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ORIGINAL RESEARCH

The clinical outcomes of oldest old patients with tuberculosis treated by regimens containing rifampicin, isoniazid, and pyrazinamide

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Objectives: To investigate the clinical characteristics, adverse drug reactions, and outcomes of the oldest old patients (aged ≥80 years) with tuberculosis (TB) treated with rifampicin, isoniazid, and pyrazinamide (RIP)-containing regimens.

Design: A retrospective chart review study.

Setting: A 1,200-bed tertiary teaching hospital in southwest Taiwan.

Participants: We conducted a retrospective observational study between January 1, 2005 and December 31, 2011. Seven hundred adult patients (aged ≥18 years) with TB treated with RIP-containing anti-TB regimens were reviewed, including 161 oldest old patients.

Outcome measures: Clinical outcomes included clinical responsiveness and microbiological eradication. Adverse outcomes included drug-induced hepatitis, and other symptoms included gastrointestinal upset (eg, abdominal pain, vomiting, diarrhea, or dyspepsia), skin rash, joint pain, and hyperuricemia.

Results: Compared with the non-oldest old adult patients, the oldest old patients more frequently had hepatitis (P=0.014), gastrointestinal upset (P=0.029), and unfavorable outcomes (P<0.001). In a multivariate analysis, hepatitis during treatment (adjusted odds ratio: 3.482, 95% confidence interval: 1.537–7.885; P<0.003) and oldest old age (adjusted odds ratio: 5.161, 95% confidence interval: 2.294–11.613; P<0.010) were independent risk factors for unfavorable outcomes. In the oldest old patients with hepatitis, rifampicin use was more common in the favorable outcome group than in the unfavorable outcome group (100% vs 37.5%; P=0.001).

Conclusion: The oldest old age and hepatitis during RIP treatment were associated with unfavorable outcomes. For the oldest old patients with TB having hepatitis during treatment, rifampicin rechallenge and use might benefit the treatment outcome.

Keywords: hepatitis, refampicin, adverse effect

Introduction

Tuberculosis (TB) remains a major problem in both developing and developed countries. In 2014, an estimated 9.6 million new cases occurred worldwide.[1] Although the annual TB incidence decreased slightly in some developed areas of the world, it continued to increase in developing countries. This increase has been more profound in the elderly population than in other age demographics in some area, such as the Eastern Mediterranean and the Western Pacific regions.[1,2]

A global demographic analysis found that "oldest old" individuals (aged ≥80 years) is the fastest growing demographic. In 2004, the oldest old comprised 18% of the world's older people and 24% of people in more developed countries, and the proportion of the oldest old people will continue to increase during the next 2 decades.[3]

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In 2014, 25% of older people (aged ≥65 years) were oldest old in Taiwan.[4] Previous studies have reported that elderly patients with TB (aged ≥65 years) exhibit unusual clinical manifestations, delayed diagnoses, and higher rates of adverse drug reactions and unfavorable outcomes.[5–11] However, the published data for the oldest old patients with TB are limited.[12,13] This retrospective study was conducted to investigate the clinical characteristics, adverse drug reactions, and outcomes of the oldest old patients with TB treated with rifampicin, isoniazid, and pyrazinamide (RIP)-containing regimens.

Methods

Study design and patients

Chang Gung Memorial Hospital at Chia-Yi, Taiwan, is a 1,200-bed tertiary teaching hospital in southwest Taiwan. A retrospective study of all adult patients with TB (aged ≥18 years) diagnosed in this hospital between January 1, 2005, and December 31, 2011 with positive *Mycobacterium tuberculosis* complex (MTB) cultures initially treated with RIP in the presence or absence of ethambutol therapy was carried out. Patients who died in the first 2 months or were lost to follow-up, those with human immunodeficiency virus infection, and those who had undergone organ transplantation were excluded. Both the electronic and paper charts of the study patients were reviewed. The data were analyzed with delinking from the patient's privacy information. This study was approved by the Institutional Review Board of the Chang Gung Memorial Hospital (Number: 100-0873B). The ethics committee granted a waiver for informed consent to be obtained.

Demography, comorbidity, and constitutional symptoms

Data regarding age, sex, and comorbid conditions were gathered by reviewing the patients' medical records. Patients aged ≥80 years were classified as the "oldest old group" and patients aged 18–79 years were the "non-oldest old adult patient group." The verified comorbidities included diabetes mellitus, heart disease, COPD, stage V chronic kidney disease, decompensated liver cirrhosis, and solid organ or hematological malignancy. Patients who were serologically positive for the hepatitis B virus (HBV) surface antigen and anti-hepatitis C virus (anti-HCV) antibody were recorded as HBV carriers and HCV-seropositive patients, respectively. The constitutional symptoms included fever, body weight loss, and cold sweating.

Diagnosis

All patients with TB infections were diagnosed according to positive MTB cultures; those infected with rifampicin-resistant and high-level isoniazid (10 μg/mL)-resistant pathogens were excluded from the study.

Pulmonary TB was defined as an MTB-positive lower respiratory tract culture; this included cultures from sputum, tracheal aspirates, bronchoalveolar lavage fluid, and lung tissue. Pleural TB was defined as an MTB-positive pleural effusion or pleural tissue culture. Upper respiratory tract TB was defined as an MTB-positive upper respiratory tract culture; these included specimens from the larynx, tonsils, and nasopharynx. Bone and joint TB, including TB arthritis, was defined as an MTB-positive synovial fluid culture, and spinal TB was defined as an MTB-positive paraspinal abscess, epidural abscess, or spinal bone tissue culture. Other sites of infection were determined by positive MTB cultures from corresponding organ systems. Disseminated TB was defined as TB involvement in at least two organ systems.

Treatment, adverse drug reactions, and outcomes

First-line anti-TB treatment was defined as the use of at least two of the RIP component drugs, and second-line treatment was defined as the use of alternative therapy. Patients who either temporarily or permanently discontinued or changed their therapeutic medicines were suspected of having adverse drug effects.[14] Patients were able to take certain anti-TB drug continuously after such represcribed drug was defined as a successful rechallenge. A hepatitis diagnosis required one of the following conditions: 1) a transaminase level increase of >5-fold above the normal upper limit; 2) a transaminase level increase of >3-fold above the normal upper limit with hepatitis-associated symptoms (eg, nausea, vomiting, abdominal tenderness, discomfort near the ribs on the right upper abdomen, and jaundice); or 3) a total bilirubin level of >3 mg/dL with hepatitis-associated symptoms. The durations between the initiation of anti-TB therapy and the onset of hepatitis were classified as <2 months, 2–4 months, and >4 months. The numbers and types of TB medications were discontinued after hepatitis, and the rates of successful rechallenge were recorded. Other adverse drug reactions included gastrointestinal upset (eg, abdominal pain, vomiting, diarrhea, or dyspepsia), skin rash, joint pain, and hyperuricemia. Patients who received a full course of TB treatment with good clinical responsiveness and microbiological eradication were considered as having favorable outcomes. Patients who died during therapeutic course were designated as having unfavorable outcomes.

Hepatitis management during RIP treatment

Management was divided into either successful first-line anti-TB rechallenge (atleast two components of the RIP) or second-line anti-TB drug therapy (including more than two second-line bactericidal anti-TB agents or one RIP component plus another second-line bactericidal anti-TB drug) or a failure to rechallenge (mortality before anti-TB drug rechallenge). In the case of successful rechallenge, the duration was classified as either <1 months or ≥1 month (≥2 types of bactericidal anti-TB drugs). Each patient's tolerance for the individual components of RIP without discontinuation and successful rechallenge was recorded.

Statistical methods

All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (Version 18.0; SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the χ^2 test or Fisher's exact test as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Variables with *P*-value <0.1 in the univariate analysis and other variables of interest were included in a logistic regression model for the multivariate analysis. All tests were two tailed, and a *P*-value <0.05 in the multivariate analysis was considered significant.

Results

Demography, comorbidity, and constitutional symptoms

A total of 700 adult patients with culture-positive TB infections were included in this study, including 161 oldest old patients (23.0%). The mean age of the 700 patients was 67.3 years with male predominance (75.7%). The comorbidity and constitutional symptoms are listed in Table 1. Compared with the non-oldest old adult patients, the oldest old patients were mostly women (34.2% vs 21.3%; *P*=0.001), with a higher rate of COPD (8.1% vs 3.5%; *P*=0.015) and lower rates of hepatitis B positivity (9.2% vs 23.4%; *P*=0.007) and body weight loss (6.2% vs 19.5%; *P*<0.001; Table 1).

Sites of infection

Pulmonary TB was the most common diagnosis (93.7%); the other sites of infection are listed in Table 1. Compared with the non-oldest old adult patient group, the oldest old group had a higher incidence of bone and joint TB (7.1% vs 3.4%; *P*=0.037; Table 1).

Adverse effects

Hepatitis (11.9%) was the most common etiology of anti-TB drug discontinuation in our study. Other adverse reactions are listed in Table 1. Compared with the non-oldest old adult patient group, the oldest old group had higher rates of hepatitis (17.4% vs 10.2%; *P*=0.014) and gastrointestinal upset (5.0% vs 1.9%; *P*=0.029; Table 1).

Outcome

Among the 700 studied patients, 69 (9.9%) had unfavorable outcomes; the oldest old group had a higher rate of unfavorable outcomes than did the non-oldest old adult patient group (23.6% vs 5.8%; *P*<0.001; Table 1).

Risk factors for unfavorable outcomes

For all studied patients, the multivariate analysis revealed that an oldest old age, malignant solid tumor, and hepatitis during treatment were independent risk factors for an unfavorable outcome. Among the oldest old patient group, hepatitis during treatment was the only independent risk factor for an unfavorable outcome in the multivariate analysis (adjusted OR: 4.417, 95% CI: 1.839–10.611; *P*=0.001; Table 2).

Risk factors for hepatitis during RIP treatment

The multivariate analysis, which also included HBV carriers and HCV-seropositive patients, showed that diabetes mellitus was the only independent risk factor for hepatitis not only in all patients but also in the oldest old patient group (Table 3).

Hepatitis during RIP treatment

A total of 67 of the 83 patients with hepatitis (80.7%) had hepatitis during the first 2 months of RIP treatment. After RIP rechallenge, 58 of these patients (69.9%) ultimately received first-line treatments containing at least two RIP component drugs. The durations between RIP treatment initiation and hepatitis onset were similar in the oldest old and the non-oldest old adult patient groups. The types and numbers of drugs that were discontinued because of hepatitis and the rechallenge success rates were also similar in both groups. Finally, the oldest old group had a significantly higher incidence of unfavorable outcomes than did the non-oldest old adult patient group in terms of hepatitis during RIP treatment (50% vs 16.4%; *P*=0.001; Table 4).

Management and outcomes after hepatitis

In the 83 patients with hepatitis, the independent factors related to outcome in the patients were oldest old age,

Table 1 Clinical characteristics of patients with tuberculosis treated with regimens containing rifampicin, isoniazid, and pyrazinamide, and the comparison analysis between the oldest old and the non-oldest old adult patient groups

Characteristics	All[a] (n=700)	Oldest old[a] (n=161)	Non-oldest old adult[a] (n=539)	*P*-value
Female	170 (24.3)	55 (34.2)	115 (21.3)	0.001
Male	530 (75.7)	106 (65.8)	424 (78.7)	
Comorbidity				
Diabetes mellitus	170 (24.3)	33 (20.5)	137 (25.4)	0.201
Heart disease	12 (1.7)	2 (1.2)	10 (1.9)	0.743
COPD	32 (4.6)	13 (8.1)	19 (3.5)	0.015
CKD stage 5	19 (2.7)	2 (1.2)	17 (3.2)	0.271
DLC	2 (0.3)	0 (0.0)	2 (0.4)	1.000
HBsAg (+)[b]	65 (20.1)	7 (9.2)	58 (23.4)	0.007
Anti-HCV antibody (+)[c]	106 (33.0)	26 (35.6)	80 (32.3)	0.592
Solid tumor cancer	72 (10.3)	15 (9.3)	57 (10.6)	0.645
Hematological malignancies	8 (1.1)	1 (0.6)	7 (1.3)	0.689
Immunosuppression	26 (3.7)	2 (1.2)	24 (4.5)	0.059
Constitutional symptom				
Fever	150 (21.4)	33 (20.5)	117 (21.7)	0.743
Body weight loss	115 (16.4)	10 (6.2)	105 (19.5)	<0.001
Cold sweat	17 (2.4)	3 (1.9)	14 (2.6)	0.774
Sites of infection				
Upper respiratory tract	5 (0.7)	1 (0.6)	4 (0.7)	1.000
Pulmonary	657 (93.9)	156 (96.9)	501 (93.0)	0.067
Pleura	19 (2.7)	4 (2.5)	15 (2.8)	1.000
Bone and joint	24 (3.4)	10 (6.2)	14 (2.6)	0.027
TB spine	16 (2.3)	5 (3.1)	11 (2.0)	0.383
TB arthritis	8 (1.1)	5 (3.1)	3 (0.6)	0.008
Lymph node	12 (1.7)	0 (0.0)	12 (2.2)	0.078
Urinary tract	12 (1.7)	3 (1.9)	9 (1.7)	1.000
Meningitis	4 (0.6)	0 (0.0)	4 (0.7)	0.579
Pericarditis	5 (0.7)	0 (0.0)	5 (0.9)	0.594
Anus abscess	2 (0.3)	1 (0.6)	1 (0.2)	0.407
Dissemination	28 (4.0)	10 (6.2)	18 (3.3)	0.103
Adverse effect				
Hepatitis	83 (11.9)	28 (17.4)	55 (10.2)	0.014
Gastrointestinal upset	18 (2.6)	8 (5.0)	10 (1.9)	0.029
Skin rash	34 (4.9)	8 (5.0)	26 (4.8)	0.940
Arthritis	17 (2.4)	4 (2.5)	13 (2.4)	1.000
Hyperuricemia	17 (2.4)	3 (1.9)	14 (2.6)	0.774
Others	7 (1.0)	0 (0.0)	7 (1.3)	0.361
Total	158 (22.6)	44 (27.3)	114 (21.2)	0.092
Unfavorable outcome[d]	69 (9.9)	38 (23.6)	31 (5.8)	<0.001

Notes: [a]Data shown represent number (%) of subjects. [b]324 patients had HBsAg data, including 76 in the oldest old group and 248 in the non-oldest old adult patient group. [c]321 patients had anti-HCV data, including 73 in the oldest old group and 248 in the non-oldest old adult patient group. [d]Patients who did not receive a full course of TB treatment with good clinical responsiveness and microbiological eradication, and patients who died during therapeutic course.

Abbreviations: COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; DLC, decompensated liver cirrhosis; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; TB, tuberculosis.

malignant solid tumor, and rifampicin use. In the 28 oldest old patients with hepatitis, rifampicin use was the only factor that correlated with a good outcome in the univariate analysis (Table 5).

Discussion

In 2014, the life expectancy was 79.84 years in Taiwan.[15] This is the first study focusing on the adverse effects and clinical outcomes of RIP treatment in the oldest old patients with TB. In the study, oldest old age and hepatitis during RIP treatment were independently associated with unfavorable outcome. Although the success rates of RIP rechallenge were similar in the oldest old and the non-oldest old adult patients with hepatitis, the former had a significantly higher rate of unfavorable outcome. In addition to the confounding of age, the oldest old patients tended to have unfavorable outcome in the second-line anti-TB treatment (3/5, 60% vs 2/15, 13.3%), especially those with treatment not containing

Table 2 Risk factors for unfavorable outcome

Variables	Unfavorable[a]	Favorable[a]	Univariate	Multivariate		
			P-value	OR	95% CI	*P*-value
All patients, number	69	631				
Oldest old	38 (55.1)	123 (19.5)	<0.001	5.161	2.294–11.613	<0.001
Body weight loss	6 (8.7)	109 (17.3)	0.068	1.275	0.374–4.374	0.697
HBsAg (+)[b]	3 (8.8)	62 (21.4)	0.084	0.449	0.126–1.599	0.217
Solid tumor cancer	16 (23.2)	56 (8.9)	<0.001	3.626	1.353–9.917	0.010
Hepatitis	23 (33.3)	60 (9.5)	<0.001	3.482	1.537–7.885	0.003
Oldest old group, number	38	123				
Solid tumor cancer	7 (18.4)	8 (6.5)	0.049	3.052	0.972–9.587	0.056
Hepatitis	14 (36.8)	14 (2.2)	<0.001	4.417	1.839–10.611	0.001

Notes: [a]Data shown represent number (%) of subjects. [b]324 patients had HBsAg data, including 34 in the unfavorable outcome group and 290 in the favorable outcome group.
Abbreviations: OR, odds ratio; CI, confidence interval; HBsAg, hepatitis B surface antigen.

Table 3 Risk factors for hepatitis during treatment

Variables	Hepatitis[a]	Non-hepatitis[a]	Univariate	Multivariate		
			P-value	OR	95% CI	*P*-value
All patients, number	83	617				
Male	71 (85.5)	459 (73.4)	0.026	1.397	0.639–3.055	0.402
Oldest old	28 (33.7)	133 (21.6)	0.013	1.885	0.967–3.676	0.063
Body weight loss	5 (6.0)	110 (17.8)	0.006	0.357	0.120–1.063	0.064
Heart disease	4 (4.8)	8 (1.3)	0.043	4.164	0.975–17.780	0.054
Diabetes mellitus	27 (33.7)	143 (23.2)	0.062	2.201	1.145–4.229	0.018
HBsAg (+)[b]	14 (23.0)	51 (19.4)	0.532	1.567	0.765–3.208	0.219
Anti-HCV antibody (+)[c]	21 (35.0)	85 (32.6)	0.718	0.974	0.521–1.822	0.935
Oldest old group, number	28	133				
Male	25 (89.3)	81 (60.9)	0.004	4.527	0.924–22.173	0.062
Diabetes mellitus	10 (35.7)	23 (17.3)	0.028	7.194	1.614–32.068	0.010
HBsAg (+)[d]	2 (10.0)	5 (8.9)	1.000	0.993	0.138–7.122	0.995
Anti-HCV antibody (+)[e]	4 (21.0)	22 (40.7)	0.123	0.434	0.118–1.596	0.209

Notes: [a]Data shown represent number (%) of subjects. [b]324 patients had HBsAg data, including 61 in the hepatitis group and 263 in the non-hepatitis group. [c]321 patients had anti-HCV data, including 60 in the hepatitis group and 261 in the non-hepatitis group. [d]76 patients had HBsAg data, including 20 in the hepatitis group and 56 in the non-hepatitis group. [e]73 patients had anti-HCV antibody data, including 19 in the hepatitis group and 54 in the non-hepatitis group.
Abbreviations: OR, odds ratio; CI, confidence interval; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus.

Table 4 Hepatitis during treatment

Variables	Oldest old[a] (n=28)	Non-oldest old adult[a] (n=55)	*P*-value
Duration between treatment and onset			
<2 months	23 (82.1)	44 (80.0)	0.815
2–4 months	3 (10.7)	10 (18.9)	0.528
>4 months	2 (7.1)	1 (1.8)	0.251
Management			
Discontinue rifampicin	25 (89.3)	52 (95.6)	0.400
Successful rechallange	16 (64.0)	33 (63.5)	
Discontinue isoniazid	24 (85.7)	49 (89.1)	0.727
Successful rechallenge	17 (70.8)	34 (69.4)	
Discontinue pyrazinamide	25 (89.3)	50 (91.0)	1.000
Successful rechallenge	7 (28.0)	12 (24.0)	
With at least two drugs of RIP in the end	20 (71.4)	38 (69.1)	0.826
Unfavorable outcome	14 (50.0)	9 (16.4)	0.001

Note: [a]Data shown represent number (%) of subjects.
Abbreviation: RIP, rifampicin, isoniazid, and pyrazinamide.

Table 5 Risk factors for an unfavorable outcome in patients with hepatitis

Variables	Unfavorable[a]	Favorable[a]	Univariate	Multivariate		
			P-value	OR	95% CI	*P*-value
All patients, number	23	60				
Oldest old	14 (60.9)	14 (23.3)	0.001	31.379	3.527–279.174	0.002
Malignant solid tumor	8 (34.8)	3 (5.0)	<0.001	112.708	7.905–1,606.911	<0.001
Rifampicin use	8 (34.8)	47 (78.3)	<0.001	0.013	0.001–0.185	0.001
Using at least two RIP drugs at the end	11 (47.8)	45 (75.0)	0.018	1.546	0.226–10.593	0.657
Oldest old group, number	14	14		–	–	–
Malignant solid tumor	4 (28.6)	0 (0)	0.098	–	–	–
Rifampicin use	5 (35.7)	14 (100)	0.001	–	–	–

Note: [a]Data shown represent number (%) of subjects.
Abbreviations: OR, odds ratio; CI, confidence interval; RIP, rifampicin, isoniazid, and pyrazinamide; –, not applicable.

rifampicin (3/3, 100% vs 2/13, 15.4%) comparing to the non-oldest old adult patients. Besides, more oldest old patients with hepatitis died before RIP rechallenge and second-line anti-TB treatment than non-oldest old adult patients did (3/8, 37.5% vs 2/17, 11.8%). In the oldest old group, the patients with hepatitis receiving treatment containing rifampicin had similar clinical outcome compared to the patients without hepatitis (the patients with unfavorable outcome: 5/19, 26.3% vs 24/133, 18.0%; P=0.365).

Hepatitis was a common side effect in standard anti-TB treatment containing RIP, and management suggestion in guidelines included discontinuation of the drugs and rechallenge after decrease of serum levels of liver enzymes.[14,16,17] In this study, both oldest old and non-oldest old adult patients with hepatitis were managed according to the guidelines. In general, the patients with hepatitis receiving second-line anti-TB treatment not containing rifampicin tended to have unfavorable outcome, especially the oldest old patients. These results revealed the risk and impact of hepatitis during standard anti-TB treatment in the oldest old patients and the importance of first-line anti-TB drugs rechallenge after hepatitis, especially rifampicin.

The recommendations for TB therapy were the same for aged patients and young adults. The incidence rates of hepatitis in anti-TB treatment ranged from 2.4% to 26% in prior studies, and the hepatitis usually developed in the first 2 months of anti-TB therapy. Some studies reported that the incidence of hepatitis was positively correlated with the aging,[6,18–20] but the correlation was not observed in the other studies.[21] Salvadó et al compared 27 oldest old patients to 82 old age patients (65–79 years old)[12] and reported that the oldest old patients had a higher rate of hepatitis than the other groups. Our study also revealed a higher rate of hepatitis in oldest old than non-oldest old adult patients, and ~80% of the cases had hepatitis in the first 2 months of anti-TB therapy. However, multivariate analyses showed that the oldest old age was not independently associated with hepatitis, and diabetes mellitus was the only independent risk factor not only in all patients but also in the oldest old group in this study. In a systemic review, diabetes mellitus might be associated with treatment failure in patients with TB.[22] Even without clinical evidence supporting the hypothesis in vivo, Wang et al reported that the hepatic cytochrome p450 2E1 activity increased in the patients with diabetes.[23] Cytochrome p450 2E1 activates several hepatotoxins and contributes to hepatotoxicity in patients with TB.[24,25]

The association between chronic viral hepatitis and hepatitis during anti-TB therapy was controversial. In the study by Hwang et al, there was no significant association between hepatitis during anti-TB treatment and HBV carrier.[26] But some studies reported that HBV carrier was a risk factor for hepatitis during anti-TB therapy.[27,28] Some studies showed that patients with HCV seropositive had a higher rate of hepatitis during anti-TB therapy than those with HCV seronegative,[29,30] but Liu et al reported that chronic viral hepatitis including hepatitis C was not significantly associated with hepatitis during anti-TB treatment.[31] In our study, HBV or HCV infection was not a risk factor for hepatitis during anti-TB treatment in all patients and in the oldest old patients.

The clinical presentation of elder patients with TB might be atypical and subtle,[7] which might lead to delayed diagnosis in the oldest old patients with TB.[32] In a meta-analysis study comparing clinical manifestations between the younger and older patients with pulmonary TB, the older patients had lower rates of fever, sweating, and hemoptysis.[33] Our study also showed that the constitutional symptoms were less common in the oldest old patient group than those in the other groups.

García-Rodríguez et al reported that female sex and age were independently associated with extrapulmonary TB.[34] In our study, extrapulmonary TB was not common either in oldest old or non-oldest old adult patient groups. However, more patients in the oldest old group had TB arthritis than those in the non-oldest old adult patient group. The invasive procedures were usually necessary in the diagnosis of extrapulmonary TB. With less enthusiasm for the invasive procedures for extrapulmonary TB diagnosis and more reliance on supportive care, extrapulmonary TB may be underestimated in the oldest old patients.

This study had some limitations. First, the exclusion of patients who died in the 2 months of diagnosis may result in an underestimation of the ratio of the unfavorable outcome. Second, only ~40% of patients were available for hepatitis B or C seromarkers; further studies for establishing the roles of hepatitis virus seromarkers in oldest old patients were needed. Finally, the term hepatitis during the anti-TB therapy was not equivalent to the term drug-induced hepatitis.

Conclusion

In the adult TB patients with RIP treatment, oldest old age and hepatitis during treatment were associated with unfavorable outcome. For the oldest old TB patients with hepatitis during treatment, rechallenge and use of rifampicin might be beneficial to the treatment outcome.

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Disclosure

The authors report no conflicts of interest in this work.

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