)  |         |
| Marital status                  |             |           |         |         |         |
| Unmarried                       | 119(24.7)   | 35(29.4)  | 42(35.3) | 42(35.3)  | 0.096   |
| Married                         | 344(71.5)   | 90(26.2)  | 85(24.7) | 169(49.1) |         |
| Divorced or widowed             | 18(3.7)     | 4(22.2)   | 5(27.8)  | 9(50.0)   |         |
| Education                       |             |           |         |         |         |
| Junior high school or below     | 197(41.0)   | 52(26.4)  | 54(27.4) | 91(46.2)  | 0.025   |
| High school or technical secondary school | 117(24.3)   | 29(24.8)  | 22(18.8) | 66(56.4)  |         |
| College degree or above         | 167(34.7)   | 48(28.7)  | 56(33.5) | 63(37.7)  |         |
| Monthly income (Yuan)           |             |           |         |         |         |
| <1000                           | 133(27.7)   | 31(23.3)  | 42(31.6) | 60(45.1)  | 0.210   |
| 1000-3000                       | 115(23.9)   | 34(29.6)  | 33(28.7) | 48(41.7)  |         |
| 3001-5000                       | 149(31.0)   | 40(26.8)  | 30(20.1) | 79(53.0)  |         |
| >5000                           | 84(17.5)    | 24(28.6)  | 27(32.1) | 33(39.3)  |         |
| Time to arrive at the medical facility (min) | 136(28.3)   | 36(26.5)  | 26(19.1) | 74(54.4)  | 0.033   |
3.3 Family support

Table 2 shows that family supervising medication, family spiritual encouragement, and family member relationships were significantly different in different groups by univariate analysis ($P<0.05$). A high proportion of low adherence (48.6%) was found in TB patients whose family members sometimes supervised their medication, while a high proportion of high adherence (47.7% and 54.5%, respectively) was found in the two groups of patients whose family members frequently supervised their medication and those who did not. Patients with frequent spiritual encouragement from family members had a higher proportion of high adherence (47.0%). The relationship between family members of most patients (95.6%) was good, and there was a little proportion of poor adherence (26.3%). A significantly higher proportion of patients (91.3%) had family member who were able to regularly help solve problems in daily life (Table 2).

Table 2. Medication adherence level by family support factors

|     | 31-60 | >60  |
|-----|-------|------|
|     | 191(39.7) | 154(32.0) |
|     | 45(23.6)       | 48(31.2)      |
|     | 62(32.5)       | 44(28.6)      |
|     | 84(44.0)       | 62(40.3)      |
Variables | Total n (%) | Adherence Level n (%) | \(P\)
---|---|---|---
| | Low | Medium | High
---
Family supervision for medication
Often | 411(85.4) | 105(25.5) | 110(26.8) | 196(47.7) | 0.002
Sometimes | 37(7.7) | 18(48.6) | 13(35.1) | 6(16.2) |
Never | 33(6.9) | 6(18.2) | 9(27.3) | 18(54.5) |
Family spirit encouragement
Often | 451(93.8) | 116(25.7) | 123(27.3) | 212(47.0) | 0.012*
Sometimes | 20(4.2) | 10(50.0) | 3(15.0) | 7(35.0) |
Never | 10(2.1) | 3(30.0) | 6(60.0) | 1(10.0) |
Family relationship
Good | 460(95.6) | 121(26.3) | 124(27.0) | 215(46.7) | 0.012*
General | 17(3.5) | 8(47.1) | 4(23.5) | 5(29.4) |
Poor | 4(0.8) | 0(0.0) | 4(100.0) | 0(0.0) |
Family members help solve problems
Often | 439(91.3) | 112(25.5) | 122(27.8) | 205(46.7) | 0.134
Sometimes | 24(5.0) | 12(50.0) | 5(20.8) | 7(29.2) |
Never | 18(3.7) | 5(27.8) | 5(27.8) | 8(44.4) |

*Means that the theoretical number is too small and adopt the Fisher's exact test method.

3.4 Society support

TB patients who had one or two close friends accounted for 46.6% of the patients included in the study, but 51 (10.6%) had no close or supportive friends. A small number of TB patients (12.3%) lived alone, while the rest lived with family, friends or colleagues. Nearly 30% of TB patients reported poor relationships with neighbors and co-workers (29.7% and 27.0%, respectively). More than half of TB patients (56.5%) reported that they never participated in group activities, while only 41 (8.5%) were regularly or actively involved in group activities. Patients generally had a good doctor-patient relationship, with a small minority (19.3%) reporting a poor relationship with the medical staff. The mean score of knowledge about TB of the included TB patients was 4.72±1.20, with 146(30.4%) getting full marks, but 24(5%) of the patients still scored less than 3 points. Univariate analysis found that doctor-patient
relationship, acquired knowledge of TB and participation in group activities were correlated with medication adherence of TB patients ($P<0.05$). (Table3).

Table 3. Medication adherence level by society support factors
| Variables                          | Total n (%) | Adherence Level n (%) | P   |
|-----------------------------------|-------------|-----------------------|-----|
|                                   |             | Low                   | Medium | High |
| The number of close friends       |             |                       |       |      |
| 0                                 | 51(10.6)    | 17(33.3)              | 12(23.5) | 22(43.1) | 0.729 |
| 1-2                               | 223(46.4)   | 62(27.8)              | 61(27.4) | 100(44.8) |
| ≥3                                | 207(43.0)   | 50(24.2)              | 59(28.5) | 98(47.3)  |
| Living condition                  |             |                       |       |      |
| Living alone                      | 59(12.3)    | 12(20.3)              | 18(30.5) | 29(49.2)  | 0.483 |
| Living with other                 | 422(87.7)   | 117(27.7)             | 114(27.0) | 191(45.3) |
| Relationships with neighbors      |             |                       |       |      |
| Poor                              | 143(29.7)   | 36(25.2)              | 45(31.5) | 62(43.4)  | 0.394 |
| General                           | 220(45.7)   | 66(30.0)              | 57(25.9) | 97(44.1)  |
| Good                              | 118(24.5)   | 27(22.9)              | 30(25.4) | 61(51.7)  |
| Relationships with colleagues     |             |                       |       |      |
| Poor                              | 130(27.0)   | 32(24.6)              | 31(23.8) | 67(51.5)  | 0.566 |
| General                           | 225(46.8)   | 64(28.4)              | 66(29.3) | 95(42.2)  |
| Good                              | 126(26.2)   | 33(26.2)              | 35(27.8) | 58(46.0)  |
| Relationships with doctors        |             |                       |       |      |
| Poor                              | 93(19.3)    | 30(32.3)              | 29(31.2) | 34(36.6)  | 0.001 |
| General                           | 223(46.4)   | 66(29.6)              | 69(30.9) | 88(39.5)  |
| Good                              | 165(34.3)   | 33(20.0)              | 34(20.6) | 98(59.4)  |
| Acquired knowledge of TB          |             |                       |       |      |
| Poor                              | 24(5.0)     | 7(29.2)               | 7(29.2) | 10(41.7)  | 0.016 |
| General                           | 149(31.0)   | 55(36.9)              | 37(24.8) | 57(38.3)  |
| Good                              | 308(64.0)   | 67(21.8)              | 88(28.6) | 153(49.7) |
| Participation in group activities  |             |                       |       |      |
| Often                             | 41(8.5)     | 11(26.8)              | 14(34.1) | 16(39.0)  | 0.008 |
| Sometimes                         | 168(34.9)   | 55(32.7)              | 53(31.5) | 60(35.7)  |
3.5 National policy support

The number of patients (59%) who knew about the country's treatment policies for TB was relatively small. There was no significant association with medication adherence ($P>0.05$), although unknown patients had a higher percentage of low adherence. Satisfaction with the national medical security policy for TB treatment and the need to increase policy support for TB treatment were proved to be relevant factors ($P<0.05$). The proportion of TB patients who were satisfied with the national medical security policy for TB treatment was 50.7%, while the proportion who were generally satisfied and less satisfied with the medical security policy was 39.3% and 10.0%, respectively. Most patients (96.7%) believed that the government still needed to increase support for TB treatment (Table 4).

Table 4. Medication adherence level by national policy support factors

| Variables                          | Total n (%) | Adherence Level n (%) | $P$  |
|-----------------------------------|-------------|-----------------------|------|
|                                   |             | Low (P)               | Medium (P) | High (P) |      |
| National TB treatment policy      |             |                       |      |         |      |
| Know                              | 284(59.0)   | 74(26.1)              | 69(24.3) | 141(49.6) | 0.083 |
| Unknown                           | 197(41.0)   | 55(27.9)              | 63(32.0) | 79(40.1)  |      |
| Medical security policy satisfaction |         |                       |      |         |      |
| Satisfaction                      | 244(50.7)   | 66(27.0)              | 52(21.3) | 126(51.6) | 0.004 |
| General satisfaction              | 189(39.3)   | 54(28.6)              | 58(30.7) | 77(40.7)  |      |
| Not too satisfaction              | 48(10.0)    | 9(18.8)               | 22(45.8) | 17(35.4)  |      |
| Increase support for TB treatment policies |         |                       |      |         |      |
| Need                              | 408(84.8)   | 98(24.0)              | 113(27.7) | 197(48.3) | 0.004 |
| General need                      | 57(11.9)    | 27(47.4)              | 15(26.3) | 15(26.3)  |      |
| Not too need                      | 16(3.3)     | 4(25.0)               | 4(25.0)  | 8(50.0)   |      |
### 3.6 Ordinal logistic regression analysis of factors independently associated with medication adherence among patients

Ordinal logistic regression analysis showed that patients whose family members regularly supervised medication \((\text{OR}: 0.34, 95\% \, 	ext{CI}: 0.16-0.71)\) and whose family members often encouraged them mentally \((\text{OR}: 0.14, 95\% \, 	ext{CI}: 0.03-0.80)\) were more likely to have a high medication adherence. Patients with better doctor-patient relationship \((\text{OR}: 0.58, 95\% \, 	ext{CI}: 0.38-0.88)\) and more TB-related knowledge \((\text{OR}: 0.49, 95\% \, 	ext{CI}: 0.33-0.72)\) were more likely to stay away from low medication adherence. Patients who want greater support for TB treatment policies \((\text{OR}: 0.39, 95\% \, 	ext{CI}: 0.22-0.67)\) were more likely to have a good medication adherence. However, patients with a college degree or higher \((\text{OR}: 1.78, 95\% \, 	ext{CI}: 1.10-2.88)\) were more likely to have a low medication adherence (Table 5).

#### Table 5. Ordinal logistic regression analysis the predictors of medication adherence
| Variables                                      | OR   | 95% CI       | P    |
|-----------------------------------------------|------|--------------|------|
| Education (Ref: College degree or above)      |      |              |      |
| Junior high school or below                   | 1.17 | 0.76-1.81    | 0.471|
| Technical secondary school or high school     | 1.78 | 1.10-2.88    | 0.018|
| Time to arrive at the medical facility (Ref: >60mins) |      |              |      |
| <31                                           | 1.21 | 0.76-1.92    | 0.434|
| 31-60                                         | 1.20 | 0.79-1.82    | 0.403|
| Family supervision for medication (Ref: Often) |      |              |      |
| Never                                         | 2.79 | 1.19-6.53    | 0.018|
| Sometimes                                     | 0.34 | 0.16-0.71    | 0.004|
| Family spirit encouragement (Ref: Often)      |      |              |      |
| Never                                         | 0.14 | 0.03-0.80    | 0.027|
| Sometimes                                     | 0.75 | 0.28-2.03    | 0.572|
| Family relationship (Ref: Good)               |      |              |      |
| Poor                                          | 2.62 | 0.22-30.60   | 0.443|
| General                                       | 0.83 | 0.30-2.28    | 0.720|
| Relationships with doctors (Ref: Good)        |      |              |      |
| Poor                                          | 0.72 | 0.42-1.23    | 0.229|
| General                                       | 0.58 | 0.38-0.88    | 0.010|
| Acquired knowledge of TB (Ref: Good)          |      |              |      |
| Poor                                          | 0.79 | 0.34-1.82    | 0.577|
| General                                       | 0.49 | 0.33-0.72    | <0.001|
| Participation in group                        |      |              |      |
activities (Ref: Often)

|             |     |          |        |
|-------------|-----|----------|--------|
| Never       | 1.28| 0.66-2.47| 0.461  |
| Sometimes   | 0.87| 0.45-1.68| 0.678  |

Medical security policy satisfaction (Ref: Satisfaction)

|                      |     |          |        |
|----------------------|-----|----------|--------|
| Not too satisfaction | 0.88| 0.47-1.65| 0.698  |
| General satisfaction | 0.80| 0.55-1.17| 0.254  |

Increase support for TB treatment policies (Ref: Need)

|                      |     |          |        |
|----------------------|-----|----------|--------|
| Not too need         | 0.85| 0.31-2.31| 0.749  |
| General need         | 0.39| 0.22-0.67| 0.001  |

Ref is reference

3.7 Patients' advice for increased policy support in an open question

Some TB patients stated one or more advice for greater policy support, and advice was received from 109 TB patients. More economic support (87.2%) was most frequently proposed, and include increased reimbursement rates (33.9 %), increased subsidies for nutrition, transportation, and other expenses (19.3 %), increased free drug coverage and time (14.7 %), free treatment (11.9%), and reduced testing costs (3.7%), especially among poor patients and patients with first-line drugs resistance. The next most common advice was to increase TB prevention and patient management (especially isolation and education of infectious patients) (9.2%), to propagandize knowledge of TB (4.6%), to increase psychological counselling (4.6%), to provide nutritious meals to inpatients or to improve the quality of food and beverage (2.8%). There are also a few patients who proposed to strengthen infrastructure construction, improve out-of-town reimbursement, provide job security and medication supply security for patients, optimize the problems of hospital transfer, reduce drug side effects, improve the success rate of treatment, and increase the special protection for patients with comorbidities and students(Fig. 1).

Discussion

As an infectious disease with high burden, the prevention and control of TB has attracted the attention in China. Improving the medication adherence of TB patients is considered to be an important way to effectively prevent and control TB. Not only does non-adherence pose a risk to the health of families and close contacts, it can also lead to the emergence of resistant bacteria that are more difficult and expensive to treat[21]. In our study, the percent of newly diagnosed TB patients with a low adherence was
26.8%, while the patients with a good adherence were only in the proportion of 45.7%. The proportion of low adherence was lower than that of the study conducted in Shandong (34.6%)\[22\] and Hubei (33.3%)\[15\]. This difference may be related to the study design and the regional context. This also suggests us that it is necessary to find an effective way to identify high-risk groups with non-adherence and measures to improve adherence.

WHO reported that the largest burden of TB was in adult men\[2\], as in our study, where there were 1.63 times more male than female. Gender was not associated with adherence, and similar results have been reported in other studies\[23\]. Most patients had a secondary or lower education level and education level had an impact on adherence. Patients with a college degree or above made up a larger proportion of low adherence, which may be related to the living and working environment, and patients with a busy schedule tend to forget to take their medicine\[12\]. This may also be due to the fear that colleague will know about their illness, so do not regularly take medicine. However, the proportion of patients with low adherence in junior high school or below education was also high. Education levels were often associated with a patient's knowledge of TB, which also had an impact on adherence\[24\]. It has been reported that time taken to reach a medical facility was associated with poor adherence, and we also found this phenomenon in univariate analysis \[14\]. Taking too long to get to the medical facility required higher transportation costs, and patients who were financially constrained by transportation costs had a higher risk of non-adherence to treatment\[25, 26\]. Some of the obstacles to treatment can be overcome by a reasonable increase in transport subsidies\[27\].

The attitudes of family members may influence the patient's decision to stop or continue treatment\[28\]. Family members, especially spouses, play an extremely important role in encouraging, supporting and supervising the patient's medication\[22\]. Our study also found that patients with frequent medication supervision by family members, patients whose family members often encouraged them mentally were more likely to have a high level of adherence. This may be because TB patients generally carry a psychological burden of fear of treatment failure and a lack of confidence in curing the disease\[29\], and hinder their adherence to treatment. However, the constant encouragement and care of the family can increase the patient's confidence and thus affect the patient's medication adherence. During the illness, family members helping to solve problems in their lives had no effect on adherence. Some experts believed that when intervening in patient adherence, it is important whether the patient feels cared for\[30\], while there was a lack of usual involvement in helping to solve the problem. Our study also found that patients whose family members sometimes supervised medication were more likely to have poor adherence, possibly due to family members not supervising when the patient forgot to take medication.

Directly observed therapy (DOT) is considered as a timely reminder and can improve medication adherence\[31\]. Studies have shown that DOT is mostly provided by family members and that well-trained family members will provide better DOT than health service personnel\[32\]. With doctors having limited time and sometimes skill to repeatedly instruct patients to stick to their medications\[33\], it may make sense to transfer DOT to family members. Therefore, we can improve patient adherence by training family members to better provide therapeutic and psychological interventions. Univariate analysis found that the relationship between family members and adherence was also related. Close family relationships
can increase patients' life satisfaction, disencumber their mind of care, and enhance their ability to fight disease, and patients with family dysfunction are more likely to be alienated and lead to negative treatment[34]. That suggests us that family members can not to be ignored in the patient's treatment process. Especially in patients with poor memory and consciousness, family supervision is particularly essential.

In our study, the patients' knowledge of TB was relatively good, with more than half getting full or near full marks, and patients who have a good knowledge of TB were more likely to show adherence. Many other studies have also shown that health education had a positive effect on adherence[35]. Patients' lack of knowledge about TB often means an incorrect understanding of TB[34]. Some patients also express a desire for knowledge and hope to popularizing the knowledge of TB. Therefore, it is necessary for hospitals to propagandize strategy on the prevention and treatment of TB and knowledge about TB to patients and their families before patients receive chemotherapy. Our research also showed that only doctor-patient relationship affected adherence rather than friends, colleagues and neighbors. This can be explained as the key to a good doctor-patient relationship is effective communication, and sometimes doctors fail to effectively explain the benefits and side effects of medications to patients, and also fail to fully consider the financial burden of patients, resulting in the occurrence of non-adherence[36]. This study is consistent with the findings of other studies, and more attention was also recommended to improve doctor-patient communication[37]. Home visits and telephone supervising contacts by health workers can improve treatment adherence, and health worker calls are generally accepted method for patient management[38]. A study in Vietnam found that digital monitoring was also a viable and acceptable adherence support method[39]. But there are also studies that suggest that when patients' adherence problems were reported to doctors through monitoring, doctors may not have enough financial incentives to manage patients more strictly[30]. Hence, improving doctor-patient relationships by training and motivating health workers and strengthening health workers telephone supervision or digital monitoring is beneficial to improving adherence.

There were still a large number of patients who were not aware of national treatment policies. In addition, consistent with other studies, our study also showed that understanding of national policy did not appear to have an impact on adherence[9]. This may be because some of the patients limitedly know what the doctor told them, not know deeply about TB knowledge. In the current study, patient need for national TB treatment policies was significantly correlated with medication adherence, and patients who listened to their doctors to take their medications on time were more likely to report stronger needs. A significant number of patients hold the belief that government should strengthen policy support, although the country has established some free policies for TB treatment, some items are not included in the free package, such as the cost of expensive tests and adjuvant drugs. A previous study in four Chinese provinces showed that although all smear-positive and some severe smear-negative patients received free drugs, patients still had to pay between 12% and 40% of their annual income for anti-TB treatment[40]. Participants also reported a small range and short duration of free drugs. Some patients simply cannot utilize the free drugs, and must spend further money elsewhere, which undoubtedly increase the financial pressure of patients. More patients also reported low reimbursement rates and high
treatment costs, especially among poor and drug-resistant TB patients. The link between poverty and TB exists throughout the course of the disease, and poverty weakens TB treatment adherence[41, 42]. With strong financial security, patients are more likely to receive regular treatment and have good adherence[9]. Some participants also suggested that the state should enhance the management of TB patients and reinforce the education of those who are infectious, so that they can isolate themselves. Therefore, it should be paid attention to increase financial support and strengthen the management of TB patients.

There were several limitations to our study that need to be addressed. Firstly, self-report questionnaires were used in this study, which resulted in recall bias to some extent. Secondly, patients were not followed up, leading to the failure to evaluate their adherence chronologically. Thirdly, only the level of TB knowledge of patients was studied, but the ways of acquiring knowledge and the types of knowledge needed by patients were not. Fourthly, the study was conducted only in Dalian, and the factors affecting adherence were different in different regions. Therefore, the results could only represent Dalian, and it was difficult to extrapolate. Finally, the adherence was measured indirectly by the scale, which was less reliable than the direct measurement. In the following study, the population should be expanded and patients should be followed up to explore adherence levels and influencing factors at different treatment stages.

**Conclusion**

Despite such limitation, our study can conclude that non-adherence is high in newly diagnosed TB patients. Patients with family members' frequent supervision of medication, family members' often spiritual encouragement, good doctor-patient relationship, more TB-related knowledge and high need for TB treatment policy support are more likely to have a good medication adherence. Therefore, training and economic incentives for medical staff, health education for patients and their families at the beginning of chemotherapy, targeted increase in patients' financial support, increase in patient management and psychological counseling for patients are recommended to improve patients' adherence.

**Abbreviations**

TB
Tuberculosis; MTBC: *Mycobacterium tuberculosis* complex; DOT:Directly observed therapy; OR:Odds ratio; CI:Confidence interval

**Declarations**

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Authors' contributions

LZ, XC provided the research design and carried forward the whole study. XC, RHW, LD analyzed the data and drafted the manuscript. XC, RHW, LD, JX, HQJ, YZ, XXZ participated in the collection and entry of the data. All authors read, revised and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethical Committee of Dalian Medical University approved this study. Before the investigation, the patients were informed of the purpose of the study and the presentation of the results, and they were assured that their personal information would not be disclosed. All patients signed informed consent in our study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures
Fig. 1 The percent of advice for more policy support for TB patients

Figure 1

The percent of advice for more policy support for TB patients