ANALYSIS ON FACTORS INFLUENCING THE DEATH OF PATIENTS WITH DUAL INFECTIONS OF MYCOBACTERIUM TUBERCULOSIS AND HIV DURING ANTI-TUBERCULOSIS TREATMENT

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ABSTRACT

Objective: This paper analyzes the specific factors that lead to death in the course of anti-tuberculosis treatment of patients with double infections of mycobacterium tuberculosis and HIV, consequently providing guidance for future clinical treatment.

Methods: The 276 patients with mycobacterium tuberculosis and HIV treated in our hospital from March 2014 to December 2016 were enrolled in this study. A prospective & retrospective analysis was conducted to estimate probability of death during the course of treatment and summarizes the factors leading to death.

Results: During the treatment period, 29 patients died, with odds of 10.51%. Statistical analysis showed that mortality was significantly lower in patients receiving antiviral therapy than those who did not (P <0.05). In addition, the probability of death occurrence could be reduced with early antiviral therapy. Based on HIV infection route, it could be noted that the mortality of intravenous drug users was significantly higher than patients with sexually transmitted infections (P <0.05). This could be observed from infection type of mycobacterium tuberculosis, whereby mortality of patients with smear positive pulmonary tuberculosis infection was substantially higher than those with smear negative pulmonary tuberculosis and patients with extrapulmonary tuberculosis alone (P <0.05). Meanwhile the mortality of patients with CD4+ T lymphocyte level > 350 cells/µl was significantly higher than patients with other cases (P <0.05).

Conclusion: HIV infection route, severity of tuberculosis, antiviral therapy and early treatment are the significant relevant factors that affect the death of patients infected with mycobacterium tuberculosis and HIV in the course of anti-tuberculosis treatment. These factors demand severe attention besides symptomatic treatment should be comprehended in all clinical institution to ensure patients’ wellbeing.

Keywords: Tuberculosis infection, HIV, dual infection, fatal cause.

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Introduction

Tuberculosis is the most common and curable, infectious disease in HIV-infected persons and AIDS patients, also the most common cause of their death1). According to the relevant clinical research reports, compared with the general population, HIV-infected persons face 113 times higher risk in active pulmonary tuberculosis, and the figure is 170 times for AIDS patients2-6). Relevant data shows that 25 -65% of HIV infected patients also faces the infection of mycobacterium tuberculosis.

In general, almost 90% cases of patient with mycobacterium tuberculosis infection could be treated and cured7). However, cure rates of anti-tuberculosis therapy for patients with dual infections are low and have shown high mortality, and is currently difficult clinical problem to overcome.

Accordingly, this study intends to elucidate the specific causes of death during anti-tuberculosis treatment of patients with HIV and coexistence of mycobacterium tuberculosis. This predictive analytics will help preventive medicine, better diagnoses
and more targeted treatments besides improve intervention effectiveness and help reduce mortality in patients with double infections. To this end, numerous papers on clinical data were analyzed and 276 cases with dual infections were opted for compilation to a comprehensive review on the specific cause of death. The detailed report was provided herewith.

Materials and methods

**General Information**

The candidate were selected from March 2014 to December 2016, a total of 276 cases. All the patients were diagnosed with dual infections of mycobacterium tuberculosis and HIV by tuberculosis and AIDS prevention and control agency which includes 162 males and 114 females; with age between 18 - 58 years (average age 35.5±6.8) years and weight in the range of 31.5 to 76.5 kg (average body weight 46.2 ± 5.8) kg and receiving anti-tuberculosis therapy: pulmonary tuberculosis 2HRZE / 4HR as well as extra-pulmonary tuberculosis 2HRZE / 10HRE; anti-HIV therapy: lamivudine + stavudine + efavirenz.

All selected patients were clearly in line with the PRC diagnostic criteria for tuberculosis, AIDS and HIV infection (Figure 1): diagnostic criteria for pulmonary tuberculosis WS288-2008, tuberculosis classification 020101, diagnostic criteria of AIDS and HIV WS293-2008.

**Methods**

First of all, prior to clinical treatment, a comprehensive analysis and collation of patient's gender, age, body weight, complications, HIV infection route, HIV infection years and antiretroviral treatment time should be available.

The number of deaths that occurred during the treatment and survival cases under the relevant factors was recorded and compared. The specific effects of factors such as patients' body weight, level of CD4 + T lymphocytes, period of antiviral treatment receival, route of HIV infection, duration with HIV infection and type of death during anti-tuberculosis therapy were analyzed. The identified factors were then made into smaller groups. Patients with different body weight was divided into 3 groups: 31-39kg, 40-49kg, 49-77kg while 4 groups with distinct level of CD4 + T lymphocytes was formed: ≤50 cells / μl, 50-199 cells / μl, 200-350 cells / μl, > 350 cells/ μl. Duration of antiviral treatment was divided into 4 groups: without antiviral therapy, with antiviral therapy 2 months after anti-tuberculosis treatment, with antiviral therapy 2 weeks after anti-tuberculosis treatment and with antiviral therapy amid (or before) anti-tuberculosis treatment. Patients were also grouped according to their HIV infection routes into 3 groups: intravenous drug infection group, sexually transmitted infection group and other route-infected group while the number of year with HIV infection were divided into 2 groups: within 2 years, > 2 years.

Patients with different tuberculosis types were divided into 3 groups: smear positive pulmonary tuberculosis, smear negative pulmonary tuberculosis and extrapulmonary tuberculosis. Besides that, patients were divided into 3 groups according to the location of lesions: tuberculosis group, group with tuberculosis accompanied by extrapulmonary tuberculosis, group with pulmonary tuberculosis alone.

**Statistical methods**

This study assesses the affected factors of HIV-infected patients’ death during tuberculosis treatment for mycobacterium tuberculosis. All the data were analyzed and processed by SPSS19.0 statistical software. The count data were expressed in (n,%) and tested by chi-square, while the measurement data were expressed in (x ± s) and tested by t. Only if P <0.05 is satisfied, the difference can be considered statistically significant.

![Figure 1: CT image analysis of AIDS-associated tuberculosis patients.](image-url)
Results

Many of these patients died during anti-tuberculosis treatment which accounted to 29 deaths with with the probabilities of 10.51%. Probability of dying during the intensive period of anti-tuberculosis treatment was the highest, 89.66% (26 patients) while another 10.34% death occurs in the continuation phase with probability of 10.34%.

The death based on patient’s body weight was 2 occurrence among 19 patients with the weight of 31-39 kg (10.52%), 12 death out of 112 patients of 40-49 kg (10.71%), and 15 patients died from 145 patients weighed 49-77 kg (10.34%). The statistical analysis shows no statistical difference between the groups.

In this study, there was no significant difference in mortality for patients with different CD4 + T lymphocyte levels. It was noted that from 150 cases with CD4 + T lymphocyte levels <50, 12 death cases with a probability of 8.00%, out of 76 cases with lymphocyte levels of 50-199, 7 death cases with probability of 9.21% while only 1 out of 16 cases with lymphocyte levels of 200-350, was noted with the probability of 6.25% but the highest death probability at 27.27% occurs to patients with lymphocyte levels of > 350 which is actually 9 out of 33 cases. Hence, the mortality rate was significantly higher with 350 patients having lymphocyte levels of > 350. However, 32 out of the 33 patients did not receive antiretroviral therapy, thus direct association between CD4 + T lymphocyte levels and patient mortality could not be affirmed.

Statistical analysis showed that the mortality rate of patients treated with antiviral therapy was significantly lower than that of patients who did not (P <0.05). From the obtained data, the highest mortality rate of 40% (14/35) for 35 cases attended shows patient did not receive antiretroviral therapy while much lower rate of 6.22% was observed for 241 cases (15/241) when patients received antiretroviral therapy. Difference between both the groups showed X2 = 37.0778, P = 0.000 <0.05, which demonstrated statistical significance. The details are provided in Table 1.

Based on the HIV infection route, mortality rate of intravenous drug users was significantly higher than that of sexually transmitted infection patients (P <0.05). The difference as displayed in Table 2 showed statistical significance with X2 = 5.738, P = 0.0017 <0.05 (Table 2).

<table>
<thead>
<tr>
<th>Antiviral treatment</th>
<th>n</th>
<th>Death/n</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated</td>
<td>35</td>
<td>14</td>
<td>40%</td>
</tr>
<tr>
<td>Simultaneous treatment</td>
<td>78</td>
<td>4</td>
<td>5.13%</td>
</tr>
<tr>
<td>Treatment after 2 weeks</td>
<td>96</td>
<td>6</td>
<td>6.25%</td>
</tr>
<tr>
<td>Treatment after 2 months</td>
<td>67</td>
<td>5</td>
<td>7.46%</td>
</tr>
</tbody>
</table>

Table 1: Mortality of patients with different antiviral treatment (n,%).

<table>
<thead>
<tr>
<th>Infection route</th>
<th>n</th>
<th>Death/n</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous drug use</td>
<td>105</td>
<td>17</td>
<td>16.19%</td>
</tr>
<tr>
<td>Sexual transmission</td>
<td>170</td>
<td>12</td>
<td>7.06%</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>0</td>
<td>--</td>
</tr>
</tbody>
</table>

Table 2: Relationship between HIV infection route and patient mortality (n,%).

<table>
<thead>
<tr>
<th>Type</th>
<th>n</th>
<th>Death/n</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear positive tuberculosis</td>
<td>85</td>
<td>18</td>
<td>21.18%</td>
</tr>
<tr>
<td>Smear negative tuberculosis</td>
<td>148</td>
<td>10</td>
<td>6.76%</td>
</tr>
<tr>
<td>Extrapulmonary tuberculosis alone</td>
<td>43</td>
<td>1</td>
<td>2.33%</td>
</tr>
</tbody>
</table>

Table 3: Relationship between tuberculosis type and patient death (n,%).

<table>
<thead>
<tr>
<th>Lesion part</th>
<th>n</th>
<th>Death/n</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis with extrapulmonary tuberculosis</td>
<td>26</td>
<td>5</td>
<td>19.23%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>203</td>
<td>22</td>
<td>10.84%</td>
</tr>
<tr>
<td>Extrapulmonary tuberculosis</td>
<td>47</td>
<td>2</td>
<td>4.25%</td>
</tr>
</tbody>
</table>

Table 4: Relationship between tuberculosis lesion and patient mortality (n,%).
Discussions

As medical studies have pointed out, tuberculosis type, severity and complications has become the main factors causing the death of tuberculosis patients \(^8\). In this context, the influencing factors of death during tuberculosis treatment in patients with mycobacterium tuberculosis and HIV infection has been conducted, mainly including factors as infected persons’ social demographic characteristics, HIV infection route, ADIS diagnostic time, highly active antiretroviral therapy as well as the CD4\(^+\) T lymph cell levels \(^8,9,10\). It has also been reported that fungal infection is one of the most common infections incidence for AIDS patients death. On the other hand, factors affecting death of mycobacterium tuberculosis and HIV-infected patients include both tuberculosis-related factors and HIV as well as AIDS related factors \(^11-17\). Patients with dual infections are easily complicated by extrapulmonary tuberculosis, with low sputum positive rate. Meanwhile, when dual-infected patients received anti-tuberculosis treatment, the prevalence of adverse reactions is higher than that of patients with tuberculosis alone.

Managing factors influencing the mortality could reduce the mortality rate. Consequently, this study was designed to investigate the effects of factors such as body weight, CD4\(^+\) T lymphocyte level, antiviral therapy, HIV infection route and infection years, TB type, and other AIDS-related infections on death of mycobacterium tuberculosis and HIV-infected patients. As can be seen from the results, intravenous drug users, smear positive tuberculosis patients, patients with tuberculosis accompanied by extrapulmonary tuberculosis and patients without antiviral treatment are more prone to death, which suggests that severity of TB lesions, patients’ functional condition are the main cause of death for patients with dual infections. Intravenous drug users’ increased mortality is considered to be related to poor functional condition, poor compliance in antituberculosis treatment of this group.

To improve the cure rate of mycobacterium tuberculosis and HIV-infected patients besides reducing their risk of death, attention should be paid to the relevant factors influencing curative effect of antituberculosis treatment. Therefore, the clinical treatment process should incorporate two-way screening work in dual infection prevention and control should be strengthened, so that patients could be diagnosed in early state and treated to reduce TB lesion damage \(^18,19\). Secondly, for those patients that meets the antiviral treatment conditions, this treatment should be given as early as possible. In addition, antiviral treatment indication for AIDS patients with TB should be appropriately widened, to actively improve patients’ functional condition \(^20\); meanwhile, focus should be given to health education, especially for those with poor compliance in treatment, to protect coherence of antituberculosis and antiviral treatment and improve treatment effect.

Conclusion

To sum up, HIV infection route, tuberculosis severity, whether one accepts antiviral therapy and specific treatment time are related factors affecting death of mycobacterium tuberculosis and HIV-infected patients. These factors should be fully considered in clinics to provide more targeted treatment for patients.

References


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