Risk Factors of Drop-Out among Tuberculosis Patients in Semarang: A Case-Control Study

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Abstract

Background: A multitude of factors are known to be associated with tuberculosis (TB) patients dropping out of treatment, such as living alone, social vulnerability, and access to health services. Semarang, the capital city of Central Java has never achieved the national TB cure rate target. Semarang city had a cure rate of 63.336% per annum in part due to the increased treatment drop-out from 2.8% in 2015 to 4.5% in 2018. The increase of drop-out TB patients in Semarang causes the decreased of the cure rate each year. The study aimed to identify independent factors associated with drop-out among TB patients and to inform the design of programs that reduce drop-out rates in Semarang, Central Java, and across Indonesia.

Methods: A case-control study was conducted to identify factors associated with treatment drop-out among TB patients. The pilot study took place in Semarang city with case-control ratio of 1:2. The case consisted of drop-out patients in 2018, whose secondary data was identified from the health district office, totaling 20 patients. Forty unmatched control patients were taken with purposive sampling technique with inclusion criteria: patients’ success treatment recorded in health centers of Semarang city area, lived in the metro area of drop-out patients and aged more than 15 years old. Results: Majority of patients in the case group has insufficient family support during their treatment course (95%) compared to the control group (45%). Inadequate DOT support was also found among the case group (80%), while the control group had less than 50%. More than half of the case group (55%) experienced a high amount of stigma.
during their treatment course. Anti-TB medications’ side effects appeared in the case group (70%) more than the control group (32.5%). In both groups, majority (case: 95%; control: 97.5%) resided close to the health facility (less than 3 km). Three variables were found to be significantly independent factors for the drop-out of TB patients. These three factors were family support (OR: 26.555 CI: 2.727-268.143), DOT or swallowing drug assistance support (OR: 5.687 CI: 1.261-25.644), and the experience of side effect of anti-TB medication (OR: 5.334 CI: 1.222-23.285). **Conclusion:** Family support is the key to success to minimize TB patients to drop out. Moreover, the experience of the side effect of anti-TB medication played five to six times higher to TB patients who are likely to drop-out the medication.

**Keywords:** Multidrug-resistant, Tuberculosis, risk factors


**Introduction**

Tuberculosis remains a major public health problem in Indonesia. In 2018, Indonesia had the third-highest rate of lung tuberculosis (TB), globally(1). The increasing trend of TB infection in Indonesia can be partially attributed to the increased number of cases detected because of the National Government’s strategic plan to combat TB, which is largely focused on increasing early detection (2).

Beyond national rates and trends, there are also important variations in TB rates across the 34 provinces and 7,024 districts of Indonesia. Central Java had the third-highest rate nationally, with a case notification rate increasing from 115.17 per 100,000 populations in 2015 to 115.36 per 100,000 populations in 2016(3). These data highlighted the need for comprehensive TB treatment and cure strategies in Central Java Province and, indeed, across Indonesia.

The Indonesian National TB Program (NTP) mission is to eliminate TB by 2030. Indonesia’s NTP is a strategic plan of strengthening leadership in district management, improving access to quality TB services, controlling TB risk factors, enhancing TB partnership through the coordination forum, engaging the community in TB control and health system strengthening. NTP’s treatment success rate target in 2017 was 90%. Central Java uses the same target.

In 2018, the success rate of confirmed cases completing treatment in Central Java was 77.1% (4). Semarang, the capital city of Central Java had never achieved the national TB cure rate target. Semarang city had a cure rate of 63.336% per annum in part due to the increased drop out from 2.8% in 2015 to 4.5% in 2018(4). TB patients dropping out from treatment is known to increase the risk of Multidrug
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Subject and Methods

A case-control study was conducted to identify factors associated with treatment drop-out among tuberculosis (TB) patients. The study pilot took place in Semarang city with case-control ratio of 1:2. The case consisted of drop-out patients in 2018, whose data were identified from secondary data in health district office of 20 patients in total. Forty unmatched control patients were taken with a purposive sampling technique with inclusion criteria; patients’ success treatment recorded in the health center of Semarang city area, lived in the metro area of drop-out patients, age greater than 15 years old.

Independent variables of the study were knowledge of TB, attitude toward TB, family’s support, directly observed therapy (DOT) support, stigma, a side effect of anti-TB medication, and distance of health facility. The variable of DOT support was measured without distinguishing the care provider i.e., health provider, family member, or community health worker. These seven variables were measured by a questionnaire that was tested for its validity and reliability before its use. It had a reliability score for family support (0.735), taking drug assistance support (0.675), stigma (0.600), and side effects of anti-TB medication (0.674). The patients’ information of case and control were collected from Bandarharjo primary health center (PHC), Karangdoro PHC, Candilama PHC, Halmahera PHC, Tlogosari Kulon PHC, Bangetayu PHC, Kedungmundu PHC, Gunungpati PHC, Simongan PHC, Lebdosari PHC, and Lamper Tengah PHC. Appointments were made with patients and data was collected between May to July 2019. This study conducted a face-to-face interview, the case respondent was visited by researcher based on the address collected from PHC.
Data were analyzed by univariate for presenting frequency and percentage of variables based on case and control groups. Bivariate analysis was applied to identify factors associated with TB treatment drop-out patients. All variables were not normally distributed. Family support was categorized into less (total score <12) and sufficient (total score ≥12), directly observed therapy (DOT) support was categorized into less (total score <7) and good (total score ≥7), stigma was categorized into low (total score <2) and high (total score ≥2), the side effect of anti-TB medication was categorized into having side effect and no side effect, Distance of health facility was categorized into <3 km and ≥3 km. The Bivariate analysis used the Chi-Square test with 95% confidence interval (CI) and closeness of correlation applied Odds Ratio (OR) value. Multivariate analysis used Regression logistic with a 95% CI and Adjusted Odds Ratio was measured.

Results

A total of 60 respondents, 20 cases, and 60 controls, participated in this study. The majority of the case group has less family support during the treatment course (95%) compared to the control group (45%). Less DOT support was also found among the case group (80%), while the control group had less than 50%. More than half of the case group (55%) experienced stigma during the treatment course. Anti-TB medications' side effects appeared on the case group (70%) more than the control group (32.5%). In both groups, the majority (case: 95%; control: 97.5%) have close access to health facilities (less than 3 km).

Table 1. Univariate analysis of factors associated with drop-out patient of tuberculosis patients treated

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Sufficient family support</td>
<td>1(5%)</td>
<td>22(55%)</td>
</tr>
<tr>
<td>• Less Family Support</td>
<td>19(95%)</td>
<td>18(45%)</td>
</tr>
<tr>
<td>Directly observed therapy support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Sufficient Support</td>
<td>4(20)</td>
<td>26(65)</td>
</tr>
<tr>
<td>• Less Support</td>
<td>16(80)</td>
<td>14(35)</td>
</tr>
<tr>
<td>Stigma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• High stigma</td>
<td>11(55)</td>
<td>15(37.5)</td>
</tr>
<tr>
<td>• Low stigma</td>
<td>9(45)</td>
<td>34(56.7)</td>
</tr>
<tr>
<td>Side-effect of anti-TB medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Has side effect</td>
<td>14(70)</td>
<td>13(32.5)</td>
</tr>
<tr>
<td>• No side effect</td>
<td>6(30)</td>
<td>27(67.5)</td>
</tr>
<tr>
<td>Distance of health facility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt;3 km</td>
<td>19(95)</td>
<td>39(97.5)</td>
</tr>
<tr>
<td>• ≥3 km</td>
<td>1(5)</td>
<td>1(2.5)</td>
</tr>
</tbody>
</table>
There was a significant difference between good and less family support of the respondents. The case group was found to have less support from the family than the control group (p-value: 0.001 OR: 23.222; CI: 2.829-190.161). Patients with less support from family during treatment had a 23.2 times higher possibility to drop out of the treatment. The support of DOT was also significantly different in both groups (p-value: 0.003; OR: 7.429 CI: 2.078-26.553). Patients who received less support on DOT have a significantly higher possibility of drop-out on a treatment course, i.e. 7.4 higher than patients with good DOT support.

Also, there was a significant difference between those who experienced the side effect of the anti-TB medication in both groups and the occurrence of drop-out. Patients that experienced the side effects of the anti-TB medication were 5.3 times more likely to drop out on treatment course than patients without the side effect of anti-TB medication (OR: 5.334 CI: 1.222-23.385). Stigma and distance of health facilities were not significantly different between the groups. (stigma p-value: 0.311 CI: 0.686-6.052; distance p-value: 1.000 CI: 0.122-34.628)

Multivariate logistic regression analysis showed three variables were found to be significant independent factors for the drop-out TB patients. These three factors were family support (OR: 26.555 CI: 2.727-268.143), DOT, or taking drug assistance support (OR: 5.687 CI: 1.261-25.644), the side effect of anti-TB medication (OR: 5.334 CI: 1.222-23.285).

Table 2. Multivariate analysis of factors associated with drop-out patient of tuberculosis patients treated

<table>
<thead>
<tr>
<th></th>
<th>Crude OR</th>
<th>95% CI</th>
<th>P-Value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Support</td>
<td>23.222</td>
<td>2.829-190.616</td>
<td>0.001</td>
<td>26.555</td>
<td>2.727-268.143</td>
<td>0.005</td>
</tr>
<tr>
<td>Directly observed therapy support</td>
<td>7.429</td>
<td>2.078-26.553</td>
<td>0.003</td>
<td>5.687</td>
<td>1.261-25.644</td>
<td>0.024</td>
</tr>
<tr>
<td>Stigma</td>
<td>2.037</td>
<td>0.686-6.052</td>
<td>0.311</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side-effect of anti-TB medication</td>
<td>4.846</td>
<td>1.515-15.504</td>
<td>0.013</td>
<td>5.334</td>
<td>1.222-23.385</td>
<td>0.026</td>
</tr>
<tr>
<td>Distance of health facility</td>
<td>2.053</td>
<td>0.122-34.628</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

This study analyzed five factors and their association with the anti-TB treatment drop-out rate in Semarang to inform the design of programs that aim to reduce the dropout in Semarang, Central Java, and throughout Indonesia. Among the studied factors, family support, DOT support, and experience of anti-TB medicinal side effects were significantly associated with TB patient treatment drop out. Whether or not the patient reported experiencing stigma and the distance of the health facility was not associated with their drop-out rate.
Family support was found to be significantly associated with the drop-out TB patients as a negative outcome of treatments. TB patients faced many obstacles during the short course treatment that can affect their psychological condition and may give rise to depressive symptoms. The support of family was needed during the treatment to avoid patients dropping out of the treatment. A previous research study found that depressive symptoms were significantly associated with loss to follow-up during TB treatment(7). A previous qualitative study showed that patients discontinued their treatment because of a lack of family and community support. The patients stated that supports are very important during the intensive phase(8).

The good support on DOT was also found as a factor related to decreasing the likelihood of drop out of TB patients. Even though, earlier research compared the DOT given by family or health workers found that family member DOT was associated with a lower rate of adherence, and a higher rate of treatment failure compared to trained health worker(9). Prior research also compared the treatment by DOT and self-administrated therapy and found that the cure rate of TB in self-administrated was low, compared to DOT(10). Overall, these studies and our results showed that both DOT support and family support are helpful in the success of TB treatment. DOT administered by a health worker or a family member is crucial for the patient’s adherence to treatment as it provided encouragement and motivation as well as assisted the administration of medication of patients.

The occurrence of side effects of anti-TB medication was significantly correlated to drop out of TB patients. Previous studies found that patients with severe side effects decided to discontinue the medication (8). Side effects that are commonly experienced by patients were body pain, vomiting, feeling weak, discoloration of urine, and lack of appetite. The lack of education on anti-TB medication seems related to the decision of TB patients to discontinue their treatment. The education of the side effect of anti-TB medication should be explained clearly before the patients begin the course. The past research found that patient’s adherence to TB treatment improved when a pharmacist led the patient with education on medication use and addressed the patient’s pharmaceutical care issues(11).

Conclusion

The combination of the DOT program, patient education of anti-TB medication side effects, and family support should be continued in Semarang and Indonesia to decrease patient drop-out rates. Semarang’s city cure rate is lower than that of the province cure rate and much lower than the national cure rate. Focusing on these three factors will avert dropouts and help maintain patient adherence to their anti-TB regimen.

Stigma and distance to the health facility were not significant factors perhaps due to the fear of the disease overpowers the fear of the stigma and distance.

Indonesia’s NTP addresses these issues and may prioritize DOT to be administered by a family member at home as this may be as effective as observation by a health worker at a clinic. Given the large
resources and cost implication of DOT, DOT at home may be more effective in Indonesia than DOT administered by a health worker.

Further studies could explore additional factors among Semarang’s TB population such as economic income, the density of their living condition, gender assessment, among other financial or logistical barriers to care.

Other approaches to help patients adhere to anti-TB treatment include defaulter follow-up and approaches to motivate patients and staff. As the “Stop TB Partnership” comes to a close, those with a higher risk of drop out need to be identified and their barriers to treatment should be addressed by the NTP so that Indonesia can eliminate TB by 2030.

References
